

Metrological traceability of measurement results in chemistry: Concepts and implementation (IUPAC Technical Report)*

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Abstract: 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 in different circumstances to arrive at metrological traceability along a metrological traceability chain. 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 provision of metrological references by a metrological institutional framework and the role of interlaboratory comparisons.

Keywords: calibration hierarchies; IUPAC Analytical Chemistry Division; measurand; measurement; metrological comparability; metrological reference; metrological traceability.

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*Sponsoring bodies: IUPAC Analytical Chemistry Division; IUPAC Interdivisional Working Party on Harmonization of Quality Assurance: see more details on page 1932.

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1. INTRODUCTION

Establishing metrological traceability of measurement results is a prerequisite to obtaining metrological comparability of measurement results. The aim of this report is to present the chemist with the supporting international framework and the tools, procedures, and current vocabulary as shown by examples of calibration hierarchies.

In commerce, society, and science, numerous comparisons of measurement results are performed daily. That requires a common, accepted definition of the concept “metrological comparability of measurement results” (see concept 1.2-1) because many of these results are obtained at different locations and at different times. Achieving metrological comparability of measurement results requires the defi-

nitions of concepts of calibration hierarchies (see concept 2.5-1) providing metrological traceability chains (see concept 2.5-2), which enable the establishment of metrological traceability (see concept 1.1-1) of measured quantity values to a common and stable metrological reference (see concept 2.6-1).

Experience has shown that the definition of the concepts involved, their relation, role, and use are insufficient and varied. Consequently, consistent definitions of the needed concepts and associated terms are offered. The reader should not expect in this study to see all the terms used in daily analytical work because their inconsistency would limit the understanding of the basic concept of metrological traceability.

When defining a concept, 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 without creating circularity.

The 3rd edition of the *International Vocabulary of Metrology: Basic and General Concepts and Associated Terms*, VIM 2008 [1] (here called VIM) provides most of the concepts needed for this Recommendation. Supplementary sources are [2–6]. Some additional concepts have been defined when necessary to convey a message.

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

A number of initialisms, acronyms, and abbreviations will be used in the text and are listed in Annex I. An alphabetical index of terms for concepts defined in the text or VIM is provided in Annex II.

1.1 Metrological traceability

In recent years, the concept “traceability” in chemical measurement has received an extraordinary amount of attention [7–17]. Still, the interpretation of “metrological traceability” varies in the literature [18]. Also, many available reference materials (RMs) often lack information about metrological traceability for assigned quantity values and associated measurement uncertainty. The lack of clarity about such an important and widely used concept makes it difficult to reach world-wide 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 college curricula and are not treated in most textbooks of analytical chemistry.

The concept and use of the term “traceability” present the following challenges.

- In spite of the definition having traceability as a property of a measurement result (see concept 1.1-1), it is common also 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 National Metrology Institute).
- Despite a growing awareness of the need for metrological traceability of measurement results, some field and routine laboratories still assert that metrological traceability is not “applicable” to their measurement results.
- It is not generally accepted that traceability to a common stated metrological reference is a precondition for metrological comparability of measurement results.
- The colloquial meaning of the term “comparability” often refers to quantity values of the same magnitude (size).

- 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 satisfactory participation in an interlaboratory comparison, proficiency testing scheme, or external quality assessment scheme automatically provides metrological traceability of the participants' measurement results.
- VIM does not define the concept "metrological reference".

In response to the group of challenges under the first bullet above, metrological traceability is only considered to be a property of a measurement result (and thereby also of a measured quantity value). 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".

1.1-1 metrological traceability

Property of a **measurement result** whereby the result can be related to a reference through a documented unbroken chain of **calibrations**, each contributing to the **measurement uncertainty**.

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 in 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 that there is an 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 [18]).

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.

[VIM-2.41]

EXAMPLES

There are three types of ‘reference’ listed in Note 1. The following examples are taken from the IFCC-IUPAC NPU terminology for laboratory medicine [19]. A question mark stands for a numerical quantity value.

Measurement unit

NPU02319 Blood–Haemoglobin(Fe); amount-of-substance concentration
= ? millimole per litre.

Measurement procedure

NPU09229 Calculus(Urine)–Carbonate; arbitrary content(measurement procedure) = ?, where “arbitrary” indicates that the measurement scale is ordinal (i.e., with no measurement unit) and is defined in the measurement procedure.

Measurement standard as a sole metrological reference is hardly possible.

In many cases, the specification comprises more than one metrological reference.

Measurement procedure and measurement unit

NPU19981 Plasma–Alanine transaminase; catalytic activity concentration (IFCC 2002)
= ? microkatal per litre.

Measurement standard and measurement unit

NPU27287 Plasma–Penicillium species antibody(Immunoglobulin G); mass concentration (WHO International Reference Preparation 67/86, Gm 27);
= ? milligram per litre.

Measurement unit, measurement procedure, and measurement standard

NPU04003 Plasma–Chorionic gonadotropin; arbitrary amount-of-substance concentration (WHO International Standard 61/6; measurement procedure)
= ? international unit per litre.

1.2 Metrological comparability

Among the many aspects of measurement that affect the reliability of a measurement result (see concept 2.1-3), the attainment of metrological traceability is essential. It underpins the ability of the analyst to claim that his or her result “is what it purports to be” [20].

A key requirement in many situations, such as in cross-border 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 parties concerned, they should be confident that they will obtain measurement results 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, meas-

urement results obtained at one time must be comparable with those obtained at another time, in the same or in another laboratory. This is assured when the results are traceable to the same metrological reference, even if calibrators or measuring systems or relative measurement uncertainties are different.

1.2-1. metrological comparability of measurement results

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.

[VIM-2.46]

The concept of metrological comparability should be distinguished from metrological compatibility of measurement results (see concept 5-3). In the treatment of metrological traceability in this IUPAC Recommendation, the *Guide to the Expression of Uncertainty in Measurement* (GUM) [2] evaluation of measurement uncertainty is assumed throughout.

2. CONCEPTS RELATED TO METROLOGICAL TRACEABILITY

2.1 General concepts in measurement

2.1-1. measurement

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.

NOTE 3: Measurement presupposes a description of the quantity commensurate with the intended use of a **measurement result**, a **measurement procedure**, and a calibrated **measuring system** operating according to the specified measurement procedure, including the measurement conditions.

[VIM-2.1]

Nominal properties, such as identity of a chemical compound or a sequence of amino acids in a polypeptide, are important in chemistry; they are not measured but rather examined and are not treated in this Recommendation.

2.1-2. quantity

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

[VIM-1.1]

The generically subordinate concepts, here called “types of quantity”:

- ordinal quantity
- “differential quantity” (also known as “difference quantity” or “interval quantity”)

- “differential logarithmic quantity” (also known as “difference logarithmic 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 differential and rational quantities have the quantity dimension one, the coherent measurement unit is one (symbol “1”). Differential logarithmic quantities all have the quantity dimension one, and the coherent measurement unit one.

The division of the concept “quantity” into various types [21] is here preferred as being more fundamental than describing the associated types of quantity-value scale [22,23].

The description of an instance of quantity should include information about the system considered, any relevant component(s) and the *kind-of-quantity*. 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 NPU format:

System(specification) — Component(specification); kind-of-quantity(specification) [24]: See specified examples in Fig. 2.1-1.

For identification of a particular system (sometimes called “instance”), 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, specification can be calibrator or measurement procedure or quantity-value scale.

This format for description of a quantity includes descriptions of “operationally defined quantities” that are measured by so-called “empirical methods” or “standard methods”.

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” [25], but see also [24].

Dedicated kinds-of-quantity [21] for each specific concept under quantity are given in Table 2.1-1.

Table 2.1-1 Dedicated kinds-of-quantity [21] for each specific concept under *quantity*.

Type of quantity	System*	Component = analyte	<i>Kind-of-quantity</i> (symbol)	<i>Measurement unit</i> (symbol)
ordinal	petroleum fuel	petroleum fuel	octane number with procedure	not applicable
differential	thermostat	water	Celsius temperature (θ)	degree Celsius ($^{\circ}\text{C}$)
differential logarithmic	lake	water	pH (pH)	one (1)
rational	butter	sodium chloride	amount-of-substance content substance content (k)	mole per kilogram (mol/kg)
	ore	iron	mass fraction (w_{B})	one = kilogram per kilogram (1) = (kg/kg)
	exhaled air	ethanol	mass concentration (γ)	kilogram per cubic metre (kg/m ³)

*Location and calendar time are necessary specifications to “system” for converting a dedicated kind-of-quantity into a singular quantity (corresponding to one instance).

The allowed mathematical treatment of *quantity values* depends on the specific type of quantity [22,23].

A *measurement* requires the following set of interacting elements:

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

2.1-3. measurement result

result of 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.

[VIM-2.9]

2.1-4. measurand

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 “particular 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.

[VIM-2.3]

EXAMPLE: The amount-of-substance concentration of sodium ion in blood plasma of a given person at a stated calendar time.

The delineation of a system carrying a measurand will influence the type of sampling plan and thereby the 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 will depend on whether the plasma comes from a group of healthy persons, a given person, or a given sample of a person.

The definition of a measurand may include a stipulated measurement procedure. Such a measurand is sometimes termed an operationally defined or standardized or procedure-defined measurand.

2.1-5. quantity value

value of a quantity
value

Number and reference together expressing magnitude of a **quantity**.

[VIM-1.19]

2.1-6. measured quantity value

value of a measured 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’.

[VIM-2.10]

A *quantity value* can be expressed as a

- product of a number and a measurement unit for a differential or rational quantity, e.g., amount-of-substance concentration of Cd²⁺ in a sample of wine = 1.2×10^{-6} mol/L; or
- number for a differential or rational quantity of metrological dimension one, e.g., pH of a blood sample = 7.2, (the *SI measurement unit* “one” is generally not written out); number fractions of lymphocytes among all leukocytes in blood; or
- number and a *metrological reference* to a measurement procedure for an ordinal quantity, e.g., Rockwell C hardness of a steel sample = 43.4 HRC; 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 = 5 400 International Units per litre.

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

2.1-7. measurement model

model of measurement
model

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

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

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

[VIM-2.48]

A measurement model accommodates algorithms as well as explicit functions and will be used for specific examples of *metrological traceability chains* in Section 9.

2.1-8. measurement function

Function of **quantities**, the value 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** $h(Y, X_1, \dots, X_n) = 0$ can explicitly be written as $Y = f(X_1, \dots, X_n)$, 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, \dots, x_n a corresponding unique output quantity value $y = f(x_1, \dots, x_n)$.

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

[VIM-2.49]

Sometimes, the measurement function may be written conditionally as

$$Y = f(X_1, \dots, X_j) | (X_k, \dots, X_n) \quad (2.1-1)$$

where X_1, \dots, X_j may be

- input quantities in a measurement model, used or measured in the experiment to establish the *measured quantity value* of Y , that are given by the defining *quantity equation* (VIM-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 measured quantity value of Y , that are different from those given by the definition of the kind-of-quantity for Y ;

- quantities, values of which have been taken from literature, such as molar masses or physical 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 hemoglobin concentration when measuring bilirubin concentration in plasma by visible light spectrometry; and
- corrections for external quantities that affect the system embodying the quantity being measured or the measuring system, such as ambient temperature, pressure, or humidity;

and X_k, \dots, X_n comprise

- *influence quantities* that affect the relation between the indication and the measurement results, and have given specified 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 and influence quantity values x_1, \dots, x_n must be metrologically traceable. They are associated with 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 $y = f(x_1, \dots, x_n)$, is an estimate of the location of the distribution of quantity values of the measurand, Y (probability density function), 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 use of the Bates–Guggenheim equation for the single ion activity for the chloride ion in the measurement function for pH determined using a Harned cell is known to be based on an incomplete theory [26]. Known and presumed deficiencies or intentional omissions in the definition of the measurand and thereby in the measurement function or measurement model contribute components to the measurement uncertainty associated with the measured quantity value. The combination of such components constitutes a

2.1-9. definitional uncertainty

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”.

[VIM-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.

2.1-10. measurement principle

principle of measurement

Phenomenon serving as the basis of a **measurement**.

[VIM-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;
- conversion of two different kinds of uncharged particles into ions (“ionization”) in a mass spectrometer for the measurement of their amount-of-substance ratio;
- separation; and
- derivatization.

A given measurement method may involve more than one measurement principle.

2.1-11. measurement method

method of measurement

Generic description of a logical organization of operations used in a **measurement**.

[VIM-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.

2.1-12. measurement procedure

Detailed description of a **measurement** according to one or more **measurement principles** and to a given **measurement method**, based on a **measurement model** and including any calculation to obtain a **measurement result**.

[VIM-2.6]

The 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, and reporting.

2.1-13. measuring system

Set of one or more **measuring instruments** and often other devices, including any reagent and supply, assembled and adapted to give information used to generate **measured quantity values** within specified intervals for **quantities** of specified **kinds**.

[VIM-3.2]

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* including a *measurement model*. The calibrated measuring system provides an *indication* that is either, directly, the *meas-*

ured quantity value of the *measurand*, or is transformed into such a measured quantity value by the measurement model. The measurement result then consists of this measured quantity value and its calculated measurement uncertainty.

2.2-1. calibration

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

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.

[VIM-2.39]

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

The outcome of the calibration may be documented in a certification report or calibration certificate.

2.3 Measurement standard

Establishing *metrological traceability* often requires a

2.3-1. measurement standard

etalon

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

[VIM-5.1]

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 VIM) 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 CRM providing certified quantity values for the mass concentration of each of 10 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 relative measurement uncertainties associated with assigned quantity values in a given *calibration hierarchy*, is often described by the following concepts:

2.3-2. primary measurement standard

primary standard

Measurement standard established using a **primary reference measurement procedure**, or created as an artifact, chosen by convention.

EXAMPLE 1: 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.

[VIM-5.4]

A *primary measurement standard* (or a *primary calibrator*) of a differential or rational quantity embodies (a multiple of) 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 2.6.

The top 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 a quantity value with associated measurement uncertainty to a primary measurement standard is done by means of a *primary reference measurement procedure* (see Section 3.3-2).

2.3-3. secondary measurement standard

secondary standard

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

[VIM-5.5]

Examples of *secondary measurement standards* (or *secondary calibrators*) can be found in the *metrological traceability chains* of the figures in Section 9.

2.3-4. reference measurement standard

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.

[VIM-5.6]

A *reference measurement standard* does not have a fixed place in the hierarchy. Any standard in the chain can be chosen for that function.

In a calibration hierarchy, the metrologically lowest measurement standard defined by VIM is

2.3-5. working measurement standard

working standard

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

[VIM-5.7]

The quantity value and associated 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” [VIM-5.2], “national” [VIM-5.3], “regional”, “travelling” [VIM-5.8], and “intrinsic” [VIM-5.10], are sometimes used as prefaces to “measurement standard”.

A measurement standard used for *calibration* in a given *measurement* should not also be used for trueness control, but can be used for precision control (see VIM-2.15).

2.4 Calibrator

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

2.4-1. calibrator

Measurement standard used in **calibration**.

