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CITAC
Cooperation on International Traceability in Analytical Chemistry

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Guide to Quality in Analytical Chemistry

An Aid to Accreditation

Fourth Edition 2026

Eurachem
A focus for analytical chemistry in Europe

CITAC

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Guide to Quality in Analytical Chemistry: An Aid to Accreditation

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Foreword

This edition is a revision of the 3rd edition of the CITAC/Eurachem Guide published in 2016. The 2016 edition was developed to fit the requirements of the 2005 version of ISO/IEC 17025.

This revision reflects changes that were introduced with the publication of the 2017 version of ISO/IEC 17025.

The Guide focuses on the requirements of ISO/IEC 17025, however the content should also be of use to organisations seeking accreditation or certification against the requirements of standards such as ISO 15189 or ISO 9001 respectively, or compliance with the Principles of Good Laboratory Practice (GLP). Similarly, although the Guide has the title 'Guide to Quality in Analytical Chemistry', it is anticipated that it will also be of benefit to disciplines other than chemistry. For those working in microbiology, it should be noted that Eurachem has published a Guide specifically for microbiological laboratories.†

The Guide will also provide useful information both for laboratories that wish to establish a quality management system but are not seeking formal recognition, and for those involved in education and training.

The bibliography section in the 2016 edition of the Guide contained only literature cited in the text. This is also the case in this edition. Additional documents related to accreditation and quality assurance can be found in a 'reading list' under the menu item 'Publications' on the Eurachem website at www.eurachem.org.

† B Magnusson and K C Tsimillis (eds.) Accreditation for Microbiological Laboratories (3rd ed. 2023). ISBN 978-91-519-6581-9. Available from www.eurachem.org.

Abbreviations and symbols

The following abbreviations and symbols appear in this Guide.

AOAC International	a globally recognised standards developing organisation
BIPM	International Bureau of Weights and Measures
CASCO	Committee on Conformity Assessment
CITAC	Cooperation on International Traceability in Analytical Chemistry
CLSI	Clinical and Laboratory Standards Institute
CMC	calibration and measurement capability
CRM	certified reference material
EA	European cooperation for Accreditation
EC	European Commission
EDQM	European Directorate for the Quality of Medicines & HealthCare
EQA	external quality assessment
EU	European Union
GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice
HPLC	high performance liquid chromatography
IEC	International Electrotechnical Commission
ILAC	International Laboratory Accreditation Cooperation
ILC	interlaboratory comparison
IQC	internal quality control
ISO	International Organization for Standardization
IUPAC	International Union of Pure and Applied Chemistry
JCGM	Joint Committee for Guides in Metrology
LIMS	laboratory information management system
LOD	limit of detection
LOQ	limit of quantification
MLA	Multilateral Agreement
MRA	Mutual Recognition Arrangement
NAB	National Accreditation Body
OIML	International Organization on Legal Metrology
PCR	polymerase chain reaction
PVC	poly vinyl chloride
QA	quality assurance
QC	quality control
QMS	quality management system
PT	proficiency testing
RM	reference material
SI	international system of units

SOP	standard operating procedure
UV	ultraviolet
VCM	vinyl chloride monomer
VIM	International vocabulary of metrology – Basic and general concepts and associated terms
WHO	World Health Organization

k	coverage factor (used in the calculation of expanded measurement uncertainty)
s	sample standard deviation
u	standard measurement uncertainty
U	expanded measurement uncertainty

Contents

1 Scope and intended audience

1.1 The aim of this Guide is to provide laboratories with guidance on best practice for the analytical operations they carry out. The guidance covers both qualitative and quantitative analysis carried out on a routine or non-routine basis. A separate Guide covers research and development work [1].

1.2 The guidance is intended to help those implementing a quality management system (QMS) in a laboratory, in particular those seeking accreditation against the requirements of ISO/IEC 17025 [2]. For those working towards accreditation it will help explain the meaning of the standard – especially in relation to the new risk-oriented approach in the 2017 version. The specific and detailed guidance contained in the Guide will focus on the requirements in ISO/IEC 17025. However, the guidance will also be useful to organisations seeking accreditation against the requirements of standards such as ISO 15189 [3] or ISO 15195 [4], certification against the requirements of ISO 9001 [5], or compliance with the Principles of Good Laboratory Practice (GLP) [6] or Good Manufacturing Practice (GMP) [7]. It should also be of use to those involved in the assessment of analytical laboratories against those requirements. Finally, the Guide should also be of value to those involved in education and training.

1.3 This Guide concentrates on the technical aspects of the quality management of a laboratory, with particular emphasis on those areas where interpretation is required for chemical testing or related measurements. The aspects of quality management not covered in detail by this Guide (for example contract review, records, reports and complaints) are fully addressed in other documents (e.g. references 5, 8).

1.4 It must be stressed – especially in the light of the more risk-oriented approach in the 2017 version – that the interpretation of the clauses in ISO/IEC 17025, and therefore the compliance with the standard, will (and should) vary from laboratory to laboratory to meet individual needs. Hence, not all recommendations in this Guide will be equally relevant for all laboratories.

2 Terminology

2.1 The Guide follows, where possible, the terminology defined in ISO/IEC 17000 [9], ISO 9000 [10] and the 3rd edition of the VIM [11]. This has been supplemented, where necessary, with terminology used in ISO/IEC 17025:2017 [2]. This version of the standard introduces a number of new definitions and explanations of terms, for example a definition of the term 'laboratory' (see Section 8).

2.2 However, in some cases, it may be difficult to decide which term to use when several similar terms are in use. For clarity, it is considered important to use a term consistently throughout the Guide. One example is the term used to describe the document that gives a detailed description of the method used in a laboratory. For quantitative analysis VIM refers to the measurement procedure, in ISO/IEC 17025 this is referred to as the method, in ISO 15189 [3] it is the examination procedure and many laboratories refer to their standard operating procedure (SOP). In line with other recent Eurachem Guides it has been decided to adhere to ISO/IEC 17025 and use the generic term 'method'. The term 'concentration' is used on its own (i.e. unqualified) when a generality is required. In the Guide this term should be taken to represent a family of terms which includes mass fraction, mass concentration, amount of substance concentration, etc.

2.3 The terms in VIM related to analytical measurement are further explained in the Eurachem Guide 'Terminology in analytical measurement' [12].

3 Terms and definitions

3.1 There are a number of important terms used in quality management and conformity assessment whose meaning may vary according to the context in which they are used. It is important for the laboratory to understand the distinction between the various terms – and to have a clear understanding of the impact of how the terms are interpreted in their discussions with their accreditation body.

3.2 A selection of terms likely to be encountered in the laboratory are presented here, but it is also recommended to refer to the Eurachem Guide on terminology [12] for further understanding of the terms in the context of analytical laboratories.

3.3 ***QUALITY:*** Degree to which a set of inherent characteristics of an object fulfils requirements (ISO 9000 [10])

3.4 ***MANAGEMENT SYSTEM:*** Set of interrelated or interacting elements of an organisation to establish policy and objectives and processes to achieve those objectives (ISO 9000 [10])

3.4.1 The notes to the definition mention that a management system can address a single discipline or several disciplines, e.g. quality management. The definition is further expanded by specifying that the management system elements establish the organisation's structure, roles and responsibilities, planning, operation, policies, practices, rules, beliefs, objectives and processes to achieve those objectives.

3.4.2 In ISO/IEC 17025 [2] (clause 8.1.1) the definition is specified in relation to the management of a laboratory: "The laboratory shall establish, document, implement and maintain a management system that is capable of supporting and demonstrating the consistent achievement of the requirements of this document and assuring the quality of the laboratory results"

3.5 ***QUALITY MANAGEMENT SYSTEM:*** Part of a management system with regard to quality (ISO 9000 [10])

3.5.1 In practice, the terms 'management system' and 'quality management system' are often used interchangeably. In both ISO/IEC 17025 [2] and ISO 15189 [3] 'management system' is used. However the latter notes that 'quality management system' was used in previous versions of the standard and is considered synonymous with 'management system'.

3.6 ***ACCREDITATION:*** Third-party attestation related to a conformity assessment body, conveying formal demonstration of its competence, impartiality and consistent operation in performing specific conformity assessment activities (ISO/IEC 17000 [9])

3.6.1 In the context of a laboratory making measurements, accreditation is a formal recognition that a laboratory is competent to carry out specific calibrations or tests. The mechanism under which accreditation is granted is described in Section 6. The core requirements are documented in ISO/IEC 17025 [2] and are the subject of further interpretation and explanation in this Guide.

3.6.2 Accreditation is also used in the context of ISO 9000-based activities [10] to describe the process whereby an accreditation body formally confirms a certification body as competent to certify organisations as being compliant with the ISO 9000 series of standards.

3.7 ***CERTIFICATION:*** Third-party attestation related to an object of conformity assessment, with the exception of accreditation (ISO/IEC 17000 [9])

3.7.1 Certification is applicable to all objects of conformity assessment except for conformity assessment bodies themselves, to which accreditation is applicable.

3.7.2 Certification primarily differs from accreditation in that technical competence is not specifically addressed. (See Section 5 for further elaboration of this.)