[VIM-5.12]

NOTE: The term “calibrant” is also used.

In addition to the assigned *quantity value* and *measurement uncertainty*, a calibrator must be accompanied by information about: the origin (material traceability, where such information has a bearing on the use of the material), production, definition of *quantity*, any matrix, homogeneity, stability, procedure used in the assignment of quantity value and measurement uncertainty, statement of metrological traceability, expiry date, intended use of the calibrator [27,28], and instructions for use.

In addition to these essential properties, its use in a *calibration hierarchy* requires that it be commutable.

2.4-2. commutability of a reference material

Property of a **reference material**, demonstrated by the closeness of agreement between the relation among the **measurement results** for a stated **quantity** in this material, obtained according to two given **measurement procedures**, and the relation obtained among the measurement results for other specified materials.

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) [13].

NOTE 3: The stability of commutable reference materials should be monitored regularly.

[VIM-5.15]

Lack of commutability in an RM leads to *measurement bias*.

2.4-3. primary calibrator

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

NOTE 1: The *quantity value* and associated *measurement uncertainty* of a primary calibrator are obtained by a direct primary reference measurement procedure or by primary preparation procedure.

NOTE 2: Such a calibrator is usually accompanied by a certification report [27] or a calibration certificate issued by an international or national metrology institute, see Figure 3.2-1.

NOTE 3: A primary calibrator is often assumed to embody a *quantity* with its quantity value having the smallest achievable measurement uncertainty, but the size of the relative measurement uncertainty is not a criterion for being called “primary”.

In case no *primary calibrator* is available, it is recommended by ISO 17511 [13] to produce an

2.4-4. international conventional calibrator

Calibrator established by international agreement.

2.4-5. secondary calibrator

Calibrator established by *measurement* according to a *secondary reference measurement procedure*.

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 [13] identifies the following two consecutive levels of material.

2.4-6. manufacturer’s working calibrator

Calibrator established by *measurement* according to the manufacturer’s selected measurement procedure or a higher-rank measurement procedure calibrated by a *primary calibrator* or *secondary calibrator* or an *international conventional calibrator*.

(adapted from ISO 17511 [13])

2.4-7. manufacturer’s product calibrator

Calibrator established according to the manufacturer’s standing measurement procedure calibrated by the *manufacturer’s working calibrator*.

(adapted from ISO 17511 [13])

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

2.5 Calibration hierarchy and metrological traceability chain

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

2.5-1. calibration hierarchy

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.

NOTE 1: **Measurement uncertainty** necessarily increases along the sequence of calibrations.

NOTE 2: The elements of a calibration hierarchy are one or more **measurement standards** and measuring systems operated according to **measurement procedures**.

NOTE 3: For this definition, the ‘reference’ can be a definition of a **measurement unit** through its practical realization, or a measurement procedure, or a measurement standard.

[VIM-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 reference 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 metrological reference to the end-user’s measuring system, but to describe metrological traceability of the measurement result, the direction of the sequence is reversed. The sequence between measurement result and metrological reference is termed and defined:

2.5-2. metrological traceability chain

traceability chain

Sequence of **measurement standards** and **calibrations** that is used to relate a **measurement result** to a reference.

[VIM-2.42]

Possible references, in this document termed “metrological reference” (see Section 2.6-1), are mentioned in “metrological traceability” (see Section 1.1-1, Note 1).

A metrological traceability chain requires a pre-established calibration hierarchy that is chosen before the measurement starts. 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.

Any given metrological traceability chain can be modified by adding or eliminating one or more calibrations, thereby creating a new chain. If the original metrological reference is eliminated, the new chain has a new reference

The generic flow chart in Fig. 2.5-1 shows possible additional strands designated by numbered triangles, circles, squares, and lozenges. Each shape refers to a *kind-of-quantity*, and the number indicates the level in the hierarchy to which the strand traces.

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 relative measurement uncertainty (runc) associated with the quantity value carried by any calibrator is necessarily greater than that of a preceding calibrator and smaller than that of a following calibrator and the even greater relative measurement uncertainty of the final measurement result. In the figures this is symbolized by a gray triangle to the left, which increases in breadth down the page.

Fig. 2.5-1 (Continued).

b) “specification of kind-of-quantity and measurement unit” that is embodied by preparing a set of one or more primary calibrators through a preparation procedure; or

c) “specification of ordinal kind-of-quantity and *ordinal quantity-value scale*” that is embodied in a set of *calibrators* through a primary preparation procedure.

unc is an abbreviation signifying a *measurement uncertainty* that is calculated according to GUM [2] in cases a) and b), but not in c).

runc signifies relative measurement uncertainty.

The symbol u will be used in specific examples of a) and b) and u_c for *combined standard uncertainty*.

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 or intermediate 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. The number in each shape is that of a measurement procedure in the hierarchy, and the type of shape refers to a particular kind-of-quantity.

Note: Q symbolizes a *quantity* embodied in a calibrator, I an *indication*.

In physics, calibration hierarchies have long been an established part of measurement [29,30]. 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 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. The Consultative Committee on Amount of Substance: Metrology in Chemistry (CCQM) has selected measurement principles and methods that have the potential for the development of primary reference measurement procedures giving component-specific quantity values in mol or its derived 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 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 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 [21]. In a single-stranded calibration hierarchy, the kind-of-quantity is the same throughout.

The term “calibration hierarchy” is used in EAL-G12 [31] and ILAC-G2 [10] in the sense of a plurilevel hierarchy of coordinated and interacting entities 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 Section 6.

2.6 Metrological reference

2.6-1. metrological reference

Specification of *kind-of-quantity* and description of how to obtain one or more *quantity values* of that kind-of-quantity.

NOTE 1: The specification is usually in the form of a normative document

NOTE 2: The types of specification comprise
definition of a measurement unit
measurement procedure
measurement standard
definition of an ordinal quantity-value scale
or combinations of the above.

NOTE 3: The metrological reference can be designated local, national, regional or international, depending on the jurisdiction of the body that maintains it.

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

- measurement, using a primary reference measurement procedure and a measuring system, assigning a differential or rational quantity value with measurement uncertainty (see Fig. 2.5-1); or
- preparation, using a primary preparation procedure, the execution of which delivers a differential or rational quantity value and its measurement uncertainty [see Fig. 2.5-1, 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 primary preparation procedure, the execution of which delivers the individual quantity values and their measurement uncertainties [see Fig. 2.5-1, 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 procedure.

2.7 Measurement uncertainty

2.7-1. measurement uncertainty

uncertainty of measurement
uncertainty

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

[VIM-2.26]

In the case of values for differential or rational quantities, but not for *ordinal quantities*, components of measurement uncertainty include *definitional uncertainty* of the *measurand*, random effects from various sources, components associated with recovery, with *measurement bias correction*, and with the assigned *quantity values* of *measurement standards* including *calibrators*. In the case where many samples of like nature, but having individual recognized systematic effects of unknown magnitude, a component that expresses the dispersion of these effects can be included in the measurement uncertainty [32].

Components of measurement uncertainty 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, here termed standard measurement uncertainties [2]. The other components, which may be evaluated by type B evaluation of measurement uncertainty, can also

be described by standard measurement uncertainties, evaluated from probability density functions based on experience, and from professional judgment, skill, or other information [2].

The overall measurement uncertainty of the measured quantity value may be expressed as a combined standard measurement uncertainty or a given multiple of it, or the half-width of a coverage interval, having a stated coverage probability.

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

The quantity value of each calibrator, except the first one, in a calibration hierarchy, associated with a combined standard measurement uncertainty that incorporates the combined standard measurement uncertainty associated with the measured quantity value of the previous calibrator, and must be evaluated and stated. Therefore, in the calibration hierarchy of, for example, Fig. 2.5-1, each relative measurement uncertainty $u(y_{i+1})/y_{i+1}$ cannot be smaller 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 any new component of measurement uncertainty incurred at step $i+1$.

How measurement uncertainties are evaluated and combined is beyond the scope of this document. Reference is made to GUM [2] and *Quantifying Uncertainty in Analytical Measurement* (QUAM) [33], and a recent supplement of GUM [34] describing approaches to deal with propagation of uncertainty using a Monte Carlo approach also for quantities that are not normally distributed.

The evaluation of measurement uncertainty requires the establishment of a calibration hierarchy for a measurement result. It is meaningless 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*.

2.8-1. target measurement uncertainty

target uncertainty

Measurement uncertainty specified as an upper limit and decided on the basis of the intended use of **measurement results**.

[VIM-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*. As the *metrological 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 validated 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 too small. Thus, the a priori fixing of a target measurement uncertainty requires a study of the intended use of the expected measurement result [35,36]. 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 either to accept a larger target measurement uncertainty than that originally desired, or that better measurement procedures, *measuring systems*, and *measurement standards* must be developed to comply with the given target measurement uncertainty. Obtaining a smaller measurement uncertainty has associated costs that will be taken into account when making decisions about these procedures.

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 *input quantities in a measurement model*, 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 to be 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 with explicit *metrological reference*, the use of the latest IUPAC relative atomic masses (atomic weights) [37], and published CODATA fundamental constants [38], with their measurement uncertainties, is sufficient, and no further documentation of metrological traceability of these quantity values is needed.

2.10 Corrections applied 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 value” must be adjusted for systematic effects by corrections applied to the *indication* or to the initially estimated quantity value itself. The effects can be caused inter alia by

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

2.10-1. correction

Compensation for an estimated systematic effect.

[VIM-2.53]

It is assumed by the GUM [2] that corrections should be applied for all recognized and significant systematic effects, e.g., due to influence quantities. Correction factors or correction addends for systematic effects may be estimated by replicate measurements of an appropriate *CRM* 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 for the systematic effects adjusted by corrections; the *measurement uncertainty* in the measurement result is the combination of the measurement uncertainty associated with 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 addends or factors correcting for the systematic effects be metrologically traceable. Therefore, in the estimation of addends or factors correcting for systematic effects, the use of measurement procedures that give metrologically traceable measurement results and CRMs with metrologically traceable quantity values are necessary.

In some cases, the definition of a measurand incorporates the necessity to measure by a specified procedure, sometimes called a “standard method”, in order to avoid a particular systematic effect.

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, and should be re-examined [39].

3. CALIBRATION OF MEASURING SYSTEMS IN A CALIBRATION HIERARCHY

3.1 Purpose of RMs in a calibration hierarchy

In any given *measurement*, an *RM* as defined below can function as either a *calibrator* or a trueness control material, not as both. In a calibration hierarchy, the first is the obvious role. Terminologically, *RM* is generically superordinate to the concept *CRM*; yet in a metrological hierarchy, *CRM* has a higher status, as it carries a certified quantity value with associated *measurement uncertainty*. The definition of *RM* in the *VIM* is naturally broad in order to cover a wide variety of meanings, used in practice:

3.1-1. reference material

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 material’ comprises materials embodying **quantities** as well as nominal properties.

EXAMPLE 1: *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.

EXAMPLE 2: *Examples of reference materials embodying nominal properties:*

colour chart indicating one or more specified colours;
DNA compound containing a specified nucleotide sequence;
urine containing 19-androstenedione**.

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

EXAMPLE 1: Substance of known triple-point in a triple-point cell.

EXAMPLE 2: Glass of known optical density in a transmission filter holder.

EXAMPLE 3: Spheres of uniform size mounted on a microscope slide.

*polychlorodibenzodioxin

**19-norandrost-4-ene-3,17-dione

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 [40].

NOTE 8: ISO/REMCO has an analogous definition [40] but uses the term “measurement process” to mean ‘examination’ (ISO 15189:2007, 3.4), which covers both measurement of a quantity and examination of a nominal property.

[VIM-5.13]

3.1-2. certified reference material

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 with assigned **quantity value** for the concentration of cholesterol and associated **measurement uncertainty** stated in an accompanying certificate, used as a **calibrator** or **measurement trueness** control material.

NOTE 1: ‘Documentation’ is given in the form of a ‘certificate’ (see ISO Guide 31:2000 [41]).

NOTE 2: Procedures for the production and certification of certified reference materials are given, e.g. in ISO Guide 34 and ISO Guide 35 [15,16].

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. “Traceability” covers both ‘**metrological traceability** of a quantity value’ and ‘traceability of a nominal property value’.

NOTE 4: Specified quantity values of certified reference materials require metrological traceability with associated measurement uncertainty [40].

[VIM-5.14]

3.2 Dissemination of calibrators

Typical disseminations of calibrators are shown in Figs. 3.2-1 and 3.2-2.

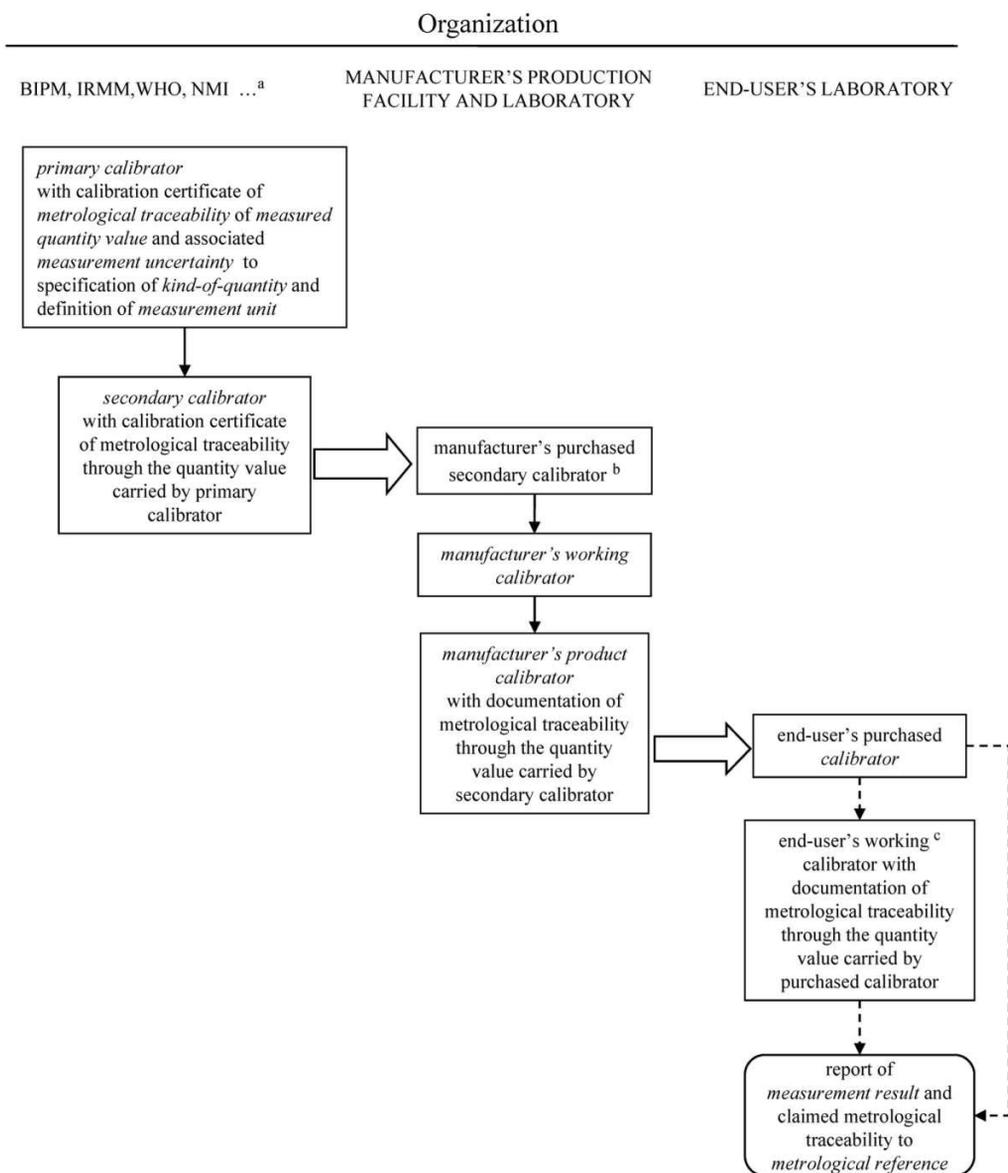


Fig. 3.2-1 A hierarchy of *calibrators* starting with a “*primary calibrator* with calibration certificate of *metrological traceability* of a *measured quantity value* and associated *measurement uncertainty* to specification of *kind-of-quantity* and definition of *measurement unit*”. A vertical arrow between boxes indicates that the measured quantity value and its associated measurement uncertainty, of the *quantity* embodied in the material described in the lower box are established by *measurement* using the calibrator in the upper box as *metrological 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.

^aThe measured quantity value and its associated measurement uncertainty of the calibrator may be assigned by a reference measurement laboratory usually designated by an NMI or an international organization.

^bThe VIM definition of *reference measurement standard* covers this hierarchical level of calibrator.

^cAn end-user may use a purchased calibrator directly for routine *measurements* or to assign the measured quantity value and its 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).

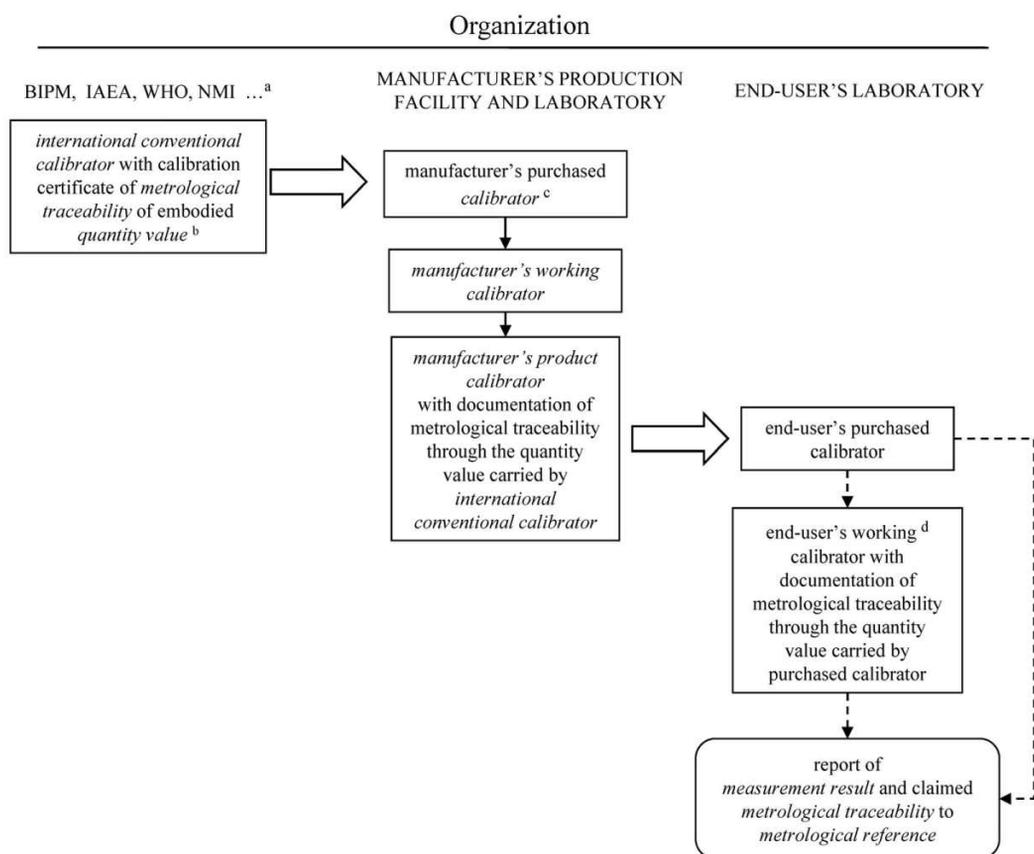


Fig. 3.2-2 A hierarchy of *calibrators* starting with “*international conventional calibrator* with a calibration certificate of *metrological traceability* of embodied *quantity value*”.

A vertical arrow between boxes indicates that the *measured quantity value* and its associated *measurement uncertainty*, of the *quantity* embodied in the material described in the lower box are established by *measurement* using the *calibrator* in the upper box as *metrological 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.

^aThe measured quantity value and its associated measurement uncertainty of the *calibrator* may be assigned by a reference measurement laboratory usually designated by an NMI or an international organization.

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

^cThe VIM definition of *reference measurement standard* covers this hierarchical level of *calibrator*.

^dAn end-user may use the purchased *calibrator* directly for routine *measurements* or to assign the measured quantity value and its 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).

3.3 Purpose of reference measurement procedures in a calibration hierarchy

Measurement procedures and *calibrators* are essential in most *calibration hierarchies* and in the ensuing *metrological traceability chain*, which ends in a definition of a *measurement unit*. The *metrological reference* may further require stipulating a *measurement procedure*.

3.3-1. reference measurement procedure

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

[VIM-2.7]

Especially in case an SI measurement 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].

The adjective “primary” in relation to measurement procedure is used with different meanings because there is a lack of commonly agreed scientific criteria.

3.3-2. primary reference measurement procedure

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).

[VIM-2.8]

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

3.3-3. secondary reference measurement procedure

secondary reference procedure

Reference measurement procedure used to obtain a **measurement result** by relation to a **measurement standard** for a **quantity** of the same **kind**.

4. ESTABLISHING AND REPORTING METROLOGICAL TRACEABILITY

The following checklist presupposes that the *measurement* will be made in a laboratory, which is operating under an accreditation scheme (e.g., ISO/IEC 17025 [7], ISO 15189 [9], ISO 15195 [8], ISO Guide 31 [41], or GLP [42]) for a specified expertise and scope, or at least has validated *measurement procedures*. The EURACHEM/CITAC guide *Traceability in Chemical Measurements* [11] gives a procedure for establishing metrological traceability. The following list shows the sequence utilizing the concepts previously defined.

- Definition of *measurand*, intended use of *measurement results*, and *target measurement uncertainty*
This will include a clear statement of the specific concept under *quantity* to be measured, including system, relevant components, and *kind-of-quantity*, with a statement of the *measurement model* or *measurement function* and a description of the *measuring system* as well as the measurement procedure including whether any *correction* is to be made for recovered quantity ratio [39]. The target measurement uncertainty will influence the stringency of the *metrological traceability chain*; the end-user’s 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 (see Section 2.6).
- 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 (laboratory technologist) should undertake appropriate *verification* to discover whether a previously validated "standard measurement procedure" can be implemented in the technologist's laboratory and validated.
- Acquisition and verification of end-user's calibrator (see Note c to Fig. 3.2-1 and Note d to Fig. 3.2-2)
Such a calibrator should be verified for absence of changes during transport and storage, validated for *commutability of a reference material*, have documented metrological traceability of its stated *quantity value* and associated measurement uncertainty.
- End-user's measurement on system or sample to obtain measurement result, including measurement uncertainty, based on an *uncertainty budget*.
- 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 together with the *measured quantity value* and associated measurement uncertainty.

The purpose of performing a measurement is to provide information, in the form of a measurement result, on the value of a measurand, embodied in a specified system. The communication of that information can be made orally, in writing, or electronically. The amount of information given directly varies with the intended use of the measurement result. When only the measured quantity value is presented, the associated measurement uncertainty and metrological traceability should be available. The documentation can take the form of a "certificate of analysis", "test report", "measurement report", "calibration certificate" or more extensively a "certification report" (4.3 in [27] and [41]). A certification report specifies all necessary details to understand the production, properties, and use of the calibrator (*measurement standard* or *CRM*), its quantity value, measurement uncertainty and their metrological traceability. The documentation of metrological traceability of the measurement result is essential 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 measured quantity value that are necessary for the calculation of the final measurement uncertainty.

In general support of this systematic approach, there should be a concerted effort to

- include basic concepts of metrology in curricula of analytical chemistry; and
- use concepts and associated terms given in the VIM [1] for description and communication of measurement.

5. THE ROLE OF METROLOGICAL TRACEABILITY IN VERIFICATION, VALIDATION, AND ESTABLISHING METROLOGICAL EQUIVALENCE OF MEASUREMENT RESULTS

The purpose of a *measurement* is to aid in the making of a decision. The definition of the *measurand* must be relevant for the subject of the decision, e.g., correct dose of correct medicine. The *measurement uncertainty* must be small enough to enable the management of risks associated with incorrect decisions. A measurement result that supports such decisions is a “valid” measurement result. A statement of validity of a measurement result for a specified intended use requires metrological traceability and measurement uncertainty against specification fixed a priori, including a target measurement uncertainty.

It is recognized that currently measures of measurement trueness and of measurement precision are often provided instead of measurement uncertainty.

The VIM defines verification and validation to make the latter subordinate to the former.

5-1. verification

Provision of objective evidence that a given item fulfills specified requirements.

NOTE 2: The item may be, e.g. a process, measurement procedure, material, compound, or measuring system

[VIM-2.44]

5-2. validation

Verification, where the specified requirements are adequate for a stated use.

[VIM-2.45]

“Validation” is seen to be more demanding than “verification”. The former subordinate concept is therefore terminologically derived from the latter superordinate concept.

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

5-3. metrological compatibility of measurement results

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.

[VIM-2.47]

A special case of *metrological compatibility of measurement results* can be characterized by the property that measurement results can be substituted for each other for a specified intended use.

5-4. metrological equivalence of measurement results

equivalence of measurement results

Property of two or more measurement results for a given *measurand* that have *metrological compatibility of measurement results*, so that they are each acceptable for the same specified intended use.

NOTE: Measurement results are either metrologically equivalent or they are not.

6. ENTITIES CONCERNED WITH METROLOGICAL TRACEABILITY

To ensure *metrological comparability of measurement results* across the world, it is necessary to establish and maintain an international framework of entities to provide the elements of metrological traceability. This framework composed of international, regional, national, and local entities, both public and private, is responsible for providing metrological references, the metrological higher elements of calibration hierarchies, and general dissemination of metrological traceability.

The preeminent part of this international framework is the International Bureau of Weights and Measures (BIPM), an international organization that was created by Article I of the Metre Convention of 1875 (<www.bipm.org>). The General Conference on Weights and Measures (CGPM) and the International Committee for Weights and Measures (CIPM) were created by Article III of the same convention. The CIPM directs and supervises the work of the BIPM under the authority of the CGPM, which is made up of delegates of the governments of the Member States, and observers from the Associates of the CGPM. The CGPM currently meets in Paris once every four years. It receives the report of the CIPM on the work accomplished; it approves the BIPM's program of work and funding for the next four-year period; it endorses the results of new fundamental metrological determinations; and it takes major decisions concerning the *International System of Units (SI)*.

The BIPM has responsibility for worldwide uniformity of *measurement*, and for ensuring the basis for a single, coherent system of measurements traceable to the SI. It assumes this mission in a number of ways, from direct dissemination of SI units, as in the case of mass and time, to international comparisons to validate the consistency of national measurement standards, as in electricity, ionizing radiation, and chemistry. To achieve this, the BIPM maintains its scientific expertise through carefully selected laboratory work, and collaborates intensively with other institutions and organizations. The principal tasks of the BIPM are to

- carefully select and target scientific and technical work to improve *measurement standards* and to improve reference facilities or measurements for the world's national metrology institutes (NMIs);
- provide specific technical services, such as the organization of international comparisons of the realizations of *base units* and *derived units* of the SI;
- further the global coordination of metrology, through, for example, the operation of the CIPM Mutual Recognition Arrangement (CIPM MRA);

- maintain, extend, and disseminate the SI, and promote the concepts of metrological traceability and measurement uncertainty; and
- establish and maintain relations with other organizations, especially those with similar missions or those having responsibilities in areas where better metrology could bring benefits to the organization and/or to its users.

The CIPM and the BIPM's direction are advised on scientific and technical matters by a number of Consultative Committees (CCs), including CCQM. The members of the committees are generally those institutions of Member States that are recognized internationally as most expert in the field. The CCs provide the focus for international evaluation of advances in science and technology that directly influence metrology and the definitions of the SI units. They prepare recommendations for the CIPM, and the CIPM in turn presents draft resolutions to the CGPM. The CCs also identify, plan, and execute key comparisons of national measurement standards (see Section 7.2).

Any measurement laboratory in a given country should have direct or indirect access to calibrators and other tools in order to establish metrological traceability of its measurements results.

The NMIs also collaborate in regional metrology organizations of which there are currently five (Table 6-1). In addition to NMIs, there are reference measurement laboratories operating under regional or international authority. A schematic of the links between the BIPM and other entities in the framework described above is given in [43].

Table 6-1 The five regional organizations providing nodes in the international framework supporting metrological traceability.

Regional organization	URL
The Asia Pacific Metrology Programme (APMP)	< http://www.apmpweb.org/ >
Euro-Asian Cooperation of National Metrological Institutions (COOMET)	< http://www.coomet.org/ >
European Collaboration in Measurement Standards (EURAMET)	< http://www.euramet.org/ >
The Inter-American Metrology System (SIM)	< http://www.sim-metrologia.org.br/ >
Forum of the Directors of the West African National Metrological and Hydrological Services (AFRIMET)	< http://www.afrimet.org/ >

7. INTERLABORATORY COMPARISON (ILC)

The concept “interlaboratory comparison” includes the proficiency testing scheme (PTS), the CCQM key comparison (KC), and the external quality assessment scheme (EQAS).

7.1 What is an ILC?

Interlaboratory comparison is a generic concept for an endeavor to obtain and compare *measurement results* obtained by two or more measurement laboratories for the same or similar *measurands* embodied in the same or similar materials. An ILC usually involves an organization or body responsible for the organizational and other aspects of the ILC.

Interlaboratory comparison is discussed in work by Thompson et al. [44], and defined in ISO/IEC 17043 [45]* as

*ISO/IEC 17043 states the term in the plural, but ISO terminology work standards advise to define concepts as singular in general.

7.1-1. interlaboratory comparison

ILC

Organization, performance and evaluation of measurements or tests on the same or similar items by two or more laboratories in accordance with predetermined conditions.