3.8 ***QUALITY ASSURANCE (QA):*** Part of quality management focused on providing confidence that quality requirements will be fulfilled (ISO 9000 [10])

3.8.1 The main quality requirements for a laboratory are specified in generic terms in ISO/IEC 17025 [2] (see Section 6).

3.9 ***QUALITY CONTROL (QC):*** Part of quality management focused on fulfilling quality requirements (ISO 9000 [10])

3.9.1 In the analytical laboratory, QC is mostly seen in the context of *Internal Quality Control (IQC)* where QC procedures relate to ensuring the quality of results obtained for specific samples or

sets of samples (see Section 28). IQC is an important quality management activity in the laboratory in combination with other external measures such as participation in Proficiency Testing (PT)/Interlaboratory Comparisons (ILCs) (see Section 29).

3.10 ***AUDIT:*** Process for obtaining relevant information about an object of conformity assessment and evaluating it objectively to determine the extent to which specified requirements are fulfilled (ISO/IEC 17000 [9])

3.10.1 In practice, quality audits take three forms. An audit carried out within the laboratory by its own personnel is often referred to as an 'internal audit' or 'first-party' audit. 'External audits' include 'second-party audits', conducted by an organisation having an interest in the laboratory (such as a customer), and 'third-party audits' which are undertaken by an independent external body, such as an accreditation body. A third-party audit carried out by an accreditation body, as part of the accreditation process, is known as an assessment.

3.10.2 In this Guide the term audit refers to an internal audit; assessment refers to a third-party external audit.

3.10.3 More details on internal audits are given in Section 32.

3.11 ***REVIEW:*** Consideration of the suitability, adequacy and effectiveness of selection and determination activities, and the results of these activities, with regard to fulfilment of specified requirements by an object of conformity assessment (ISO/IEC 17000 [9])

3.11.1 In the laboratory this kind of review is referred to as *'Management Review'*, which is a requirement of ISO/IEC 17025 [2].

3.11.2 More details on management review are given in Section 32.

3.12 ***MEASURAND:*** Quantity intended to be measured (VIM [11])

3.12.1 The specification of the measurand should be sufficiently detailed to avoid any ambiguity. It is important to remember that measurand is not an alternative for analyte (this is explained further in the Eurachem terminology Guide [12].)

3.13 ***STANDARD:*** This word has a number of different meanings in the English language. It is used routinely to refer both to written standards, i.e. widely adopted procedures, specifications, technical recommendations, etc., and to measurement standards used, for example, for calibration purposes. A written (documentary) standard is defined by ISO and IEC as "a document, established by consensus and approved by a recognised body, that provides, for common and repeated use, rules, guidelines or characteristics for activities or their results, aimed at the achievement of the optimum degree of order in a given context." A measurement standard is defined as the "realisation of the definition of a given quantity, with stated quantity value and associated measurement uncertainty, used as a reference" (VIM [11]). Certified reference materials (CRMs) are one (important) category of measurement standards.

3.13.1 In this Guide, to minimise confusion, the term 'standard' is used only in the sense of written standards, whereas the term 'measurement standard' is used to describe chemical or physical standards, used for calibration or validation purposes, such as: chemicals of established purity and their solutions of known concentration; UV filters; weights, etc.

3.13.2 ISO/IEC 17025 [2] also uses the term 'consensus standard' (clause 6.5.3) which is based on an intrinsic measurement standard (measurement standard based on an inherent and reproducible property of a phenomenon or substance VIM [11]). The VIM notes that an intrinsic measurement standard usually consists of a system produced according to the requirements of a consensus procedure and subject to periodic verification (for example, the triple point of water).

3.14 ***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 (VIM [11])

3.14.1 More details on the handling and use of RMs are given in Sections 13 and 22.

3.15 ***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 (VIM [11])

3.15.1 More details on the handling and use of CRMs (and the possibility of claiming metrological traceability to such) are given in Sections 13 and 22.

3.16 ***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

NOTE 1 A measurement procedure is usually documented in sufficient detail to enable an operator to perform a measurement.

NOTE 2 A measurement procedure can include a statement concerning a target measurement uncertainty.

NOTE 3 A measurement procedure is sometimes called a standard operating procedure, abbreviated SOP. (VIM [11])

3.16.1 Note that in ISO/IEC 17025 [2] and this Guide the term 'method' is used (see Section 2.2). A note to section 7.2.1.1 of ISO/IEC 17025 states that in the context of the standard, 'method' can be considered synonymous with the term 'measurement procedure' as defined in the VIM. It should be noted that according to the VIM [11], a 'measurement method' is a more generic concept.

3.16.2 Further explanation of the concepts of measurement procedures and methods in the analytical laboratory can be found in the Eurachem Guide on terminology [12].

3.16.3 More details on dealing with analytical methods are given in Sections 20 and 21.

3.17 ***METROLOGICAL TRACEABILITY:*** Property of a measurement result whereby the result can be related to a reference through a documented unbroken chain of calibrations, each contributing to the measurement uncertainty (VIM [11])

3.17.1 An explanation of how to understand and deal with the concept of traceability in the analytical laboratory is given in the Eurachem Guides on traceability [13] and terminology [12].

3.17.2 In this Guide, further information on how to deal with metrological traceability in the analytical laboratory is given in Section 22.

3.18 ***CALIBRATION:*** operation that, under specified conditions, in a first step, establishes a relation between the quantity values with measurement uncertainties provided by measurement standards and corresponding indications with associated measurement uncertainties and, in a second step, uses this information to establish a relation for obtaining a measurement result from an indication (VIM [11])

3.19 ***MEASUREMENT UNCERTAINTY:*** Non-negative parameter characterising the dispersion of the quantity values being attributed to a measurand, based on the information used

NOTE 1 Measurement uncertainty includes components arising from systematic effects, such as components associated with corrections and the assigned quantity values of measurement standards, as well as the definitional uncertainty. Sometimes estimated systematic effects are not corrected for but, instead, associated measurement uncertainty components are incorporated. (VIM [11])

3.19.1 More details on the evaluation of measurement uncertainty are given in a Eurachem/CITAC Guide [14] and in Section 24 of this Guide.

3.20 ***VERIFICATION:*** Provision of objective evidence that a given item fulfils specified requirements (VIM [11])

3.20.1 In this Guide, more details on method verification are given in Section 21.

3.21 ***VALIDATION:*** Verification, where the specified requirements are adequate for an intended use (ISO/IEC 17025 [2], VIM [11])

3.21.1 Further discussion of the terminology relating to method validation can be found in the Eurachem Guides on terminology [12] and method validation [15].

3.21.2 In this Guide, more details on method validation are given in Section 21.

3.22 ***CONFORMITY ASSESMENT:*** Demonstration that specified requirements are fulfilled (ISO/IEC 17000 [9]).

3.22.1 A note to the definition states that conformity assessment includes activities such as testing, inspection, validation, verification, certification, and accreditation.

3.23 ***DECISION RULE:*** Rule that describes how measurement uncertainty is accounted for when stating conformity with a specified requirement (ISO/IEC 17025 [2])

3.23.1 Further information on decision rules is available in a Eurachem/CITAC Guide [16] and in Section 26 of this Guide.

3.24 ***IMPARTIALITY:*** Presence of objectivity

Note 1: Objectivity means that conflicts of interest do not exist, or are resolved so as not to adversely influence subsequent activities of the laboratory

Note 2: Other terms that are useful in conveying the element of impartiality include “freedom from conflict of interests”, “freedom from bias”, “lack of prejudice”, “neutrality”, “fairness”, “open-mindedness”, “even-handedness”, “detachment”, “balance”. (ISO/IEC 17025 [2])

4 Introduction to quality in analytical measurement

4.1 The importance of analytical quality

4.1.1 Measurements affect our lives on a daily basis. Reliable measurements, whether physical, chemical or biological, are essential to the functioning of society. Every measurement will be carried out for a reason and decisions will be made on the basis of the results obtained. Whether results are being used to check compliance with a regulatory limit, to confirm that a product meets specifications, to support process optimisation or to inform patient diagnosis and treatment, it is essential that the results are of sufficient quality to allow reliable decisions to be made.

4.2 What is quality?

4.2.1 What is meant by 'quality' in the context of measurement results? In ISO 9000 [10] quality is defined as the "degree to which a set of inherent characteristics of an object fulfils requirements". So quality is about making sure that a product or service meets the requirements of a customer or end-user. This is often described as 'fitness-for-purpose'. In the laboratory, 'quality' does not necessarily mean getting the most accurate result possible. Instead, it relates to ensuring that results are sufficiently reliable that they are of use to the customer, and that they are produced within agreed timescales and budgets. In this context, 'fitness-for-purpose' means that results are sufficiently accurate that any decisions based on them can be taken with confidence.

4.3 How is quality achieved in practice?

4.3.1 Producing reliable data consistently doesn't happen by chance! Generally, laboratories are aware of the importance of ensuring the quality of their data and over the last decades agreement has been reached as to what is required – although the details of how it is achieved will be different from laboratory to laboratory.

4.3.2 The starting point to achieving quality in the laboratory is to have a clear understanding of what the customer requires. This requires knowledge of the materials to be tested and the quantity to be measured, as well as an understanding of the expected end use of the data. The laboratory should also agree customer expectations in relation to the timescale for reporting the results and the budget available. This information will then allow the laboratory to identify or develop a suitable method to carry out the measurements.