[ISO/IEC 17043-3.4]

In some circumstances, one of the laboratories involved in the intercomparison may be the laboratory that provides the assigned quantity value for the material. The operation enables the determination of the *metrological equivalence of measurement results* of the participants but does not, by itself, establish *metrological traceability*.

7.2 Purposes of an ILC

Interlaboratory comparisons are arranged by many organizations and companies with the aim to evaluate analytical *measurement procedures* and their *measurement results*. Harmonization of such studies has benefited from recommendations by the IUPAC/ISO/AOAC Interdivisional Working Party on Harmonization of Quality Assurance Schemes for Analytical Laboratories [44,46,47]. The scope of an ILC evolved from being a measurement procedure *validation* study to performing proficiency testing and further to assessing the *metrological equivalence of measurement results*. Infrastructural requirements were described [48] and used in ISO/IEC 17043 [45]. A special category of ILCs is a study aimed at assigning *quantity values with measurement uncertainties* to materials [16]. Categories, names, and purposes of ILCs are given in Table 7.2-1.

Table 7.2-1 Types of *interlaboratory comparison* and their purposes.

Category	Usual term	Purpose	Comment
assessment of participant's <i>measurement capability</i>	proficiency testing scheme; intercomparison study; intercomparison run; external quality assurance scheme; laboratory measurement evaluation program	to test the ability of a laboratory to obtain <i>measurement results</i> similar to those of peer laboratories or to document participant's measurement performance or for education	often required as part of an accreditation (e.g., to ISO/IEC 17025 or ISO 15189) or when taking regulatory or legal action; sometimes external <i>reference measurement procedure quantity values</i> rather than the average of participants' measurement results are used to assess performance
	interlaboratory <i>measurement bias</i> study; International Measurement Evaluation Program (IMEP)	to determine measurement bias of measurement results obtained through a <i>measurement procedure</i> , assessment of measurement capability	based on a <i>reference quantity value</i> with demonstrated <i>metrological traceability</i> and associated measurement uncertainty, external to the participants
cooperative trial, or measurement audit		one-off comparison of participant's performance	may be for contractual purposes

(continues on next page)

Table 7.2-1 (Continued).

Category	Usual term	Purpose	Comment
mutual recognition of national <i>measurement standards</i> and of calibration certificates and measurement certificates	CIPM key comparison	determine degree of equivalence of national measurement standards, expressed quantitatively in terms of their deviations from the comparison reference value and the measurement uncertainties of those deviations	organized in the frame of the CIPM-MRA to support claims of NMIs related to their measurement and calibration capabilities
measurement procedure validation	method validation study, or collaborative trial	to provide data for the validation of a measurement procedure	determines inter alia the <i>measurement reproducibility</i> of measurement results obtained using a given measurement procedure and, if a CRM is used, the measurement bias of each participant's measurement result may be calculated
material characterization	multi-laboratory or multi- <i>measurement method</i> approach to assign quantity values and measurement uncertainties embodied in materials	to provide measurement results to be used in assigning quantity value and measurement uncertainty embodied in an RM or CRM	A <i>measured quantity value</i> 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 <i>metrological reference</i> .

All of these are tools in quality assurance. Assessment may be based on the evaluation of the participants' measurement results against those assigned to the interlaboratory comparison material before the ILC by a reference measurement laboratory or against an agreed *measured quantity value*. ILCs are announced by the organizers as open or closed, and participation may either be voluntary or compulsory. Participation in ILCs in many cases is an integral part of a laboratory's quality assurance program, and is complementary to the laboratory internal quality control and on-site assessments by peer experts, but cannot replace them. According to the ISO/IEC 17025 [7] and the ISO 15189 [9] International Standards, regular laboratory participation in ILCs is a requirement for accredited laboratories.

Key comparisons are organized in the frame of the CIPM-MRA between NMIs or NMI-designated institutions, following protocols established for the comparison. The main aim of a KC is a practical support to the MRA in the assessment and confirmation of the metrological equivalence of measurement results obtained by any pair of participating NMIs or laboratories designated by them. In chemistry, a pilot study is normally organized to enable the participants to familiarize themselves with

any problems arising in the *measurement* of a particular *quantity* embodied in a particular material. After a KC is performed, a key comparison reference value (KCRV) may be established from participants' measurement results. However, different approaches for calculating the KCRV and associated measurement uncertainty are used and agreed for each KC. Potential harmonization related to KCRV assignment is still the subject of discussion.

Measurement procedure validation studies (usually called “method validation studies”, or “collaborative trials”) require the use of the same measurement procedure by all laboratories on the same well-characterized material or set of such materials.

In material characterization studies aiming at measuring quantity values embodied in candidate RMs, the organizing body, e.g., an RM 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 [15,16] yielding quantity values with established *metrological traceability* and associated measurement uncertainty.

7.3 Measurement capability

7.3-1. measurement capability

Ability to measure a *quantity* of a given *kind*, in a specified interval of *quantity values*, embodied in a specified material, as demonstrated by a *measurement uncertainty*.

NOTE: 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.

7.4 Obtaining a reference value of a quantity embodied in an ILC material

A *reference quantity value* [VIM-5.18] assigned to a *quantity* embodied in an ILC material is usually obtained in one of the following ways:

- *measurement* by a reference measurement laboratory;
- use of materials carrying one or more pre-established *quantity values*, e.g., an RM or CRM, or *international measurement standard*;
- using a reference preparation procedure such as spiking;
- using an agreed quantity value decided by selected or expert laboratories; or
- using an agreed quantity value derived from *measurement results* reported by the participants.

7.5 ILCs and metrological traceability

Each laboratory participating in an ILC establishes its own *metrological traceability chain* for its *measurement results*. If the measurement results of all participants are to be comparable, their metrological traceability chains must end in the same *metrological reference*. With the exception of measurement procedure validation studies, a *measurement procedure* is usually not prescribed in proficiency testing, intercomparison studies, external quality assurance schemes, and laboratory measurement evaluation programs. In some cases, the establishment of metrological traceability is arranged as a part of the ILC by provision of a common *calibrator* and is decided by the organizer *prior* to the *measurements*.

7.6 ILCs and laboratory performance

An assessment of the ILC participants' *measurement results* can be performed by evaluating properties associated with these results. Which laboratory performance properties might be assessed in a specific ILC depends 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 *metrological compatibility of measurement results*, or the *metrological equivalence 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* assigned to the ILC comparison material used.

Use of "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 to assess a participant's *measurement capability*. This would constitute a circular approach because the participants' measurement results will influence the ILC quantity value, and they will be evaluated using that same ILC quantity value. In addition, such an evaluation cannot detect a *measurement bias* that is common to all *measurements*. Also, it is perfectly possible that a laboratory identified as submitting an outlier, may actually be reporting the most correct measurement result, thus demonstrating the importance of an external metrologically traceable reference quantity value.

Nevertheless, in certain types of ILCs, an agreed quantity value is the only quantity value possible to arrive at, e.g., in an ILC assessing laboratory performance of the measurement results obtained for procedure-defined *measurands*. In that case, the ILC can only establish *metrological equivalence* of the participants' measurement results, not their *metrological traceability*.

7.7 ILCs and the assignment of quantity values and measurement uncertainties to RMs

Currently there are many open questions related to *metrological traceability* of quantity values assigned to materials using results from participants in ILCs. Although it is clear that combination of *measurement results* that are metrologically traceable to the same *metrological reference* leads to a traceable value, a description of the *metrological traceability chain* becomes a very complex issue. The assessment of measurement uncertainty associated with such a derived result becomes even more difficult. It is metrologically contradictory that the uncertainties of consensus quantity values are sometimes much smaller than the spread of measured quantity values used for calculation and also that the final measurement uncertainty associated with the consensus value is often smaller than the smallest measurement uncertainty of the measurement results reported by individual laboratories.

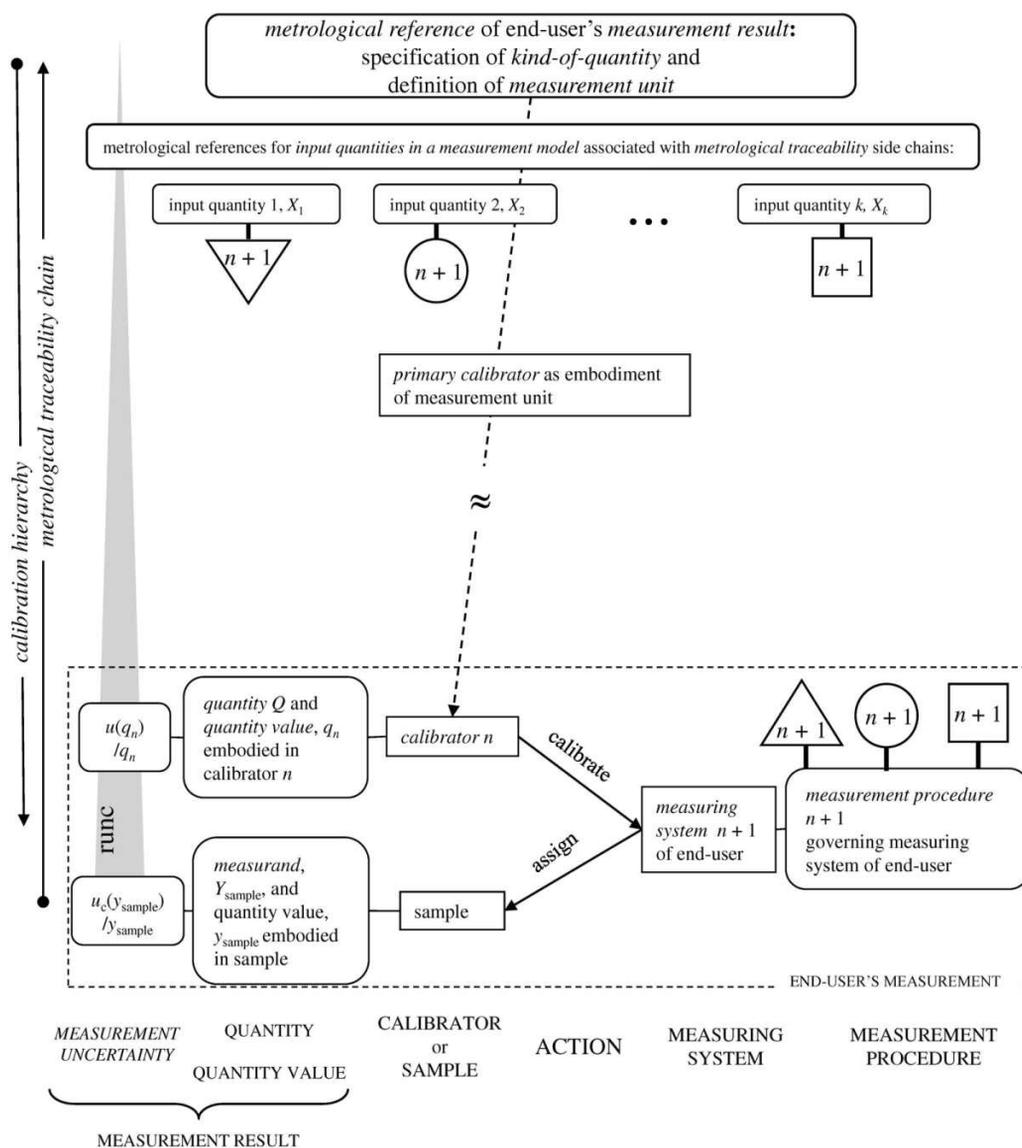
8. METROLOGICAL TRACEABILITY OF MEASUREMENT RESULTS FROM FIELD LABORATORIES

8.1 Function of metrological traceability in quality assurance

Understanding of, and appropriate dealing with, metrological traceability and *measurement uncertainty* are important considerations in achieving a reliable *measurement result*. 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 defining the *measurand*, choosing a *calibration hierarchy*, and agreeing on the required *target measurement uncertainty*.

8.2 Demonstration of metrological traceability by field laboratories

The establishment by the field analyst of the metrological traceability of his/her *measurement results* is simple and is illustrated in Fig. 8.2-1. The lower levels in any *calibration hierarchy* are the end-user's



measurement model for the end-user $h(Y_{\text{sample}}, Q_{n+1}, I_{\text{sample}}, X_1, \dots, X_k) = 0$

Fig. 8.2-1 Metrological traceability chain available to an end-user.

Note 1: The scheme does not apply in the case of an ordinal quantity.

Note 2: Q symbolizes a quantity embodied in a calibrator, I an indication.

Note 3: See Fig. 2.5-1 for an explanation of symbols and abbreviations.

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 provider of RMs or CRMs.

Figure 8.2-1 implies that the calibrator should be sold with an established metrological traceability chain for the measured quantity value with associated measurement uncertainty that is to be included in the end-user measurement uncertainty budget. Knowing the measurement uncertainty associated with any assigned quantity value of a quantity 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.

It is recognized that routine measured quantity values are often not delivered with their associated measurement uncertainties, but accreditation according to ISO/IEC 17025, or ISO 15189, requires that the measurement uncertainty be available to the customer, if relevant.

9. EXAMPLES OF METROLOGICAL TRACEABILITY CHAINS OF MEASUREMENT RESULTS

In this section, examples of metrological traceability chains for measurement results are presented. The examples have been chosen to illustrate the application of various *measurement principles*.

Metrological traceability chains may be longer or shorter than those given, or modified as the circumstances of the end-user require. The set of details presented for each example is only to be regarded as one possible solution to a particular measurement problem.

A chemist in a field laboratory will probably establish *metrological traceability of quantities* such as a mass, temperature, and volume by purchasing and maintaining suitably calibrated equipment such as balances, thermometers, and volumetric equipment. A metrological traceability chain for a given *measured quantity value* may have other metrological traceability chains as side chains. For explanation of the conventions used in the flow charts of *calibration hierarchies*, see the legend of Fig. 2.5-1.

9.1 Amount-of-substance concentration of an acid in a solution

Titration of an acid with a base, using *measurement of pH* or the color change of an added indicator to obtain the end point, is a long-established *measurement principle* for the measurement of amount-of-substance concentration of an acid. In this example the amount-of-substance concentration of a solution of hydrochloric acid (HCl) is measured by titration with a solution of sodium hydroxide (NaOH). The amount-of-substance concentration of NaOH is first measured by titration of a solution of potassium hydrogen phthalate (KHP), which has been prepared from a solid of known and metrologically traceable amount-of-substance content.

It is noted that the *measurement uncertainty* for an example of this kind of measurement is presented in Appendix A.3 of the QUAM [33].

9.1.1 The measurement model

The amount-of-substance concentration of HCl can be expressed in terms of a *measurement function*

$$c_{\text{HCl}} = c_{\text{NaOH}} \frac{V_{\text{T2}}}{V_{\text{HCl}}} \quad (9.1.1-1)$$

where c_{HCl} and c_{NaOH} are amount-of-substance concentrations of HCl and NaOH, respectively, V_{T2} is the end point volume of the titration of HCl by NaOH, and V_{HCl} the aliquot of HCl taken for the titration.