4.3.3 The next step is to ensure that the method has undergone appropriate validation or verification. Validation allows the laboratory to establish that key performance characteristics such as precision, bias and capability of detection are adequate (see Section 21). Method verification allows the laboratory, before introducing the method into operation, to ensure the measurements can achieve specified parameters. Data obtained during method validation and verification can be used to estimate the measurement uncertainty associated with results produced by the method. The uncertainty establishes the range of values attributable to the quantity being measured (the measurand) and therefore provides a quantitative measure of the accuracy of a result (see Section 24). Method validation or verification and knowledge of the measurement uncertainty alone are insufficient to ensure that results obtained at different times and in different locations can be compared. For this to be achieved the metrological traceability of results needs to be established by linking them to a common reference point through an unbroken chain of calibrations (see Section 22). To ensure that all processes related to undertaking a measurement are carried out effectively, the laboratory needs to have documented procedures in place, and all staff need to be trained and have demonstrable competence in the activities relevant to their roles (see Section 9). While method validation or verification provides confidence that the chosen test method is capable of delivering fit-for-purpose results, the reliability of results obtained during routine use of the method needs to be monitored. IQC procedures verify that the method is still 'under control' (i.e. its performance has not deteriorated significantly since the validation was undertaken) and that particular sets of results can be released to the customer (see Section 28). Finally, regular participation in ILCs such as PT schemes provides an independent assessment of a laboratory's performance (see Section 29).

4.3.4 All of the activities mentioned above need to be addressed by laboratories to ensure the quality of results, regardless of their size or the nature of the tests that they carry out. For this reason these activities are also core requirements of standards used for laboratory accreditation such as ISO/IEC 17025 [2] and ISO 15189 [3]. To help laboratories address some of these issues, Eurachem has published guides on method validation [15],

evaluating measurement uncertainty [14], establishing metrological traceability [13], and selecting and participating in PT schemes [17].

4.3.5 This Guide explains where these technical issues fit into QA and provides guidance on other activities required to ensure that measurement results are fit-for-purpose. Figure 1 shows how all these different aspects fit together to ensure the quality of measurement results.

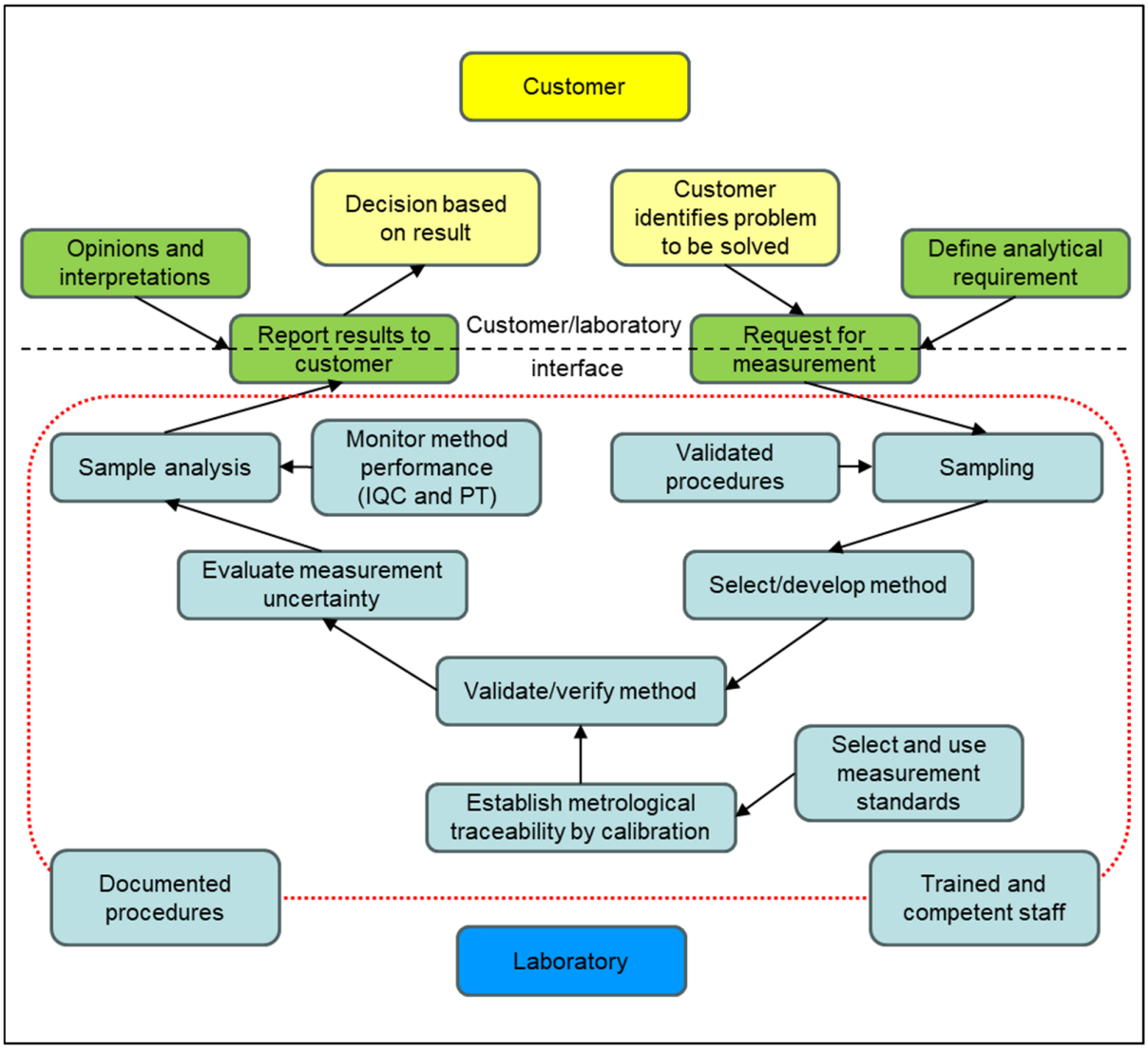

Figure 1 – Illustration of typical 'measurement cycle' and the issues that need to be addressed to ensure results are fit-for-purpose

5 Demonstrating competence – the international framework

5.1 It should be noted, that despite the fact that both the definition of 'accreditation' and 'certification' are related to a 'third-party attestation' (implying verification of the fulfilment of some specified requirements), the two types of 'attestation' are significantly different in background and impact. It was already noted in the definition of 'certification' (3.7), that certification is applicable to all objects of conformity assessment except for conformity assessment bodies themselves (such as laboratories), to which accreditation is applicable. Furthermore the following important differences should be mentioned:

- accreditation of testing laboratories is (normally) based on ISO/IEC 17025 [2] (except for medical laboratories where ISO 15189 [3] is used instead), which states a number of requirements for the technical competence of the laboratory in addition to the requirements on management;
- accreditation is not granted to a laboratory as such, but only for the accreditation scope, i.e. a number of specified testing methods, for which the laboratory can document its specific competence.

In addition, in the EU only one accreditation body (i.e. the National Accreditation Body (NAB)) operates; its authority is generally derived from the government in accordance with Regulation No 765/2008 [18]. In contrast, a certification body is a private company in competition with other certification bodies.

5.2 The references to accreditation in this and successive sections refer to fulfilment of the requirements in ISO/IEC 17025 [2]. Note that the standard itself does not deal with the concept of accreditation (except in the scope, where it is mentioned that it can be used by accreditation bodies as a basis for judgement on competence). Its requirements form the basis for accreditation granted by an NAB and international agreements are in place to support the equivalence of assessments done by the individual NABs (see Section 5.6).

5.3 Accreditation is granted to a laboratory for a specified set of activities, i.e. tests, calibrations or sampling following assessment of that laboratory by an accreditation body (see Section 6). Such assessments will typically involve an examination of the methods in use, the facilities, environment, equipment and personnel involved, and the means of controlling the procedures being performed, looking for evidence of compliance with the requirements in ISO/IEC 17025 [2]. Furthermore, the QMS and the related documentation of the laboratory will be examined.

5.4 Each accreditation body has established procedures against which it operates, assesses laboratories and grants accreditation. To ensure harmonised assessments, the accreditation bodies themselves must work in accordance with the requirements of ISO/IEC 17011 [19].

5.5 Assessors are chosen against specified criteria. The selection criteria for assessors appointed by accreditation bodies are specified in ISO/IEC 17011 [19]. These include the requirement for technical expertise in the specific areas of operation being assessed.

5.6 The benefit of accreditation is that it provides potential customers with confidence in the quality of the work performed by the accredited laboratory. Since the introduction of formal requirements for the competence of laboratories, the endorsement conferred by accreditation has gained worldwide recognition and plays an important role in trade. Many accreditation bodies in the European region (which have been evaluated and found to satisfy relevant requirements, see Section 5.4) have signed a Multilateral Agreement (MLA) with European Accreditation (EA) members, and/or a Mutual Recognition Arrangement (MRA) under the International Laboratory Accreditation Cooperation (ILAC).*

5.7 Accredited laboratories and others working towards obtaining accreditation need the support of competent RM producers and PT providers. This competence is based on the requirements of relevant standards, i.e. ISO 17034 [20] and ISO/IEC 17043 [21], respectively.

*On 1 January 2026, Global Accreditation Cooperation Incorporated assumed the roles of the International Accreditation Forum (IAF) and the International Laboratory Accreditation Cooperation (ILAC), becoming the single international authority on the accreditation of laboratories, certification bodies, inspection bodies, proficiency testing providers, validation/verification bodies, reference material producers and biobanks.

6 The accreditation process

6.1 The standard ISO/IEC 17025 [2] contains five sets of requirements; they are classified as follows:

- Clause 4: general requirements – dealing with impartiality and confidentiality;
- Clause 5: structural requirements – organisation and responsibilities;
- Clause 6: resource requirements – related to the basic resources (personnel, facilities, equipment etc.) which must be in place for a laboratory to function;
- Clause 7: process requirements – ensuring proper handling of the testing/calibration/sampling process from initial contact with the customer to final delivery of the report;
- Clause 8: management requirements – setting the minimum requirements for the structure and content of the management system which must be in place.

This structure is one of the main differences from the 2005 version of the standard [22].

6.2 Under these five headings are a number of more specific requirements, summarised below (and further elaborated in this Guide):

- a QMS;
- a suitable laboratory environment;
- educated, trained and skilled personnel;
- training procedures and records;
- specifications for reagents, calibrants and measurement standards (including RMs);
- measuring instruments suitably maintained and calibrated;
- procedures for sampling (where the laboratory is responsible for this activity);
- procedures for sample handling;
- documented, verified and validated methods;
- metrological traceability of results;
- evaluation of measurement uncertainty;
- IQC procedures;
- participation in ILCs [for example PT/external quality assessment (EQA)];
- procedures for checking and reporting results;
- procedures for dealing with nonconforming work and corrective actions;
- internal audit and review procedures.

According to the new approach in the revised ISO/IEC 17025 from 2017 [2], the laboratory is furthermore responsible for addressing any risks and opportunities which can be identified in relation to all these requirements (see Section 7).

6.3 Requirements relating to the management of a laboratory (in clause 8, but also included in clauses 4-7 of ISO/IEC 17025 [2]) are very much in line with the requirements given in ISO 9001 [5]), i.e. ensuring that policy, procedures and appropriate documentation are in place for:

- safeguarding impartiality in the laboratory's activities and relationships, and in the relationships of its personnel;
- organisation and delegation of responsibilities;
- establishment, assessment and improvement of the QMS;
- control of documents and records;
- ensuring customers are dealt with consistently (contracts, cooperation, feedback);
- safeguarding the quality of supplies, services and any subcontracted work;
- identifying and dealing with any nonconformities in relation to the established QMS;
- confirming the management's current awareness of the effectiveness and appropriateness of the QMS;
- handling risks and opportunities.

NOTE: This Guide does not deal specifically with any of these management issues – except for the requirements on risks and opportunities (see Section 7) and internal audits and management reviews (see Section 32).

6.4 Requirements relating directly to the technical competence of the laboratory to carry out specific types of tests, calibrations or sampling are given in clauses 6 and 7 of the standard. These are the subject of the more detailed recommendations found in the following sections of this Guide.

6.5 As mentioned above, ISO/IEC 17025 [2] incorporates the ISO 9001 [5] management system elements which are applicable to laboratories. For

laboratories within organisations that are seeking certification according to ISO 9001 (and therefore not looking to obtain a third-party evaluation of their technical competence as in the case of an accreditation), ISO/IEC 17025 and this Guide can still be recommended as useful tools for securing good quality work in that laboratory. The equivalence of the management system documentation clauses of ISO/IEC 17025 and the requirements of ISO 9001 is described in clause 8 of the standard (Options A and B) and Figure 2.

6.6 Laboratories that comply with the requirements of ISO/IEC 17025 [2] will operate a QMS that meets the principles of ISO 9001 [5]. Therefore they will not require separate certification to the requirements of ISO 9001 for those activities covered by the ISO/IEC 17025 accreditation. However, the organisation may choose to obtain certification for non-technical activities which are not covered by the accreditation, such as finance, human resources or sales and marketing.

6.7 The methods to be covered by the accreditation will be examined to ensure they are technically appropriate for the intended purpose, that they have been verified (or validated; see Sections 20 and 21) and are documented clearly and unambiguously. The methods will also be examined to confirm that their performance is under control (e.g. through establishment of IQC procedures and use of statistically based QC charts; see Section 28).

6.8 The performance of tests may be witnessed to ensure documented procedures are being followed and interpreted in a consistent way. The laboratory's performance in PT schemes or other ILCs when using the accredited methods will also be a focal point.

6.9 In addition to following the documented test methods, the laboratory must have a number of procedures in place for securing appropriate compliance with the various requirements in the standard.

6.10 It is the responsibility of the laboratory to ensure that all procedures used are appropriate for their intended purpose, and to what degree such procedures need to be documented. The 2017 version of the standard is more focused on requirements related to evidence of appropriate performance than prescriptive requirements.

6.11 The consistency of operation of laboratory activities is one of the pillars of the standard (along with competence and impartiality). It is the responsibility of the laboratory to guarantee that the latest version of all the documents is available when and where needed, and to whoever needs them.

6.12 The assessment process examines whether the procedures are fit-for-purpose and looks specifically for evidence of their appropriate accomplishment.

6.13 A laboratory may apply quality management to all or part of its operations. Where a laboratory claims accreditation it is important to be clear as to which activities the accreditation applies. The formal statement of the activities which have been accredited against ISO/IEC 17025 [2] is known as the 'scope'.

6.14 For laboratories seeking accreditation to ISO/IEC 17025 [2] a clear statement of the activities complying with the standard is required, which excludes externally provided laboratory activities on an ongoing basis.

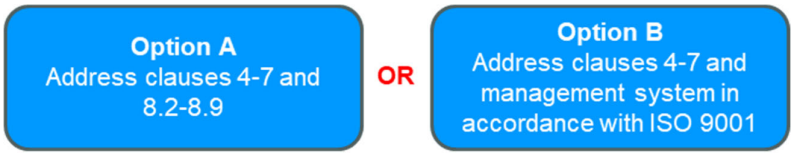

Figure 2 – Illustration of management system options in ISO/IEC 17025

6.15 This scope of accreditation is typically defined for testing laboratories (including medical laboratories) in terms of:

i) the range of products, materials or sample types tested or analysed;

ii) the properties to be determined;

iii) the specification or method, equipment or technique used.

6.16 For calibration laboratories the scope of calibration and measurement capability (CMC) can be expressed in terms of:

i) measurand or RM;

ii) calibration or measurement method or procedure and type of measuring instrument or material to be calibrated or measured;

iii) measurement range and additional parameters where applicable;

iv) measurement uncertainty.

6.17 The scope of accreditation should also be clear in regard to the objective of the sampling activities and the type of sampling, regardless of whether sampling is done as a stand-alone activity or is associated with subsequent testing.

6.18 Guidance on how to define the scope of accreditation for a testing, calibration or medical laboratory according to the relevant standards is given in ISO/IEC 17011 [19] and ILAC G18 [23].

6.19 This type of scope is often referred to as a 'fixed scope'. The test/calibration laboratory's accreditation schedule will contain the information indicated above for the tests/calibrations for which accreditation has been obtained. For testing laboratories the range of values to be determined and the measurement uncertainty do not have to be stated in the scope of accreditation, however relevant documentation must be available to meet the requirements of ISO/IEC 17025 [2].

6.20 It should be noted here that there might be slight variations in practices in different countries, as the NABs will have established their own accreditation procedures (in accordance with ISO/IEC 17011 [19]) which may express different approaches in how to state the scope.

6.21 Definition of scope in specific terms is clearly most easily applied to laboratories carrying out routine tests/calibrations using established methods. However, the 'fixed scope' approach can be restrictive as it does not readily enable new or modified methods to be added to a laboratory's scope of accreditation, even where competence in a general area of testing/calibration has already been demonstrated. An alternative is for the laboratory to be granted a 'flexible scope'. A laboratory must maintain a list of the tests/calibrations included under its flexible scope, but this approach allows the laboratory to include additional activities in its scope of accreditation on the basis of its own validations, without having to apply to the accreditation body for an extension to scope (as described in Section 6.23) [23-25]. In a testing laboratory, flexible scope can cover scenarios such as:

i) use of new or amended tests in accordance with a generic method;

ii) modification of existing methods to broaden their applicability (e.g. to deal with new sample types or analytes);

iii) inclusion of newly revised methods or standard methods that are technically equivalent to methods already covered by the laboratory's accreditation.

6.22 A flexible scope puts more responsibility on the laboratory in terms of demonstrating that methods are fit-for-purpose. Flexible scope also requires a laboratory to be able to demonstrate that it has procedures in place to adequately manage the accreditation of new or revised methods, and the updating of accredited methods. Although the concept of flexible scope is widely accepted, there are differences in its implementation in different countries.

6.23 Unless it has a 'flexible scope' accreditation a laboratory wishing to change its scope, either by adding additional tests/calibrations or changing the method of existing tests/calibrations may require the approval of the accreditation body, which will have a specified policy for such situations. Typically, it is possible to grant simple changes by examination of documentation. For more complex changes, particularly where new techniques are involved, additional assessments may be required.