9.1.2 Primary calibrator, pure potassium hydrogen phthalate

The primary calibrator is solid potassium hydrogen phthalate with an amount-of-substance content measured by coulometric titration. This *calibrator* is purchased as a *CRM* with calibration certificate stating the purity (mass fraction, or amount-of-substance content) with an *expanded measurement uncertainty*.

9.1.3 Secondary calibrator, standard solution of sodium hydroxide

The *calibrator* for the end-user's *measurement* of the amount-of-substance concentration of the HCl solution is a solution of sodium hydroxide that is freshly standardized* against a *primary calibrator* of dissolved potassium hydrogen phthalate according to the *measurement function*

$$c_{\text{NaOH}} = \frac{m_{\text{KHP}} k_{\text{KHP}}}{V_{\text{T1}}} \quad (9.1.3-1)$$

where m_{KHP} is mass of KHP, k_{KHP} is amount-of-substance content of KHP [50], and V_{T1} is the end point volume of the titration of KHP by NaOH.

Note that in the EURACHEM example, the equations of the two titrations are combined to give the measurement function, which also expresses the purity of the KHP as a mass fraction. The equivalent measurement function from equations 9.1.1-1 and 9.1.3-1 is

$$c_{\text{HCl}} = \frac{m_{\text{KHP}} k_{\text{KHP}} V_{\text{T2}}}{V_{\text{HCl}} V_{\text{T1}}} \quad (9.1.3-2)$$

With eqs. 9.1.3-1 and 9.1.3-2, the measurements are separated to show the role of the *secondary calibrator* (the NaOH solution).

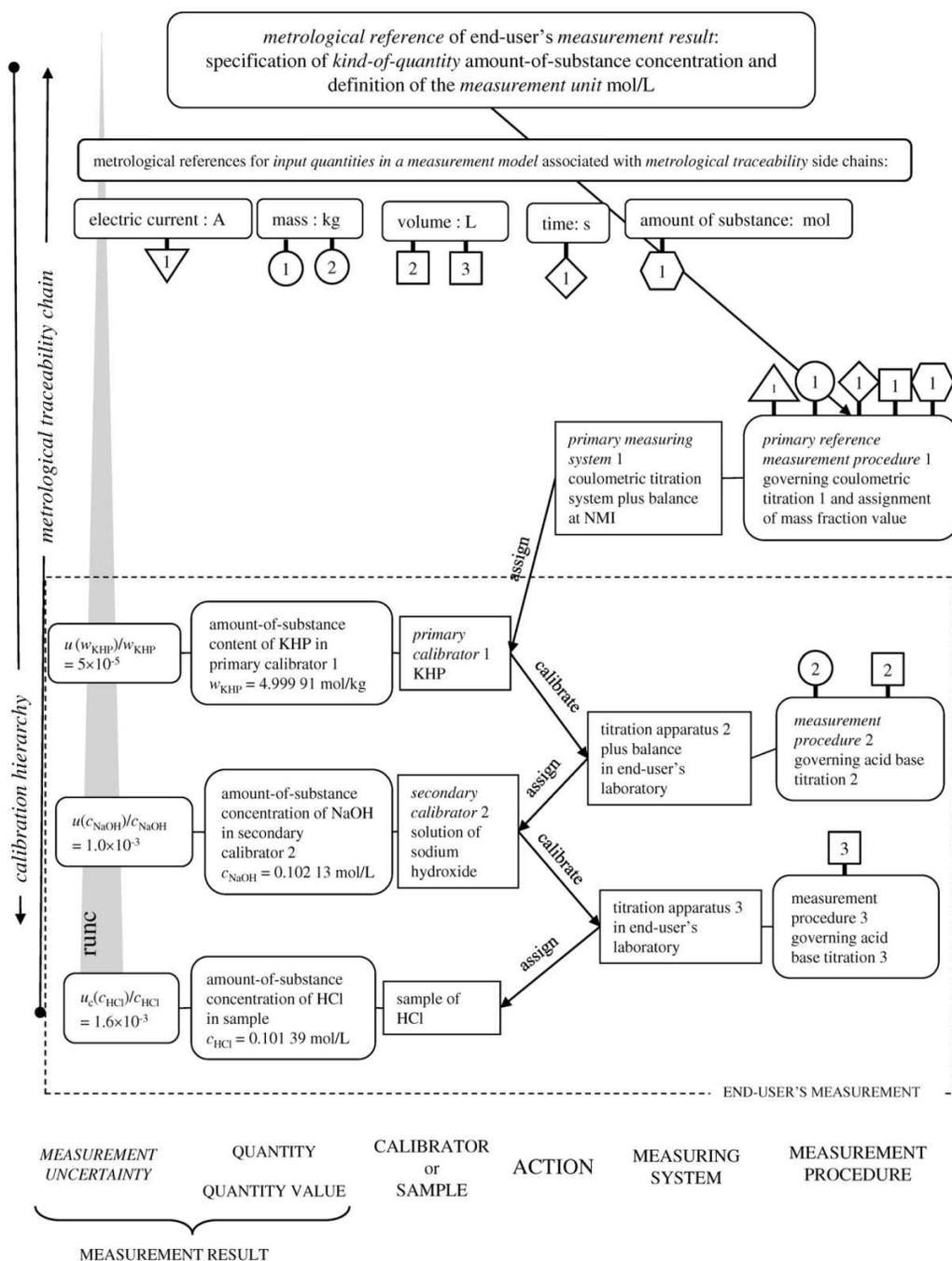
9.1.4 Measuring systems

The measuring systems for the titrations both include a titration apparatus with a means of obtaining the end point of the titration. For the *quantity value* assignment of the *secondary calibrator*, a balance is used to weigh an aliquot of KHP. In the end-user's *measurement*, volumetric equipment is required to deliver a known volume of the HCl solution for titration by NaOH.

9.1.5 Metrological traceability of the measured amount-of-substance concentration of HCl

Figure 9.1.5-1 shows the metrological traceability of the *measurement result* of amount-of-substance concentration of HCl. The amount-of-substance concentration of the *secondary calibrator* (NaOH solution) is metrologically traceable to the amount-of-substance content of a solution of the *primary calibrator*, and the volumes of glassware and titrating systems. The amount-of-substance content of the primary calibrator is in turn metrologically traceable to the definition of the *SI measurement units* mole and kilogram through metrologically traceable *measured quantity values* for time, electric current, and mass. In addition, the value of the Faraday constant, to relate amount of electricity to amount of substance, is also required.

*"Standardization" or "calibration" is a term in common use to describe the assignment of a *quantity value*.



measurement model for end-user $h(w_{\text{KHP}}, c_{\text{HCl}}, c_{\text{NaOH}}, V_{\text{HCl}}, V_{\text{T2}}) = 0$

Fig. 9.1.5-1 Metrological traceability chain of a measurement result of an amount-of-substance concentration of an HCl solution by titration. Titration apparatus 3 may be identical to titration apparatus 2. See Fig. 2.5-1 for an explanation of symbols and abbreviations.

9.2 pH of a solution

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

In 2002, IUPAC issued a recommendation for revision of the pH scale based on the concept of a *primary reference measurement procedure* for pH [26]. The use of the Harned cell fulfills the criteria for a primary reference measurement procedure so that a pH value thus obtained is unequivocally metrologically traceable to the *International System of Units*, here the *SI measurement unit* one. A buffer solution, the pH of which 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 operated 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, gives buffers that are classed as *secondary measurement standards*.

9.2.1 Primary reference measurement procedure—the Harned cell

The Harned cell [26] is a cell without transference comprising a hydrogen electrode and a silver, silver chloride electrode:



the use of which leads to the following *quantity equation*

$$\text{pH} = \lim_{b_{\text{Cl}^-} \rightarrow 0} \left\{ \frac{(E_1 - E^\circ)F}{RT \ln 10} + \lg \left(\frac{b_{\text{Cl}^-}}{b^\circ} \right) \right\} - \frac{AI^{1/2}}{1 + 1.5(I/b^\circ)^{1/2}} \quad (9.2.1-1)$$

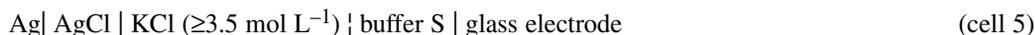
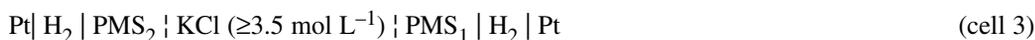
where A is the Debye–Hückel constant, which is given in tables for the temperature of the experiment, I is the ionic strength of the solution, E_1 is the cell potential difference, E° is the standard electrode potential of the cell, F is the Faraday constant, b° is the standard molality (1 mol/kg), and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

An *uncertainty budget* has been prepared [50], and buffer solutions that fulfill requirements for *calibration* of a pH *measuring system* have been identified as candidates for *primary measurement standards*.

9.2.2 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



Issues concerning the minimization and estimation of residual liquid junction potentials are discussed in detail in ref. [26].

9.2.3 Metrological traceability of pH measurement results

It is argued that the *measurement procedure* using a Harned cell to measure the pH of a solution meets the criteria of a *primary reference 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 associated with the pH value, arising from the use of the Bates–Guggenheim convention to establish $-\lg(\gamma_{\text{Cl}^-})$ (the value 1.5 in the term $-\frac{AI^{1/2}}{1+1.5(I/b^\circ)^{1/2}}$ in eq. 9.2.1-1), 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 ($k = 2$) of a typical primary measurement result 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 eq. 9.2.1-1. By not including the full measurement uncertainty, if in the future an improved *quantity value* for the activity coefficient of chloride ion were used ($\gamma_{\text{Cl}^-}^\circ$), 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 Fig. 9.2.3-1.

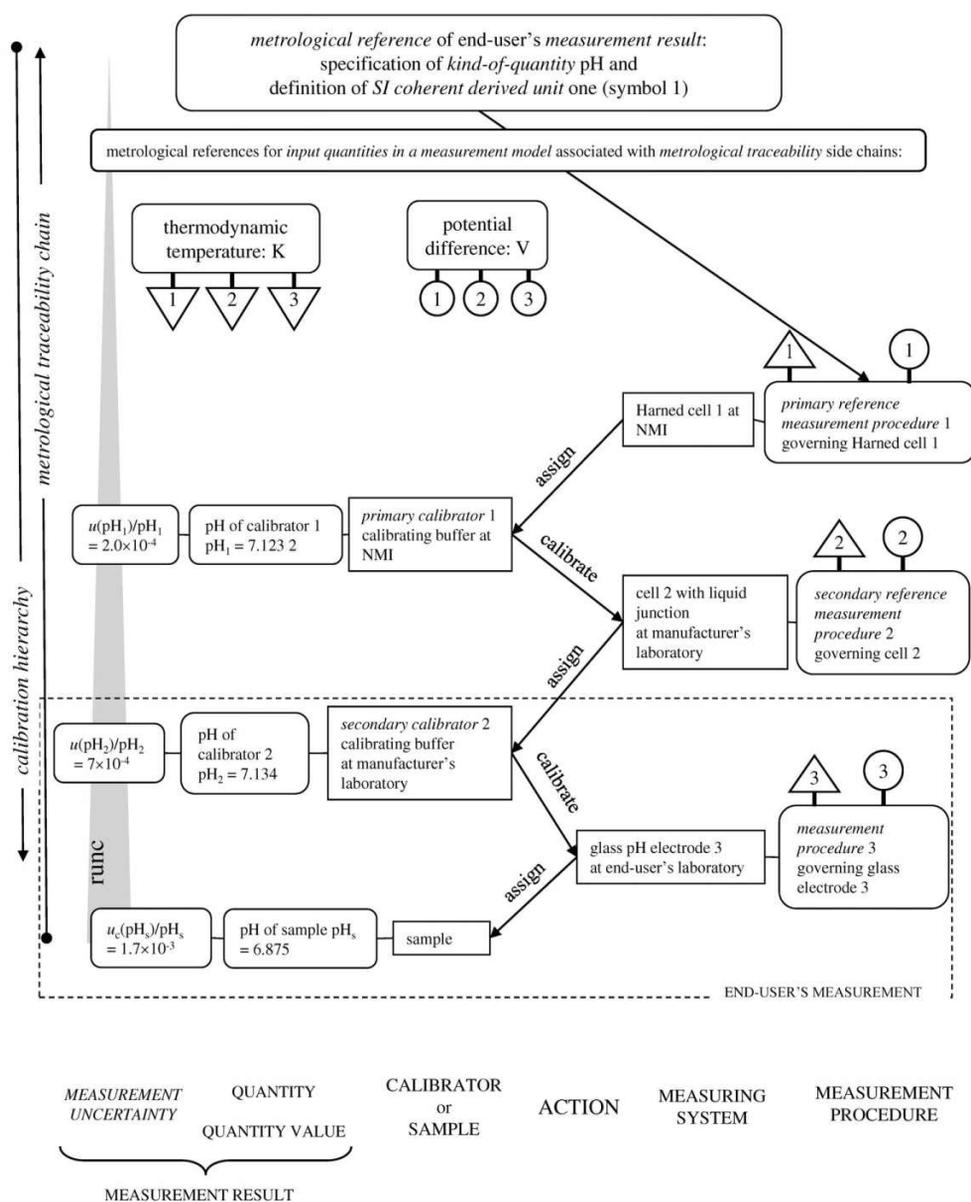
There is, therefore, an interesting, but unfortunate dilemma; if we wish to have *metrological traceability* to the SI without specification, rather than involving a conventional measurement procedure, then we must accept a *measurement uncertainty* that turns out to be about 2 ½ times greater, even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

9.2.4 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 reference measurement procedure* described above. Aqueous buffer solutions are usually made up from pH *RMs* dissolved in a prescribed mass of water. However, in general, the preparation of a buffer solution from compounds according to a recipe cannot 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 be termed primary buffer solutions, and can be considered directly metrologically traceable. It is usually not known 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 [51].

If it is necessary, for any reason, to prepare buffers similar in composition to the primary ones from solids of different kinds it is recommended to use cell 2 for comparison.

If the published pH value of some material has been determined by *ILCs* between NMIs on many samples of buffer solution made from different sources of solids, then the measurement uncertainty of that pH value may be deemed to include batch-to-batch variation. If not (i.e., 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*.