7 Risks and opportunities

7.1 According to ISO/IEC 17025 [2], the laboratory shall consider the risks and opportunities associated with its activities [26-28]. This risk-based thinking is reflected not only in a number of sub clauses of ISO/IEC 17025 but in its philosophy as a whole. The laboratory needs to plan and implement appropriate actions, proportional to the impact risks and opportunities have on the validity of results, and to evaluate their effectiveness. It is the laboratory's choice which risks and opportunities to address, as well as how to address them. No reference is made to 'preventive' actions since this need is covered by the risk (and opportunity)-based provisions as well as those clauses relating to improvement. ISO 15189 [3] also provides for the risk-based philosophy.

7.2 It is important to implement a culture of risk-based thinking at all relevant levels and functions of the laboratory, making it a part of all activities and practices. Particular reference is made in clauses regarding statements of conformity, nonconforming work, risks and opportunities and management reviews. Defining and endorsing a risk management policy, and aligning the laboratory risk management objectives with the objectives and strategies of the organisation, can help with pursuing such a culture.

7.3 The laboratory management shall be committed to impartiality and, to this end, it shall identify risks to its impartiality on an on-going basis. If a risk to impartiality is identified, the laboratory shall be able to demonstrate how it eliminates or minimises such risk.

8 Definition of laboratory – Legal entity

8.1 In order for a laboratory to receive accreditation, it shall be a standalone legal entity or a part of an existing legal entity. That is, it shall be recognised as a company, organisation or person that has legal rights and responsibilities. It should be noted that both ISO/IEC 17025 [2] and ISO 15189 [3] deem that a governmental laboratory is a legal entity on the basis of its governmental status. As a legal entity, the laboratory possesses the legal capacity to engage in contractual agreements, hold ownership of assets (including equipment, intellectual property, and facilities), assume liabilities, and is legally responsible for its conduct. When the laboratory is a component of a larger legal entity it maintains separate legal obligations and operational independence for its laboratory functions. Thus, it is ensured that there is a clear accountability for the quality and reliability of the laboratory work.

8.2 A laboratory, as a legal entity, can engage in commercial activities, issue invoices, pay taxes, and be subject to legal actions in its name.

8.3 It has defined management structures and processes to ensure effective decision-making, compliance with legal and regulatory requirements, and the achievement of its operational objectives.

8.4 The laboratory, as a legal entity, is accountable to its stakeholders, including customers, regulatory bodies, employees, and the community, for upholding ethical standards and delivering quality services.

8.5 According to ISO/IEC 17025 [2] a laboratory performs one or more of the following activities:

- testing;
- calibration;
- sampling, associated with subsequent testing or calibration.

8.6 The management of the laboratory with overall responsibility for the activities should be identified. A laboratory bears responsibility for its activities. It is directly responsible for the outcomes and integrity of its work, including the accuracy and reliability of its test results and the confidentiality of sensitive information. Within the organisation, the management should define the units or teams which are responsible for undertaking particular activities. The responsibilities, authorities, and relations between personnel who manage, perform, or verify work affecting the results of laboratory activities shall be specified, elaborating on how these specifications are documented, communicated, and enforced within the organisation.

8.7 The laboratory shall define in detail its organisation and management structure, its place in its parent organisation (if applicable), and the relationship between management and the other services. An ‘organisational chart’ is a useful way of meeting this requirement but is not mandatory. Such provision underscores the importance of a structured approach to quality management and accountability within a laboratory.

8.8 The range of laboratory activities shall be defined and documented so that all parties are aware of where the activities start and end. According to ISO/IEC 17025 [2], the laboratory shall only claim conformity for this range of laboratory activities, excluding externally provided laboratory activities, for which the laboratory only ensures compliance with the standard’s requirements.

8.9 The procedures shall be documented to the extent necessary to ensure the consistent application of the laboratory’s activities and the validity of its results.

8.10 The laboratory management shall ensure communication takes place regarding the effectiveness of the management system and the importance of meeting customer and other requirements. This is a significant output requirement of the management review (see Section 32). Effective communication is essential to ensure that every member of staff understands their duties and obligations in upholding the quality objectives of the management system and in fulfilling the expectations of customers and other interested parties.

8.11 The laboratory management is responsible for maintaining the integrity of the management system when changes are planned and implemented, ensuring that any modifications to processes, procedures, or organisational structures do not adversely affect the system’s effectiveness or compliance with established standards.

9 Personnel

9.1 The laboratory management has to identify and document the different functions within the laboratory. The roles within the laboratory and its structure are often summarised in one or more organisational charts (also known as 'organograms').

9.2 The laboratory management should formulate the goals and job description for each role and, based on these, the required education, training and skills of the personnel appropriate for their functions. Present and anticipated tasks of the laboratory have to be considered in order to achieve continual quality improvement.

9.3 The laboratory management should document, the minimum level of academic or vocational qualification and experience necessary for the key functions within the laboratory. Personnel who are required to perform specialist tasks, (e.g. particular types of test or sampling) or who issue test reports and/or provide 'opinions and interpretations', will need specific training and competence appropriate for the task. All analyses must be carried out by, or under the supervision of, a qualified, experienced and competent analyst. Lower formal qualifications may be acceptable when personnel have extensive relevant experience and/or the scope of their activities is limited. Personnel undergoing training or with no relevant qualifications may undertake analyses provided that they have received an acceptable level of training to carry out the particular task, have demonstrably achieved an appropriate level of competence and are adequately supervised. All education and training requirements should be documented, and procedures for and records of training and monitoring of competence maintained.

9.4 In certain circumstances, the minimum requirements for qualifications and experience of personnel carrying out particular types of analysis may be specified in regulations.

9.5 The laboratory management must ensure that all personnel receive sufficient training to enable the competent performance of the tests and operation of equipment. Therefore a programme of continuous training shall be carried out and documented. Where appropriate, this will include training in the principles and theory underpinning particular techniques. Where possible, objective measures (performance criteria) should be used to assess the attainment of competence during training. Only analysts who can demonstrate the necessary competence, or who are adequately supervised may be authorised to perform tests on samples. Training and development plans for all personnel shall be in place to support the attainment of appropriate competencies and ensure the future needs of the laboratory are met. Continued competence shall be monitored, for example, by reviewing the performance achieved in IQC and PT. The need to periodically retrain personnel shall be considered, particularly (but not only) where a method or technique is not in regular use. Authorisation shall be given before personnel can begin undertaking analysis on their own.

9.6 The laboratory management shall maintain an up-to-date record of the training that each member of staff has received. The purpose of these records is to provide evidence that every individual has been adequately trained and their competence to carry out particular tasks has been assessed. In some cases, it may be pertinent to state any particular limitations to evidence about competence. Typically the record for each person should include:

- academic qualifications;
- external and internal courses attended;
- relevant on-the-job training (and retraining as necessary).

Possibly also:

- participation in IQC activities and/or PT schemes, with associated data;
- participation in intralaboratory comparisons;
- involvement in method validation activities;
- technical papers published and presentations given at conferences.

9.7 In some cases it may be more appropriate to record competence in terms of particular measurement techniques rather than complete methods.

9.8 Access to training records will be necessary in the course of everyday work. Access to other personal details, usually held centrally, may be restricted by national legislation on data protection.

9.9 Appropriate procedures shall be followed in the case of temporary staff, contractors, trainees and other newly employed personnel with regard to their competence and awareness of the relevant QMS requirements.

9.10 Personnel (including individuals acting on the laboratory's behalf and personnel of external

bodies/organisations) shall act impartially and keep confidential all information obtained or generated during the course of laboratory activities. In line with other standards produced by ISO/CASCO, ISO/IEC 17025 [2] contains specific clauses on impartiality and confidentiality.

10 Environment

10.1 Samples, reagents and measurement standards (including RMs) must be stored so as to ensure that their integrity is maintained. In particular, they must be stored and used or tested in such a way that cross contamination is not possible. It is advisable that the reagents, measurement standards and samples are stored in different locations. The laboratory should guard against their deterioration, contamination and loss of identity, taking into account any specific requirements stated by the supplier or specified in the method (e.g. storage temperature).

10.2 The laboratory environment, services and facilities should be sufficiently uncrowded, clean and tidy to ensure that the quality of the work carried out is not compromised. Where it is critical to the quality of its work, the laboratory shall maintain documented procedures and records relating to cleaning processes.

10.3 It may be necessary to restrict access to particular areas of a laboratory because of the nature of the work carried out there. Only authorised personnel may have access and this must be described in procedures and their names recorded. Restrictions might be made because of security, safety, or sensitivity to contamination or interferences. Typical examples might be work involving explosives, radioactive materials, carcinogens, forensic examination, polymerase chain reaction (PCR) techniques and trace level analysis. Where such restrictions are in force, personnel should be made aware of:

i) the intended use of a particular area;

ii) the restrictions imposed on working within such an area;

iii) the reasons for imposing such restrictions;

iv) the procedures to follow when such restrictions are breached.

Depending on the needs and requirements for the improvement or optimisation of its activities, the laboratory shall monitor and periodically review the measures to control access to facilities.

10.4 Where incompatible activities are carried out in neighbouring work areas, provision needs to be made to ensure effective separation. The separation can be in terms of space (i.e. by carrying out the activities in different laboratory areas) or time (i.e. by scheduling work so that the incompatible activities happen sequentially with adequate cleaning procedures between the two).

10.5 When selecting designated areas for new work, account must be taken of the previous use of the area. Before use, checks should be made to ensure that the area is free of contamination. Decontamination procedures may be appropriate where the environment or equipment is subject to change of use or where accidental contamination has occurred.

10.6 The laboratory shall provide the appropriate environmental conditions and controls necessary for particular tests or operation of particular equipment. This should include consideration of the effects and required control of, for example:

- temperature;
- humidity;
- pressure;
- vibration;
- airborne and dustborne microbiological contamination;
- lighting.

10.7 In addition, the need for radiation screening and particular services (e.g. gas lines or demineralised water supply) should also be considered.

10.8 Critical environmental conditions must be monitored and kept within predetermined limits. Monitoring equipment needs to be adequately maintained, verified and/or calibrated.

10.9 A breakdown of critical environmental conditions may be indicated either by monitoring systems or by the QC results produced during the particular tests. The impact of such failures may be assessed as part of ruggedness testing during method validation (see Section 21.14) and, where appropriate, emergency procedures established. Any such event has to be followed up as a nonconformity in the QMS.

10.10 When activities are performed at sites outside the laboratory's permanent control, the laboratory shall ensure that the requirements related to facilities and environmental conditions are met.

10.11 The correct disposal of reagents and samples does not directly affect the quality of sample analysis, however it is a matter of good laboratory practice and should comply with national environmental and health and safety regulations.

11 Equipment

11.1 Equipment qualification

11.1.1 Although it is not a requirement of ISO/IEC 17025 [2] the process of equipment qualification, which is widely adopted in the pharmaceutical sector, provides a useful framework for managing equipment. Equipment qualification is defined as the process of ensuring that equipment performance is appropriate for its intended use and is usually divided into four stages, each dealing with different aspects of the equipment's history [29]:

- Design Qualification, DQ – Selection of an instrument and supplier;
- Installation Qualification, IQ – Installation and release for use;
- Operational Qualification, OQ – Periodic and motivated instrument checks;
- Performance Qualification, PQ – In-use instrument checks.

11.1.2 Note that some guidance, for example that published by EDQM, identifies the different stages of equipment qualification as Level I, II, III and IV instead of DQ, IQ, OQ and PQ [30].

11.1.3 DQ deals with the initial stage of selecting the equipment and supplier. At this stage, key functions are specified and levels of performance are defined. In addition, requirements for other services, such as calibration, maintenance and training, are defined, according to the needs related to the intended use of the equipment and the laboratory's capabilities.

11.1.4 IQ addresses the operations to be performed and documented when the equipment is received and installed, before it can be released for routine use. Such operations will usually include checks that the equipment is received in good condition, as ordered, and assessment of its full functionality in the selected environment. This includes the start-up checks done by the supplier, followed by a full check of the equipment's key performance parameters, irrespective of any analytical method. Whenever required, calibration is performed as part of this stage. Start-up, full checks of performance parameters and the first calibration data should be documented and archived. The release for use shall be documented and authorised by the person responsible for the equipment.

11.1.5 The checks performed before release (IQ) also form the basis for periodic assessments of the equipment's ongoing functionality (OQ). These shall be performed at intervals which will depend on the frequency of use and knowledge of the stability of the equipment in the conditions of use. The checks shall also be performed if the equipment is moved to a new environment, or undergoes significant repair or maintenance operations. For measuring instruments, a process of 'metrological confirmation' (further explained in Section 11.2.2) shall be devised, to ensure that relevant metrological characteristics are kept under control. Acceptance criteria for the tested parameters should take into account the specification from the manufacturer of the equipment as well as the requirements for the intended use of the equipment.

11.1.6 Finally, PQ should be planned to check the performance of the equipment during routine use, to confirm, on a day-to-day basis, that the same quality level is achieved. These checks are usually built into the analytical methods themselves, in terms of analytical response for calibration standards, blanks and other QC materials. Control charts for such responses allow the recording and monitoring over time of the equipment's performance (see Section 28). Further guidance and practical examples (e.g. for the qualification of spectrophotometers, mass spectrometers, HPLC) is available [30].

11.2 Categories of equipment

11.2.1 All equipment used in laboratories (including any associated software) should be of a specification sufficient for the intended purpose, and kept in a state of maintenance and metrological control consistent with its use (see Section 11.2.2). Equipment normally found in an analytical laboratory can be categorised as:

i) general service equipment (e.g. hotplates, stirrers, non-volumetric glassware and glassware used for approximate volume measurements) and laboratory heating or ventilation systems;

ii) measuring instruments, including volumetric equipment (e.g. flasks, pipettes, pyknometers, burettes) and other instruments (e.g. hydrometers, U-tube viscometers, thermometers, timers, spectrometers, chromatographs, electrochemical meters, balances);

iii) physical measurement standards (weights, reference thermometers);

iv) reference data (e.g. molecular weights, physical constants);

v) computers and data processors.

Note that in ISO/IEC 17025 [2] reagents and other consumables, and RMs are also considered under the heading of equipment. In this Guide these are dealt with separately in Sections 12 and 13, respectively.

11.2.2 Laboratories can obtain guidance on managing measurement processes and the metrological confirmation of measuring equipment from ISO 10012 [31], which can help with developing effective metrological processes. According to the definition given in that standard, 'metrological confirmation' typically includes: calibration and checks of the calibration status; maintenance and/or repair, followed by re-calibration as necessary; a comparison with the metrological requirements for the intended use; and sealing and/or labelling as required. Typical examples of characteristics for which metrological requirements should be established are: measuring interval, resolution, repeatability and trueness.

11.3 General service equipment

11.3.1 General service equipment will typically only be maintained by cleaning and safety checks as necessary. Metrological controls will be necessary where the setting can significantly affect the test or analytical result (e.g. the temperature of a muffle furnace or constant temperature bath). Such checks need to be planned, documented and recorded.

11.4 Measuring instruments

11.4.1 The performance of some volumetric (and related) glassware is dependent on particular factors, which may be affected by cleaning methods etc. As well as requiring strict procedures for maintenance, such measuring instruments may require more regular and scheduled metrological control, depending on use. For example, the performance of pyknometers, U-tube viscometers, pipettes, and burettes is dependent on 'wetting' and surface tension characteristics. Cleaning procedures must be chosen so as not to compromise these properties. Such scheduled maintenance and metrological control activities need to be documented and recorded.

11.4.2 Attention should be paid to the possibility of contamination arising either from the fabric of the measuring instrument itself, which may not be inert, or from cross-contamination from previous use. In the case of volumetric glassware, cleaning procedures, storage, and segregation of equipment may be critical, particularly for trace level analyses where leaching and adsorption can be significant.

11.4.3 Correct use combined with periodic servicing, cleaning and calibration will not necessarily ensure that a measuring instrument is performing adequately. Where appropriate, periodic performance checks should be carried out (e.g. to check the response, stability and linearity of sources, sensors and detectors, the separating efficiency of chromatographic systems, or the resolution, alignment and wavelength accuracy of spectrometers) – see Annex B. Laboratories need to ensure that the test and measuring instruments (and any associated software) are protected against unauthorised adjustments, and have a systematic approach to transferring correction factors. Additional controls may be required when the measuring instrument has been used outside of the laboratory, for example when performing field tests.

11.4.4 The frequency of such performance checks may be specified in manuals or operating procedures. If not, then it will be determined by experience and based on need, type and previous performance of the measuring instrument. Intervals between checks should be shorter than the time the measuring instrument has been found to take, in practice, to drift outside acceptable limits.

11.4.5 It is often possible to build performance checks – system suitability checks – into test methods (e.g. based on the expected detector or sensor response to RMs, the resolution of component mixtures by separation systems, or the spectral characteristics of measurement standards). These checks must be satisfactorily completed and recorded before the measuring instrument is used.

11.4.6 In some cases, a test and its performance is actually defined in terms of a particular measuring instrument and checks will be necessary to confirm that the instrument conforms to the relevant specification. For example, the flashpoint value obtained for a particular flammable sample is dependent upon the dimensions and geometry of the apparatus used in the testing.

11.5 Physical measurement standards

11.5.1 Wherever physical parameters are critical to the correct performance of a particular test, the laboratory shall have access to the relevant measurement standard as a means of calibration, for example standard weights [32].

11.5.2 Measurement standards should be stored and used in a manner consistent with preserving their

calibration status. Particular consideration should be given to any storage advice given in the documentation supplied with the measurement standard. Certificates and other relevant documentation should be stored in such a way as to be readily available while the measurement standards are in use, and afterwards filed for as long as deemed necessary to document the metrological traceability of the measurements linked to them. Checks on the calibration status should be performed at regular intervals and laboratories should establish acceptance criteria for the results of their metrological control.

11.6 Computers and data processors

11.6.1 Requirements for computers are given in Section 30.

12 Reagents and consumables

12.1 The quality of reagents and other consumable materials must be appropriate for their intended use. Consideration needs to be given to the selection, purchase, receipt and storage of reagents.