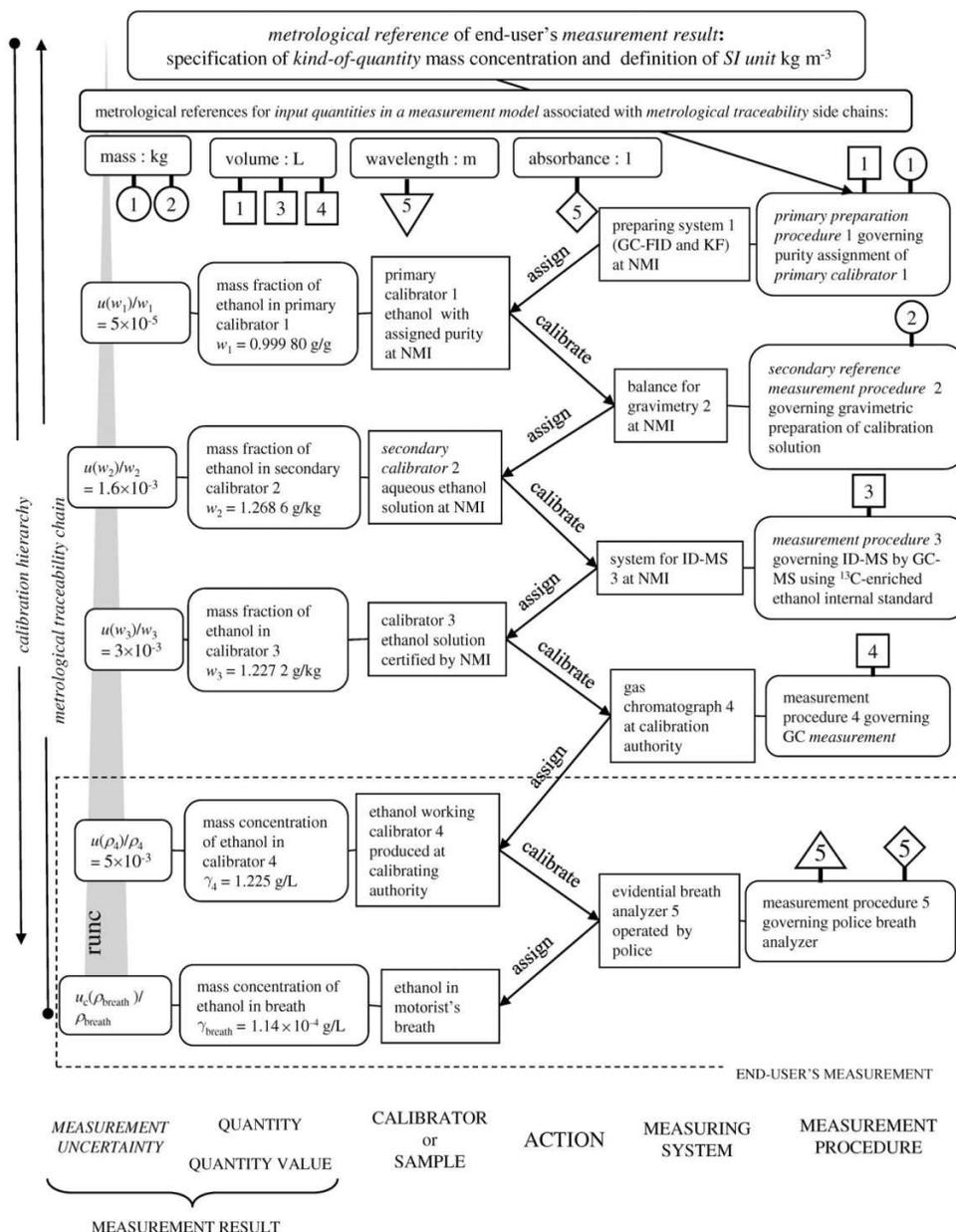
measurement model for end-user: $h(\text{pH}_{\text{sample}}, E^\circ, k') = 0$

Fig. 9.2.3-1 Metrological traceability chain of a pH measurement result using a primary reference measurement procedure (Harned cell). The input quantities in the measurement model, standard electrode potential E° and constant k' are obtained from calibration using the secondary calibrator 2. See Fig. 2.5-1 for an explanation of symbols and abbreviations. Note that cell 2 in Fig. 9.2.3-1 could be cell 2 described in the text above.

9.3 Mass concentration of ethanol in breath

Mass concentration of ethanol in breath is measured by infrared spectroscopy. Evidential breath analyzers are verified and calibrated using aqueous ethanol solutions or dry gas mixtures consisting of ethanol and air. In former times, the solutions have been made by gravimetric dilution of absolute

ethanol with water. The hygroscopic nature of ethanol causes an unknown deviation of the solution concentration from the supposed one. It is difficult to obtain a reasonable estimate of the *measurement bias* that this effect causes, and so to correct the deviation and estimate the *measurement uncertainty*. It is



$$\text{measurement model for end-user: } h(\gamma_{\text{breath}}, \gamma_4, \alpha_{l,\text{breath}}, \alpha_{l,4}) = 0$$

Fig. 9.3-1 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. Note that the legal limit in this example is a mass concentration of ethanol in the motorist's breath. See Fig. 2.5-1 for an explanation of symbols and abbreviations.

therefore necessary to measure the ethanol mass fraction in the calibration solution. This is done by several methods, including titration with dichromate, and by gas chromatography. To ensure international *metrological comparability of measurement results* and to become aware of possible measurement biases, international comparisons have been organized by the CCQM. For ethanol water mixtures, a first comparison (CCQM-K27.a) for forensic matrices was made in 2002, a study that included the Australian NMI. It showed that even at the highest level of *measurement capabilities* measurement biases can arise. As an example, it is shown how the *metrological traceability chain* of a breath alcohol measurement back to a national standard has been realized in Australia, where a metrologically traceable *quantity value* for an ethanol *measurement standard* is obtained by the *measurement* of the ethanol mass fraction of a solution by isotope dilution-mass spectrometer (ID-MS). This *calibrator* (calibrator 3 in Fig. 9.3-1) is provided to calibration authorities who prepare working calibrator ethanol solutions that are supplied to the police to calibrate field breath analyzer *measuring systems*.

9.4 Number-ratio of isotopes of an element in a material

Measurements of the *quantity* “number-ratio R of numbers of two atoms of different isotopes of element E of a sample” are of key importance in the determination of the relative atomic mass A_r (atomic weight) of an element E because, nowadays, all relative atomic masses are computed from such measured number-ratios.

9.4.1 The measurement model

For any given element E , *measurements* of the *measurand* $R_{i,j}$

$$R_{i,j} = N(^iE)/N(^jE) \quad (9.4.1-1)$$

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 that is separated in a magnetic field into as many composing ion currents as there are isotopes. The pairwise ratios of the resulting isotope ion currents $I(^iE^+)/I(^jE^+)$ are measured. These electric current ratio measurements must be calibrated in order to yield the corresponding isotope number-ratios.

That requires a *measurement model*, which is

$$h[R_{i,j}, K_{i,j}, I(^iE^+)/I(^jE^+)] = 0 \quad (9.4.1-2)$$

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

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

$$R_{i,j} = K_{i,j} \cdot I(^iE^+)/I(^jE^+) \quad (9.4.1-3)$$

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

$$K_{i,j} = (R_{i,j})_{\text{cal}} / [I(^iE^+)/I(^jE^+)]_{\text{cal}} \quad (9.4.1-4)$$

where $(R_{i,j})_{\text{cal}}$ and $[I(^iE^+)/I(^jE^+)]_{\text{cal}}$ are the number-ratios and their corresponding measured electric current ratios of the chosen isotopes in the element E in a *calibrator*. This is an isotope *measurement standard*. It is termed and marketed as a “certified isotope reference material”. Such a calibrator enables measurement of the calibration factor used in the measurement function described in eqs. 9.4.1-3 and 9.4.1-4.

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

9.4.2 The definition of the measurement unit

Examining the *measurement model*, the relevant *SI* measurement unit for number-ratio is the *coherent derived unit* one per one (symbol 1/1), which is equal to one (symbol 1). The embodiment of the measurement unit requires a *primary reference measurement procedure* or a primary preparation procedure.

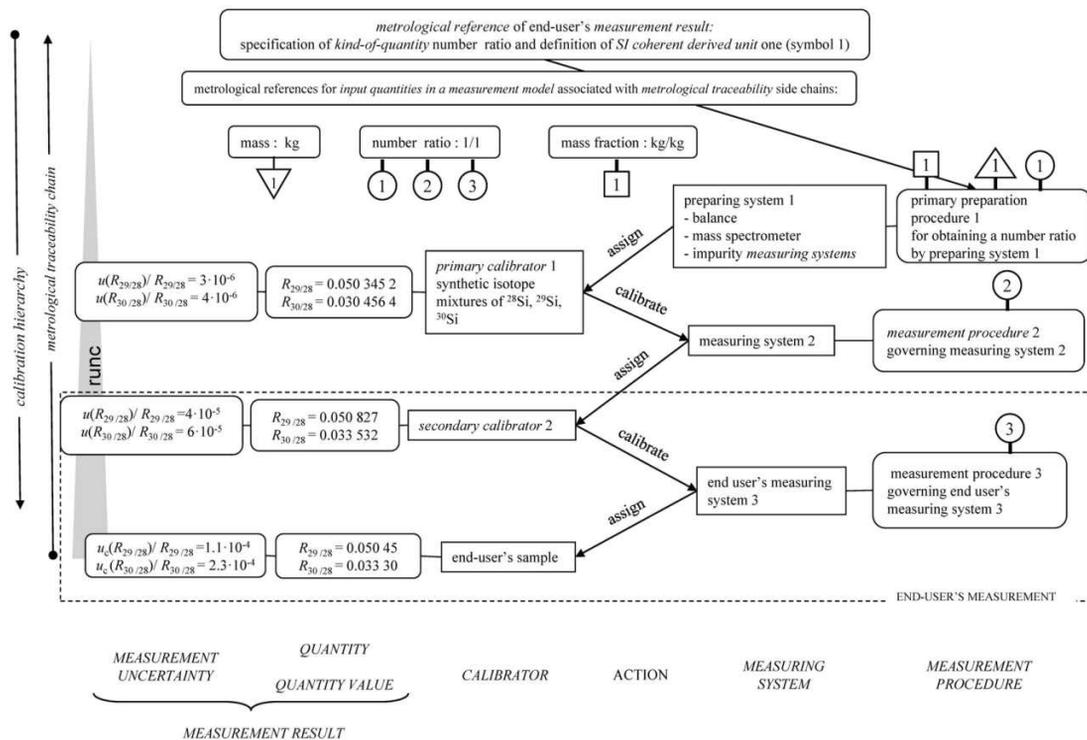
So far, there is no *measurement procedure* meeting the VIM definition of a primary reference measurement procedure, hence a primary preparation procedure is used to embody the measurement unit.

9.4.3 The primary preparation procedure governing the preparation system 1

A primary preparation procedure can be realized by using chemically purified and (highly) enriched or pure isotopes that are built into stoichiometrically well-known molecular compounds. These are weighed and mixed in a solution or in a gas to achieve homogeneity of the atoms of the isotopes on the atomic level. The mass ratios of the compounds can be converted to number-ratios for the isotopes concerned by measuring the relative atomic mass of the element E in the enriched isotopes ⁱE 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 relative combined standard measurement uncertainties of the relative atomic masses of the enriched isotopes approach the measurement uncertainties of the relative atomic mass values of 100 % pure isotopes, typically 10⁻⁷ or better.

9.4.4 The measuring system 2

The measuring system 2, governed by *measurement procedure 2*, can be used to assign calibrated *measured quantity values* of a number-ratio to a *secondary calibrator 2*. See Fig. 9.4.3-1.



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

Fig. 9.4.3-1 Metrological traceability chain of a measurement result for an isotope number-ratio. $R_{i,j}$ defined by eq. 9.4.1-3. See Fig. 2.5-1 for an explanation of symbols and abbreviations.

9.4.5 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 number-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* and the *quantity value* with associated *measurement uncertainty* assigned to the calibrator.

In many practical cases, the metrological traceability chain is longer than in the example of Fig. 9.4.3-1.

9.4.6 Quantities derived from isotope number-ratio

9.4.6.1 Isotope abundance $x(^i\text{E})$

In isotope *measurements*, much use is made of the *kind-of-quantity* “isotope abundance” $x(^i\text{E})$, which is the number fraction of atoms of one isotope ^iE in the total number of atoms of the element E in a given sample. Hence, the sum of abundances $\sum x(^i\text{E})$ is, by definition, always equal to 1 exactly, i.e.

$$\sum x(^i\text{E}) \equiv 1 \quad (9.4.6.1-1)$$

and

$$x(^i\text{E}) = N(^i\text{E}) / \sum N(^j\text{E}) \quad (9.4.6.1-2)$$

$$x(^i\text{E}) = [x(^i\text{E}) / x(^j\text{E})] / [\sum N(^i\text{E}) / N(^j\text{E})] \quad (9.4.6.1-3)$$

$$= R_{i;j}(^i\text{E}) / \sum R_{i;j}(^i\text{E}) \quad (9.4.6.1-4)$$

An isotope number-ratio measuring device enables measurement of ratios $R_{i;j}$ of an isotope abundance relative to a conveniently chosen abundance of another isotope (^jE), thus enabling calculation of any isotope abundance $x(^i\text{E})$.

Measurement uncertainty $u_c[x(^i\text{E})]$ is obtained by propagating the measurement uncertainties of $R_{i;j}$.

9.4.6.2 Relative atomic mass $A_r(\text{E})$

The relative atomic mass $A_r(\text{E})$ is calculated from $x(^i\text{E})$ by

$$A_r(\text{E}) = \sum x(^i\text{E}) \cdot A_r(^i\text{E}) \quad (9.4.6.2-1)$$

where $A_r(^i\text{E})$ is the atomic mass of that isotope.

Substitution of $x(^i\text{E})$ in eq. 9.4.6.2-1 according to eq. 9.4.6.1-4 leads to

$$A_r(\text{E}) = \sum R_{i;j}(^i\text{E}) \cdot A_r(^i\text{E}) / \sum R_{i;j}(^i\text{E}) \quad (9.4.6.2-2)$$

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

Note: A relative atomic mass $A_r(\text{E})$ of an element E is the ratio of the relative atomic mass value of that element to $1/12^{\text{th}}$ of the relative atomic mass value of the ^{12}C atom, the latter being set by convention to 12 g/mol exactly. This may change in the future with a redefinition of the SI base units.

9.5 Mass fraction of glyphosate in an agricultural chemical

There are different *measurement procedures* available for the *measurement* of the purity of a chemical substance. These include approaches based on the subtraction of the sum of mass fractions of impurities from 1, and those based on chromatography with appropriate detection.

Since its discovery, nuclear magnetic resonance spectroscopy (NMR) has been used as a nominal examination principle for the identification and elucidation of structures of an enormous variety of inor-

ganic, organic, and biological materials. Quantitative NMR (QNMR) has been reported as the basis of a *primary reference measurement procedure* for measurement of mass fractions of organic compounds such as agricultural chemicals [52]. 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”): $\text{HOOCCH}_2\text{NH}_2\text{CH}_2\text{PO}(\text{OH})_2$ uses a CRM of dimethyl sulfone ($\text{CH}_3\text{SO}_2\text{CH}_3$) as a ^1H calibrator and a CRM of sodium phosphate (Na_3PO_4) as a ^{31}P calibrator. The successful application of these *measurement methods* relies on the presence of suitable peaks in the NMR spectrum that are uncontaminated with any impurity peaks. Very high field NMR allows discrimination between closely related compounds.