12.2 Suppliers of critical reagents and consumables should be evaluated and approved; relevant documentation and records should be maintained. The purpose of such evaluation is to prevent possible deviations from the expected quality of the measurement results that may arise from failure of any critical supply to meet the requirements. The process should be based on a risk assessment for the reagents and materials supplied. Key questions to be asked include:

- What may happen and why, should a given product fail to match the relevant specifications?
- What would be the consequences for the laboratory work?
- What is the chance of such a failure occurring?
- Are there any factors that may reduce either the probability of the failure or its consequences? Is the level of risk acceptable?

Further guidance on risk assessment and management is provided in ISO documents [26-28].

12.3 Documents referring to the purchase of reagents and other items affecting the quality of laboratory operations must contain an adequate description of the order. The order must clearly identify the specification required and the purpose for which the reagent is purchased. These documents should be reviewed and approved as appropriate prior to release.

12.4 Where the quality of a reagent is critical to a test, the quality of a new batch should be verified against the outgoing batch before use, provided that the outgoing batch is known to be still serviceable. However, in all cases, the reagents and other consumables should be inspected and verified as complying with set specifications.

12.5 Reagents received into the laboratory should be labelled with the dates of receipt, opening and expiry, plus the name of the person opening the reagent. The laboratory must ensure compliance with the expiry dates of reagents. For this purpose, the rule of FIFO (First In-First Out) or of FEFO (First Expired-First Out) should be applied.

12.6 The grade of any critical reagent used (including water) should be stated in the method description, together with guidance on any particular precautions which should be observed in its preparation, storage and use. These precautions relate to toxicity, flammability, stability to heat, air and light; reactivity to other chemicals; reactivity to particular containers; and other hazards. Reagents and RMs prepared in the laboratory should be labelled to identify substance, concentration, solvent (where not water), any special precautions or hazards, restrictions of use, and date of preparation and/or expiry. The person responsible for the preparation shall be identifiable either from the label or from records.

13 Measurement standards and reference materials

13.1 A series of ISO documents relating to RMs is available [20, 33-37].

13.2 RMs and CRMs are defined in Section 3. They are used for calibration, method validation, evaluating measurement uncertainty, QC and for training purposes. However, a specific RM can only be used for one purpose in a measurement, e.g. for calibration or for QA purposes. Figure 3 shows a typical analytical process and illustrates the role of RMs in relation to calibration, method validation and QC.

13.3 RMs may take a variety of forms, including pure substance RMs, matrix RMs, metals, alloys, solutions or mixtures. The following are all examples of RMs:

- 99% pure sodium chloride;
- an aqueous solution with mass concentrations of copper (II) sulfate equal to 10 g/l and magnesium chloride equal to 20 g/l;
- a powdered polymer with a particular molecular weight distribution range;
- a crystalline solid melting in the range 150-151 °C;
- a dried milk powder containing a known amount of vitamin C.

13.4 For many types of analysis, calibration may be carried out using materials prepared within the laboratory from chemicals of known purity and composition (for example solutions of known composition). Some chemicals may be purchased with a manufacturer's certificate stating purity. Alternatively, chemicals of a stated but uncertified purity may be purchased from reputable suppliers. Whatever the source, it is the user's responsibility to establish that the quality of such materials is fit-for-purpose. Sometimes additional tests will need to be carried out by the laboratory. Normally a new batch of a chemical should be checked against the previous batch. Ideally, all chemicals to be used as RMs should be purchased from producers with demonstrated quality management systems. However, a QMS does not automatically guarantee the quality of the producer's products and laboratories should take all reasonable steps to confirm the quality of critical materials. The control of impurities is important, especially for trace level analysis, where they may cause interferences. Due regard should be paid to the manufacturer's recommendations on storage and shelf life. In addition, caution is needed, as suppliers do not always provide information about all impurities.

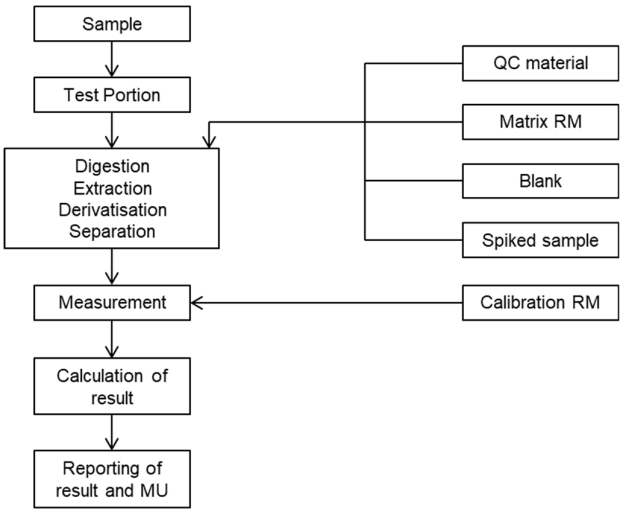

Figure 3 – Example of a typical analytical process, showing the role of RMs

13.5 The use of appropriate RMs enables analysts to demonstrate the metrological traceability of results by calibrating measuring instruments, to validate methods and to monitor the method's performance. They may also be used as transfer (measurement) standards for comparison of methods. Their use is strongly encouraged wherever appropriate.

13.6 The uncertainty associated with the stated purity of a pure substance CRM needs to be considered in relation to the uncertainty associated with other aspects of the method. Ideally, the uncertainty associated with the property value of a RM or CRM, used for calibration purposes, should not contribute more than one third of the overall measurement uncertainty.

13.7 An important factor in selecting RMs is their commutability. This is the property of a RM whereby it is demonstrated to behave similarly to test samples under the same measuring conditions. The concept is defined in VIM [11] and discussed further in the Eurachem terminology Guide [12]. Specific guidelines for RMs used in laboratory medicine are published by the Clinical and Laboratory Standards Institute (CLSI) [38]. In general, the composition of the RM should be as close as possible to that of the samples routinely tested in the laboratory. Where matrix interferences potentially exist, ideally a method should be validated using a matched matrix RM certified in a reliable manner. If such a material is not available it may be acceptable to use a sample spiked with a RM.

13.8 It is important that any CRM used has been produced and characterised in a technically valid manner. Users of CRMs should be aware that not all materials are produced with the same degree of rigour. Details of homogeneity and stability studies, the methods used in certification, and the uncertainties and variations in the stated analyte values, are usually available from the producer and should be used to judge their reliability. The material must be accompanied by a certificate, which includes an estimate of the uncertainty associated with the certified value. ISO 17034 [20] specifies criteria for the competence of RM producers.

13.9 RMs and CRMs should be clearly labelled so that they can be unambiguously identified and referenced against accompanying certificates or other documentation. Information should be available indicating shelf life, storage conditions, applicability, and restrictions of use. RMs prepared within the laboratory, e.g. as solutions, should be treated as reagents for the purposes of labelling (see Section 12.6).

13.10 The handling of measurement standards should safeguard against them becoming contaminated or degraded. Procedures for training personnel should reflect these requirements.

14 Externally provided products and services

14.1 No laboratory is a stand-alone unit. While the previous edition of this Guide covered externally provided products and services only in terms of subcontracting work (either to meet a short term need or on a continuing basis), ISO/IEC 17025:2017 [2] requires that the laboratory has strategies in place to cover the quality aspects of all external products and services that may affect its activities. 'Products' covers any items that a laboratory might use in the course of carrying out its activities, including RMs and other measurement standards, reagents, measuring instruments and laboratory consumables. The scope of 'services' is equally broad, encompassing calibration services, testing services, sampling services, equipment maintenance and PT services to name a few.

14.2 The laboratory needs to ensure that any externally provided products and services are of sufficient quality so as not to adversely affect its activities. This means that the laboratory shall ensure that whatever is externally provided:

- conforms to requirements, regardless of whether it is used in its own laboratory or provided directly to the customer;
- remains within the control of its own QMS, which means defining the controls and their effectiveness for both the products/services and the provider, and understanding their potential impact on the laboratory's own ability to consistently meet requirements;
- is tested and verified before being used.

14.3 The laboratory shall therefore:

- have a procedure for evaluating, selecting, approving and monitoring external providers, including controls, quality criteria and an action plan in case anything goes wrong;
- keep records of the verification processes;
- have a communication strategy with the external providers covering
    - what is required and expected;
    - the relevant criteria;
    - the qualifications and competence of the people performing the services;
    - any control and monitoring to be applied that might be reviewed by the laboratory or their customer.

14.4 There is a distinction between externally provided products and services that support a laboratory in carrying out its day to day activities, and externally provided laboratory activities (i.e. subcontracting of work). Where an external provider is to be used to deliver a particular activity requested by a customer, in addition to addressing the issues in 14.2, the laboratory must inform the customer about the external provider and get their approval.

14.5 There are implications on subcontracting work, especially on a regular basis. It is most likely a management decision to outsource a process, and the risks and opportunities associated with this decision have to be carefully considered. The laboratory must ensure that externally provided services meet the requirements of the customer. In the test report the laboratory must state that the activities have been performed by an external provider, and are therefore outside the scope of accreditation of the laboratory.

15 Analytical task and analytical strategy

15.1 Analysis is a complex multistage activity and analytical work is often an iterative process rather than the linear series of steps shown below. This is especially true for cases where there is no standard method available. All analytical work should be adequately planned and documented. The level of detail required will depend on the complexity of the task.