9.5.1 Measurement method

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

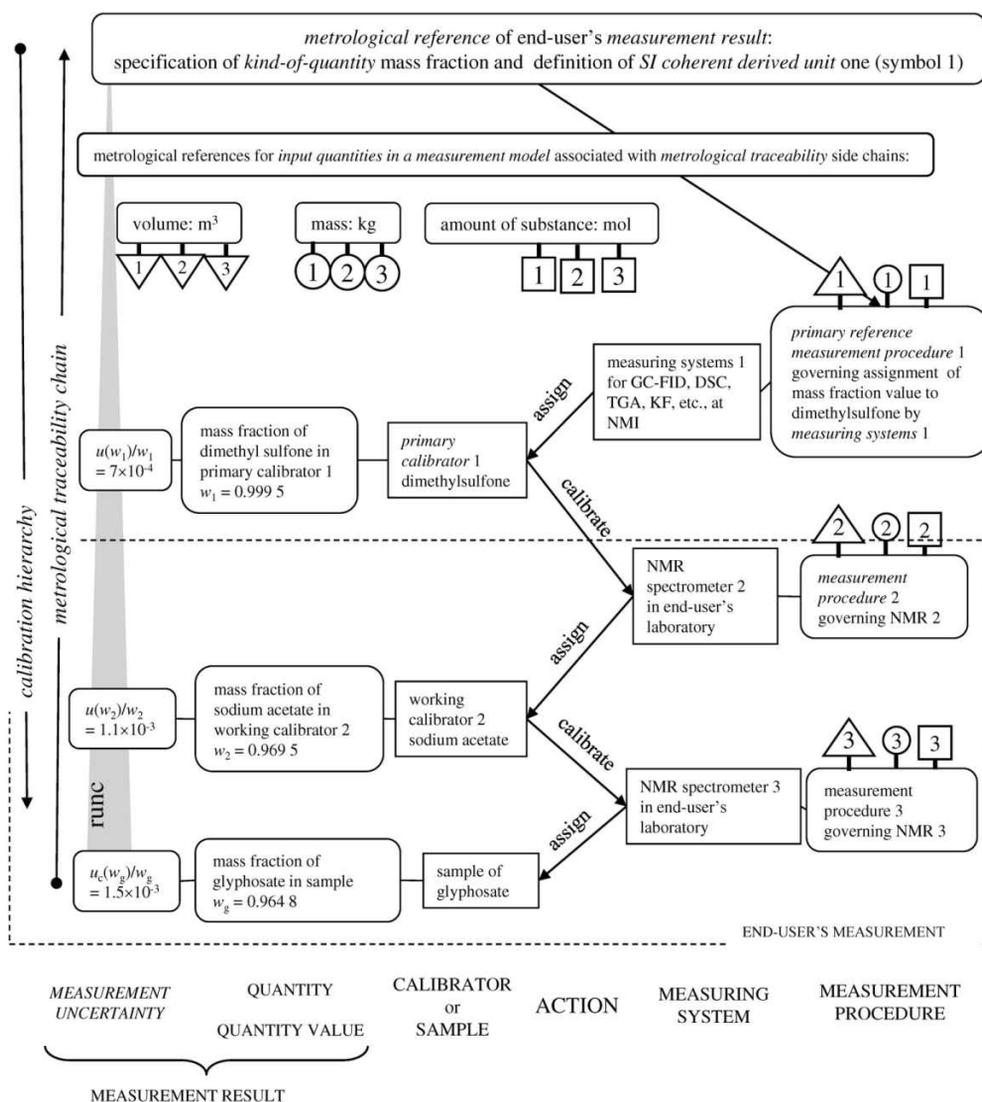
- Weigh a mass of sample into an NMR tube by difference (about 5 mg glyphosate).
- Weigh a mass of the *calibrator* into the NMR tube by difference to give approximately the same amount of substance of the target isotope as of the component.
- Add deuteriated solvent to an appropriate level in the NMR tube.
- Introduce the NMR tube into the instrument. Allow to equilibrate at the set temperature of the probe and measure with instrumental settings for full relaxation (and suppression of the nuclear Overhauser effect as required).
- Record the free induction decay (FID) spectrum.
- Process the FID with window function as required, phase the spectrum manually, and establish the baseline.
- Integrate the peaks to obtain the ratio of the integrated peak for the sample to the integrated peak for the calibrator ($I_{\text{sample}}/I_{\text{cal}}$).

9.5.2 Measurement function

The measurement function for the mass fraction of a sample based on the observation of the NMR signal for ^1H is

$$w_{\text{sample}} = \frac{I_{\text{sample}}}{I_{\text{cal}}} \frac{m_{\text{cal}}}{m_{\text{sample}}} \frac{N_{\text{cal}}}{N_{\text{sample}}} \frac{M_{\text{sample}}}{M_{\text{cal}}} w_{\text{cal}} \quad (9.5.2-1)$$

where “sample” and “cal” refer to the sample being measured and working calibrator respectively; I is an integrated peak area of the NMR spectrometer for a given chemical shift, m is the mass, N is number of protons in one molecule, M is molar mass, and w is mass fraction. The mass fraction of the *primary calibrator* is measured at an NMI by a combination of measurement principles, including GC-FID, NMR, thermogravimetry, differential scanning calorimetry, Karl Fischer 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* [53]. For QNMR *measurements* in which the isotope of interest is a proton, the mass fraction of a *working measurement standard* (working calibrator) of sodium acetate can be measured by QNMR calibrated by the dimethylsulfone primary calibrator. The *metrological traceability chain* is shown in Fig. 9.5.2-1.



measurement model for end-user

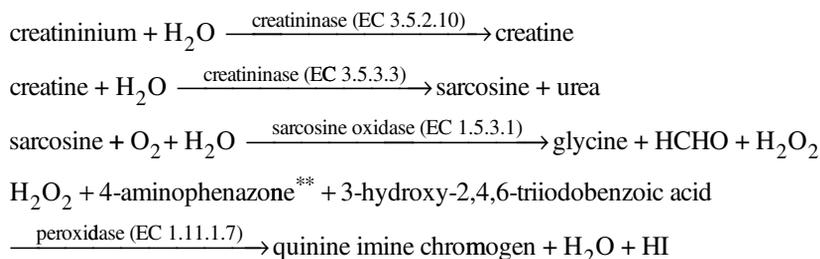
$$h(w_{\text{sample, gly}}, w_{\text{cal, 2}}, m_{\text{cal, 2}}, N_{\text{cal, 2}}, I_{\text{cal, 2}}, M_{\text{cal, 2}}, I_{\text{sample, gly}}, m_{\text{sample, gly}}, N_{\text{sample, gly}}, M_{\text{sample, gly}}) = 0$$

Fig. 9.5.2-1 Metrological traceability chain of a measurement result of the mass fraction, w , of a sample of the agricultural chemical glyphosate. I = peak area, m = mass, M = molar mass, N = number of protons contributing to the NMR signal. GC-FID = gas chromatography with flame ionization detector, DSC = differential scanning calorimetry, TGA = thermogravimetric analysis, KF = Karl Fischer titration procedure. See Fig. 2.5-1 for an explanation of general symbols and abbreviations.

9.6 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 [54,55]. The reactions involved are



where the color intensity change of the chromogen is directly proportional to the creatininium concentration and is recorded at an end point by absorbance at 552 nm corrected for blank at 659 nm [56].

The *measurement* may be performed on a Roche COBAS INTEGRA 800 and the *metrological traceability* to an *SI unit* is claimed [57,58]. The *calibration hierarchy* shown in Fig. 9.6-1 should reflect this information.

9.6.1 Primary measurement

A *primary reference measurement procedure* involving an 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 have a good *measurement trueness*.

9.6.2 Secondary measurement

The *primary calibrator* is used to calibrate the manufacturer’s *measuring system* operating according to his standing *secondary reference measurement procedure*. Both equipment, i.e., COBAS INTEGRA 800 with reagents, and secondary reference 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.

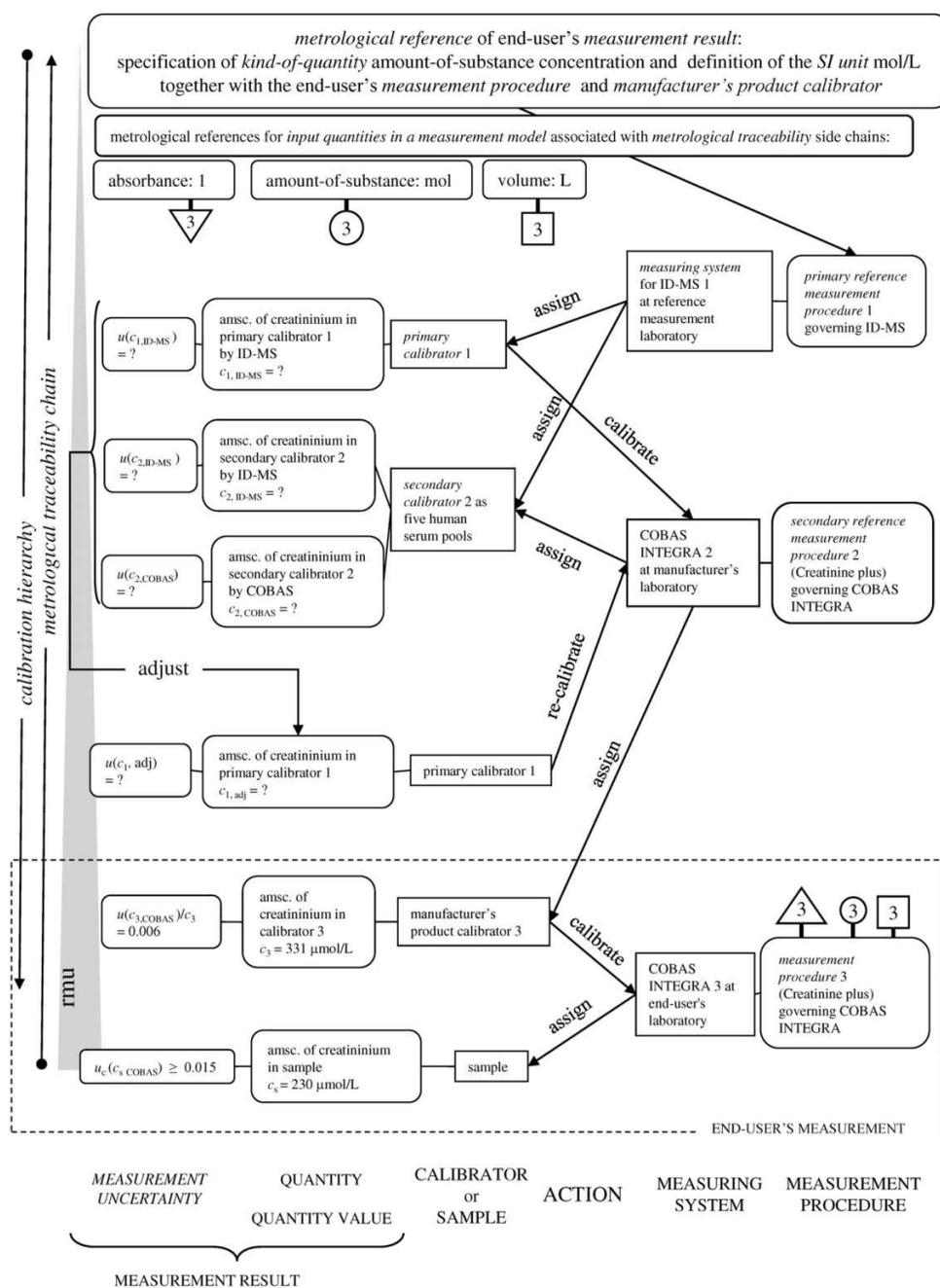
The manufacturer’s standing secondary reference measurement procedure and COBAS INTEGRA calibrated with the primary calibrator are used to assign a second set of *quantity value* and *measurement uncertainty* to each of the five serum pools.

9.6.3 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 equation ($y = bx + a$). 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 an appropriate 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*.

^{*}2-imino-1-methylimidazolidin-4-one

^{**}4-amino-1,5-dimethyl-2-phenyl-1,2-dihydro-3H-pyrazol-3-one



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

where I symbolizes an indication.

Absorbance, amount-of-substance and volume have their respective *measurement models* (not shown).

Fig. 9.6-1: *Metrological traceability chain 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. See Fig. 2.5-1 for an explanation of general symbols and abbreviations.

Only data concerning the manufacturer's product calibrator 3 are available to the end-user.

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 reference 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.

9.6.4 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 reference 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.

9.6.5 End-user's measurement

Using the *manufacturer's product calibrator* 3 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 adequate for the given purpose because the measuring system and measurement 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 *measurand*,
- measurement uncertainty associated with an 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-examination and examination 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 of measurement* (which subsumes some other sources).

The pre-examination 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 $\mu\text{mol/L}$:

- $u = 2.12 \mu\text{mol/L}$ [58]
- CV within run 0.7 % [56] (repeatability)
- CV between run 0.9 % [56] (reproducibility, presumably meaning *intermediate measurement precision*)

With an end-user's quantity value of, say, 230 $\mu\text{mol/L}$, 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 condition of measurement:

$$\begin{aligned} & \sqrt{2.12^2 + (0.007 \times 230)^2 + (0.009 \times 230)^2} \mu\text{mol/L} \\ & = \sqrt{4.49 + 2.59 + 4.28} \mu\text{mol/L} = 3.37 \mu\text{mol/L} \\ & \text{or CV (intermediate)} = 3.37 \mu\text{mol/L} \times 100 / (230 \mu\text{mol/L}) = 1.5 \% \end{aligned}$$

The calculation of measurement uncertainty assumes no correlation between the *quantities* contributing to the calculation. The quantity values were obtained in the manufacturer's laboratory and the end-user should expect somewhat higher quantity values for measurement uncertainty and increasing relatively with lower *measured quantity value*.

9.6.6 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 measurement unit* $\mu\text{mol/L}$. As the *calibration hierarchy* includes an empirical "holistic" adjustment element, it is necessary to specify the *measurement procedure* and *manufacturer's product calibrator* in the metrological reference.

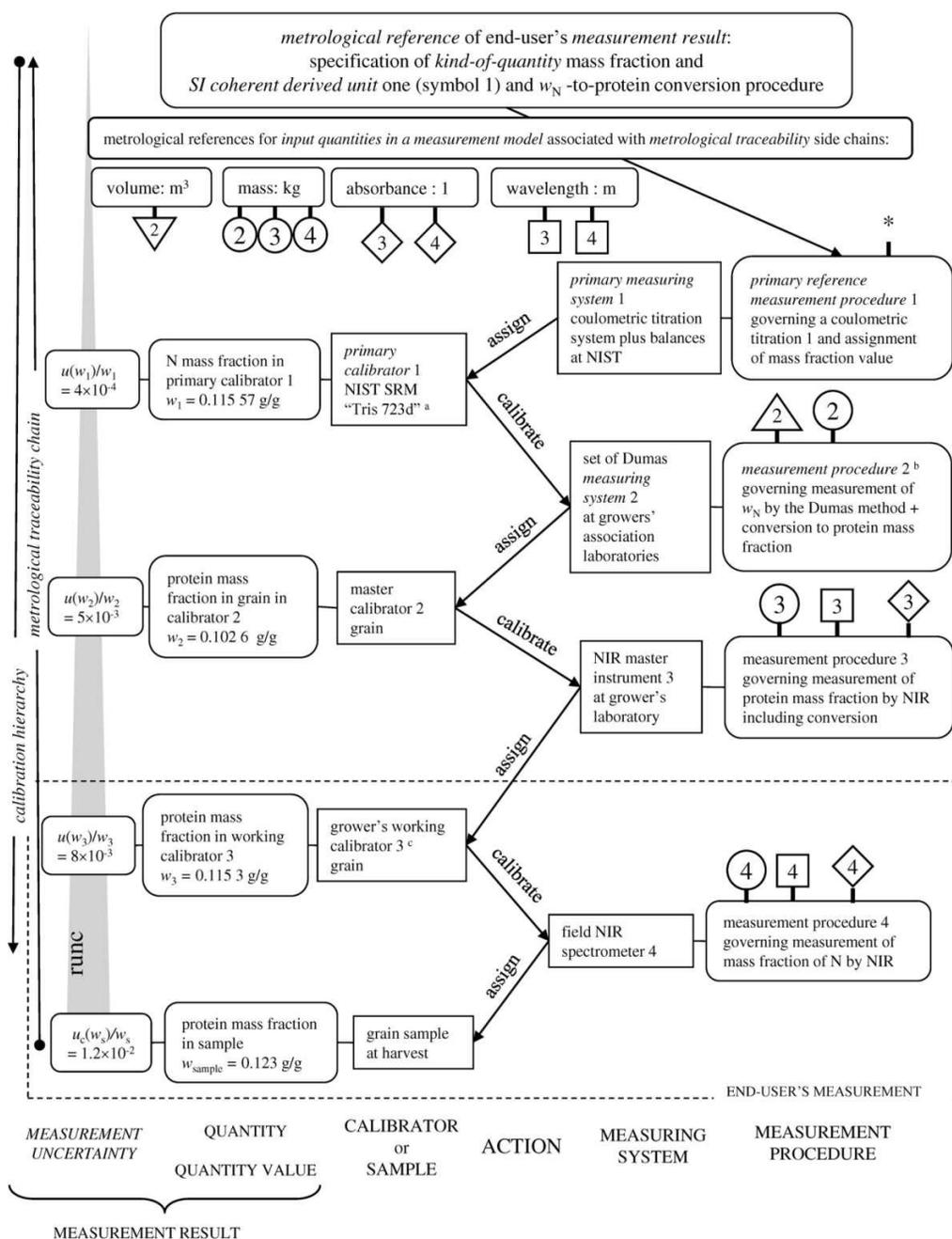
It should be added that various types of adjustment procedure such as the above are not infrequent in commercial *measuring systems*. It would be an aid to the end-user in evaluating their appropriateness if the data were available on request. In this respect, regulatory rules could help.

9.7 Mass fraction of protein in grain

The price of a harvested grain, such as wheat, depends on its protein content. The mass fraction of nitrogen is measured in the field by near infrared (NIR) spectrometry and multiplication by a conventional factor gives a *measurement result* for the operationally defined *measurand* "mass fraction of protein in the sample of grain using the conventional factor to convert mass fraction of nitrogen to mass fraction of protein". The absorbances at several infrared wavelengths provide highly correlated indications, and the calibration function is obtained by a multivariate method such as partial least squares regression. *Metrological comparability of 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 measurement unit* one for the *kind-of-quantity* mass fraction. The *primary calibrator* selected is a NIST SRM 723d (Tris = 2-amino-2-(hydroxymethyl)propane-1,3-diol) 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 a trademark for a *CRM* issued by NIST) has been established by a *primary reference measurement procedure* giving *metrological traceability* to the SI unit.

9.7.1 Description of the calibration hierarchy

Measurement results are metrologically traceable to the mass fraction of nitrogen of a NIST standard RM (Tris). The mass fraction of titratable acid (purity) of the material has been established by coulometric titration, and the material is claimed to have an assigned *quantity value* that is metrologically traceable to the *SI measurement unit* one for mass fraction. This *CRM* is used to calibrate *measuring systems* for the *measurement* of nitrogen mass fraction by the Dumas method, which involves combustion of the sample followed by gas chromatographic analysis of the nitrogen oxides that are produced. The protein mass fraction 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,



measurement model for end-user: $h(w_{\text{sample}}, w_{\text{cal3}}, \alpha_{\lambda, \text{sample}}, \alpha_{\lambda, \text{cal3}}) = 0$

Absorbance (α) and wavelength (λ) have their respective measurement models, 3 and 4.

*See Fig. 9.1.5-1 for side chains associated with a coulometric titration and assignment of mass fraction.

^aTris = 2-amino-2-hydroxymethyl-1,3-propanediol.

^bMeasuring systems are calibrated and then certify grain samples in an interlaboratory comparison.

^cThe master instruments each measure grain samples to act as grower's working calibrator for field measurements.

Fig. 9.7.2-1 Metrological traceability chain of a measurement result of mass fraction of protein in harvested grain. Measurement uncertainties are given as relative standard measurement uncertainties.

using the calibrated Dumas systems. The continuity of the *metrological traceability chain* rests on the assumption of *commutability of the reference material*, i.e., Tris. The measurement result from each laboratory, and hence the *quantity 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 an NIR instrument in each of their laboratories, the so-called master instruments. The *calibration* is based on a large number of samples and is regularly updated. 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 mass fraction of protein of the harvested grain.

9.7.2 Metrological traceability chain

A schematic of the *metrological traceability chain* is shown in Fig. 9.7.2-1.

CONCLUSIONS

The need of *metrological comparability of measurement results* is met by establishing their *metrological traceability* to a common *metrological reference*. Necessary concepts with definitions and associated terms for their use in practice have been identified to aid common understanding. *Metrological traceability chains of measurement results* for various *kinds-of-quantity* in chemistry are given as examples utilizing the nomenclature developed. They show a surprising possibility of a common approach and structure for many measurement results in chemistry and likely in other fields.

ANNEX I: INITIALISMS, ACRONYMS, AND ABBREVIATIONS

AAS	atomic absorption spectrometry
AOACI	Association of Official Analytical Chemists International
BIPM	Bureau International des Poids et Mesures International Bureau of Weights and Measures, <www.bipm.org>
CASCO	Committee on Conformity Assessment (of ISO)
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 on 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 web site 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
DFM	Danish Fundamental Metrology
DIN	Deutsches Institut für Normung
DSC	differential scanning calorimetry
EA	European co-operation for Accreditation
EAL	European co-operation for Accreditation of Laboratories (now called EA)

EC	European Commission
EC	Enzyme Commission (historical) of International Union of Biochemistry and Molecular Biology and IUPAC
EN	European norm
EQA	external quality assurance
EQALM	European Committee for External Quality Assurance Programs in Laboratory Medicine
EQAS	external quality assurance scheme
EU	European Union
EURAMET	European Association of National Metrology Institutes
FID	free induction decay
GC	gas chromatography
GLP	good laboratory practice
GUM	<i>Guide to the Expression of Uncertainty in Measurement</i> [2] <i>Guide pour l'Expression de l'Incertitude de Mesure</i>
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 Program (at IRMM)
INRIM	National Institute of Metrological Research (Italy) L'Istituto Nazionale di Ricerca Metrologica
IRMM	Institute for Reference Materials and Measurements (of the Joint Research Center 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 titration procedure (measurement of mass fraction of water in a material)
METAS	Bundesanstalt für Metrologie und Akkreditierung Schweiz
MLA	multilateral recognition arrangement (under ILAC)
MRA	mutual recognition arrangement (under CIPM)
MU	measurement uncertainty
NARL	National Analytical Reference Laboratory (NMI, Australia)
NATA	National Association of Testing Authorities (Australia)
NIR	near infrared
NIST	National Institute for Standards and Technology (USA)
NMI	national metrology institute, national measurement institute
NMIA	National Measurement Institute of Australia
NMR	nuclear magnetic resonance
NPU	Nomenclature for Properties and Units, indicating terms from the IFCC-IUPAC Subcommittee on NPU
OIML	Organisation Internationale de Métrologie Légale

	International Organization of Legal Metrology
PAC	<i>Pure and Applied Chemistry</i>
PCR	polymerase chain reaction
PMS	primary measurement standard
PRMP	primary reference measurement procedure
PTB	Physikalisch-Technische Bundesanstalt (Germany)
PTS	proficiency testing scheme
QNMR	quantitative nuclear magnetic resonance
QUAM	quantifying uncertainty in analytical measurement [33]
REIMEP	Regular European Interlaboratory Measurement Evaluation Program (at IRMM) (for nuclear measurements)
REMCO	Council Committee on Reference Materials (under ISO)
RM	reference material
RMP	reference measurement procedure
runc	relative measurement uncertainty
RSC	Royal Society of Chemistry
SI	Le Système International d'Unités The International System of Units
SRM	standard reference material, trademark for NIST certified reference material
TC	technical committee
TGA	thermogravimetric analysis
TMU	target measurement uncertainty
unc	measurement uncertainty
UNIDO	United Nations Industrial Development Organization
USGS	United States Geological Survey
UTC	coordinated universal time
VIM	JCGM. <i>International Vocabulary of Metrology (VIM)</i> , JCGM 200:2008 (in the name of BIPM, IEC, IFCC, ILAC, ISO, IUPAC, IUPAP, OIML), BIPM, Sevres [1]
WHO	World Health Organization
WMO	World Meteorological Organization

ANNEX II: ALPHABETICAL INDEX OF TERMS FOR CONCEPTS DEFINED IN TEXT OR VIM

Term	Number	VIM
base unit	–	1.10
calibration	2.2-1	2.39
calibration hierarchy	2.5-1	2.40
calibrator	2.4-1	5.12
certified reference material	3.1-2	5.14
combined standard measurement uncertainty	–	2.31
combined standard uncertainty	–	2.31
commutability of a reference material	2.4-2	5.15
conventional reference scale	–	1.29
correction	2.10-1	2.53
coverage factor	–	2.38
coverage interval	–	2.36
coverage probability	–	2.37
CRM	3.1-2	5.14
definitional uncertainty	2.1-9	2.27
derived quantity	–	1.5
derived unit	–	1.11
equivalence of measurement results	5-4	–
etalon	2.3-1	5.1
expanded measurement uncertainty	–	2.35
indication	–	4.1
influence quantity	–	2.52
input quantity in a measurement model	–	2.50
instrumental bias	–	4.20
interlaboratory comparison	7.1-1	–
intermediate measurement precision	–	2.23
intermediate precision condition of measurement	–	2.22
international conventional calibrator	2.4-4	–
International System of Units	–	1.16
kind-of-quantity (VIM: kind of quantity)	–	1.2
manufacturer's product calibrator	2.4-7	–
manufacturer's working calibrator	2.4-6	–
measurand	2.1-4	2.3

(continues on next page)

Term	Number	VIM
measured quantity value	2.1-6	2.10
measured value	2.1-6	2.10
measurement	2.1-1	2.1
measurement accuracy	–	2.13
measurement bias	–	2.18
measurement capability	7.3-1	–
measurement function	2.1-8	2.49
measurement method	2.1-11	2.5
measurement model	2.1-7	2.48
measurement precision	–	2.15
measurement principle	2.1-10	2.4
measurement procedure	2.1-12	2.6
measurement reproducibility	–	2.25
measurement result	2.1-3	2.9
measurement standard	2.3-1	5.1
measurement trueness	–	2.14
measurement uncertainty	2.7-1	2.26
measurement unit	–	1.9
measuring system	2.1-13	3.2
method of measurement	2.1-11	2.5
metrological comparability	1.2-1	2.46
metrological comparability of measurement results	1.2-1	2.46
metrological compatibility of measurement results	5-3	2.47
metrological equivalence of measurement results	5-4	–
metrological reference	2.6-1	–
metrological traceability	1.1-1	2.41
metrological traceability chain	2.5-2	2.42
model	2.1-7	2.48
model of measurement	2.1-7	2.48
nominal property	–	1.30
ordinal quantity	–	1.26
ordinal quantity-value scale	–	1.28
output quantity in a measurement model	–	2.51
primary calibrator	2.4-3	–
primary measurement standard	2.3-2	5.4
primary reference measurement procedure	3.3-2	2.8
primary reference procedure	3.3-2	2.8
primary standard	2.3-2	5.4
principle of measurement	2.1-10	2.4
quantity	2.1-2	1.1
quantity equation	–	1.22

(continues on next page)

Term	Number	VIM
quantity value	2.1-5	1.19
quantity-value scale	–	1.27
reference material	3.1-1	5.13
reference measurement procedure	3.3-1	2.7
reference measurement standard	2.3-4	5.6
reference quantity value	–	5.18
reference standard	2.3-4	5.6
relative standard measurement uncertainty	–	2.32
repeatability condition of measurement	–	2.20
result of measurement	2.1-3	2.9
RM	3.1-1	5.13
secondary calibrator	–	
secondary measurement standard	2.3-3	5.5
secondary reference measurement procedure	3.3-3	–
secondary reference procedure	3.3-3	–
secondary standard	2.3-3	5.5
SI	–	1.16
standard measurement uncertainty	–	2.30
target measurement uncertainty	2.8-1	2.34
target uncertainty	2.8-1	2.34
traceability	1.1-1	2.41
traceability chain	2.5-2	2.42
type A evaluation of measurement uncertainty	–	2.28
type B evaluation of measurement uncertainty	–	2.29
uncertainty	2.7-1	2.26
uncertainty budget	–	2.33
uncertainty of measurement	2.7-1	2.26
unit	–	1.9
unit of measurement	–	1.9
validation	5-2	2.45
value	2.1-5	1.19
value of a quantity	2.1-5	1.19
value of a measured quantity	2.1-6	2.10
verification	5-1	2.44
working measurement standard	2.3-5	5.7
working standard	2.3-5	5.7

SUPPLEMENTARY INFORMATION

Concept diagrams are available online (doi:10.1351/PAC-REP-07-09-39).

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ACKNOWLEDGMENTS

This document was submitted in the drafting stage to two reviews by the AOAC-Int (M. Walsh), BIPM (A. Wallard), CCQM (R. Kaarls, R. Wielgosz), CITAC (I. Kuselman), DFM (P. Jakobsen), EURACHEM (S. Ellison), EURAMET-MetChem (P. Charlet), IAEA (M. Gröning), IFCC (F. Pontet), ILAC (A. Squirrel, H. Imai), IRMM (H. Emons), ISO-CASCO (S. MacCurtain), ISO-REMCO (A. van der Veen, H. Emons), ISO-TC 12 (A. Thor), OIML (J. F. Mangana), PTB (P. Spitzer and WG on pH), RSC (D. Barden, C. Burgess), UNIDO (O. Loesener), USGS (T. Coplen), WHO (A. Padilla), and WMO (L. A. Barrie), IUPAC Divisions.

Personal comments were requested and received from M. Kuehne (BIPM), L. Mackay (NMIA), F. Pavese (INRIM), and W. Woeger (retired from PTB).

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