15.2 Although different standards emphasise different aspects of quality management and some of the steps below are not specifically covered, it is important that the quality management of each stage is considered, and where relevant addressed. Not every step will be required each time a routine measurement is performed, and analytical steps in *italics* are of more significance in the context of non-routine analysis.

- Specification of requirements (Section 17);
- *Information review;*
- *Creative thought;*
- *Study plan*;
- Sampling (Section 18);
- Sample preparation;
- *Preliminary analysis;*
- Identification/confirmation of composition;
- Quantitative analysis;
- Data collection and review;
- Data interpretation/problem solving;
- Reporting/advice.

15.3 Plans will typically indicate the starting and intended finishing point of the particular task together with the strategy for achieving the desired aims. Where, during the course of the work, it is appropriate to change the strategy, the plan should be amended accordingly. Any amendments should be documented and significant changes communicated to and agreed with the customer.

16 Routine vs non-routine analysis

16.1 Non-routine analysis can be considered as:

- tasks which are carried out infrequently, but where reliable methodology is already established;
- tasks where every sample requires a different approach and methodology has to be established at the time.

The latter case is sometimes referred to as 'ad-hoc analysis'. Guidance on QA for research and development and non-routine analysis is given in Eurachem/CITAC Guide CG2 [1].

16.2 The cost of measurements reflects the costs associated with method development, method verification or validation, instrumentation, consumables, ongoing maintenance of equipment, input from personnel, calibration, QC, etc. Many of these costs are independent of the number of samples subsequently analysed using that method. Thus where a single method can be used for a large throughput of samples, the unit analytical cost will be comparatively low. Where a method has to be developed specifically for the analysis of a small number of samples, the unit analytical cost can be very high. For such non-routine analysis some of the costs can be reduced by use of generic methods, i.e. methods which are very broadly applicable. In other instances, subcontracting the work to a laboratory that specialises in the particular type of work would be the most cost-effective solution. When work is subcontracted, the requirements outlined in Section 14.4 apply.

16.3 Many measurements can conveniently be described in terms of an isolation stage and a measurement stage. The purpose of the isolation stage is to simplify the matrix in which the concentration of the analyte is finally measured. Often the isolation procedure may vary very little for a wide variety of analytes in a range of sample matrices. A good example of a generic isolation procedure is the digestion technique used to extract trace metals from foods.

16.4 Similarly, once analytes have been isolated from the sample matrix and are presented in a comparatively clean environment, such as a solvent, it may be possible to have a single generic method to cover the measurement of the concentration of a wide variety of analytes (for example, gas chromatography or UV/visible spectrophotometry).

16.5 The documentation of such generic methods should be designed so that it can easily accommodate the small changes which relate to the extraction, clean-up or measurement of different analytes, for example by the use of tables. Parameters which might be varied include sample size, volume and type of extraction solvents, extraction conditions, chromatographic columns, separation conditions, or spectrometer wavelength settings.

16.6 The value of generic methods for non-routine analysis is that when a new analyte/matrix combination is encountered, it is frequently possible to incorporate it within an existing generic method with appropriate additional validation, measurement uncertainty calculations and documentation. Thus the additional costs incurred are minimised in comparison to the development of a whole new method. The method should define the checks which will need to be carried out for the different analyte or sample type in order to confirm that the analysis is valid. Sufficient information will need to be recorded in order that the work can be repeated in exactly the same manner at a later date. Where a particular analysis subsequently becomes routine, a specific method may be validated and documented.

16.7 It is possible to accredit non-routine analysis and most accreditation bodies will have a policy for assessing such methods and describing them in the laboratory's accreditation scope or schedule. Accreditation of a 'flexible scope', as described in Section 6.21, is one possible option. It is the laboratory's responsibility to demonstrate to the assessors that in using these techniques, it is meeting all of the criteria of the relevant quality standard. In particular, the experience, expertise and training of the personnel involved will be a major factor in determining whether or not such analyses can be accredited.

17 Analytical requirement

17.1 There is a whole section (7.1) in ISO/IEC 17025 [2] devoted to the question 'what exactly does the customer want and need, and does the laboratory have the capabilities and resources to meet the requirements?'

17.2 The laboratory has a duty to provide an analytical service for its customers that is appropriate to solving the customers' problems.

17.3 The key to good analysis is a clear and adequate specification of the requirement. This will need to be produced in co-operation with the customer who may need considerable help to translate their functional requirements into a technical analytical task. The analytical requirement may evolve during the course of a commission but should eventually be agreed by both customer and laboratory. Each party should confirm they have the same understanding of the analytical problem and its solution. Procedures must be in place that address differences between requests and contract before the work commences.

17.4 The specification of the analytical request should address the following issues:

- analytical context;
- information required;
- criticality of test result;
- time constraints;
- cost constraints;
- sampling;
- metrological traceability requirements;
- measurement uncertainty;
- method requirements, including sample preparation;
- required method performance (e.g. targets for measurement uncertainty and/or for individual performance characteristics such as precision and limit of detection (LOD));
- identification/confirmation/fingerprinting;
- QA/QC requirements;
- method development/approval.

17.5 Table 4 in the Eurachem Method Validation Guide [15] contains a number of possible analytical questions which might be posed in formalising an analytical requirement, and the related performance characteristics of the method to be evaluated.

17.6 One of the key steps in agreeing the analytical requirement is to determine the level of method performance required. This can be defined in terms of targets for individual method performance characteristics such as precision, bias and LOD, or by setting a target measurement uncertainty [39]. How the performance criteria are set will vary in different situations. In some cases the performance requirements may be specified in regulations. In other cases they may be agreed with the customer on the basis of analysis they have previously commissioned, or they may be set in relation to the established performance levels for similar methods. If a standard method is being used, it is likely that some performance characteristics will be documented within the method.

17.7 The laboratory shall have procedures in place for the review of requests, tenders and contracts. The review should also cover any work that is subcontracted by the laboratory. Good communication between laboratory and customer is crucial, especially when contracts need to be amended or delays can be expected. Customers value advice and guidance in technical matters. Needless to say, records of reviews and significant changes need to be maintained, as well as of any discussions with the customer. Note that in the case of internal customers, it is likely that these procedures can be simplified.

17.8 In the event that the customer requests a statement of conformity from the laboratory, before formalising the contract, the decision rule to be applied in the statement of conformity shall be defined and agreed (see Section 26).

17.9 Subcontracting, if deemed necessary, is already covered in Section 14.

17.10 The laboratory shall cooperate with customers in clarifying the customer's request and also in monitoring the laboratory's performance. If requested, the laboratory shall provide the customer with reasonable access to relevant areas of the laboratory for the witnessing of tests and/or calibrations performed for the customer.

17.11 The laboratory should inform the customer about the significance of accreditation, and of the accreditation status of the tests, calibrations and/or sampling covered by the customer's request.

18 Sampling

18.1 Measurement and test results may be required for a variety of reasons, including identifying the presence of a substance in a material, establishing an average analyte value across a material, establishing an analyte concentration profile across a material, or determining local contamination in a material. In some cases, for example forensic analysis, it may be appropriate to examine the entire material. In others, it is appropriate to take a sample. Clearly the way samples are taken will depend on the reason for the analysis.

18.2 If the test portion is not sufficiently representative of the original material, it will not be possible to relate the analytical result obtained to the properties of the original material, no matter how good the analytical method is or how carefully the analysis is performed.

18.3 When a laboratory carries out sampling for subsequent testing it must have a documented sampling plan and documented procedures for undertaking the sampling. The sampling plan and procedures should be developed in such a way as to ensure the validity of results obtained. As mentioned above, inappropriate sampling will seriously impact the fitness-for-purpose of results obtained. Where possible, sampling plans should be based on appropriate statistical methods and both the plan and the documented sampling procedures must be available at the location where the sampling is undertaken.

18.4 Note that ISO/IEC 17025 [2] considers sampling to be a laboratory activity (along with testing and calibration). The clauses of the standard may therefore apply to sampling, depending on the accreditation scope and sampling activity.

18.5 Sampling always contributes to the measurement uncertainty [40]. As analytical methodology improves and methods allow or require the use of smaller test portions, the uncertainties associated with sampling become increasingly important and can significantly increase the total measurement uncertainty associated with the measurement result. The measurement uncertainty introduced by subsampling carried out within the laboratory should always be included in the test result measurement uncertainty. However, the measurement uncertainty associated with the primary sampling process (carried out prior to submission of a sample to the laboratory, and often outside of its control) is commonly treated separately, but ideally treated as an integral part of the whole measurement process [40] and included in the validation [41]. ISO/IEC 17025 [2] requires that all significant contributions to the measurement uncertainty are taken into account, including those arising from sampling.

18.6 In many areas of testing the problems associated with sampling have been addressed and methods have been validated and published. Sampling procedures are sometimes prescribed in legislation as in, for example, the EU Regulation relating to certain contaminants in food [42]. Analysts should also refer to national or sectoral standards as appropriate. Where specific methods are not available, the analyst should rely on experience or adapt methods from similar applications. When in doubt, the material of interest, and any samples taken from it, should always be treated as heterogeneous.

18.7 Selection of an appropriate sample or samples, from a larger amount of material, is a very important stage in the measurement process. It is rarely straightforward. If the final results produced are to be of any practical value, the sampling stages should be carried out by, or under the direction of, a skilled sampler with an understanding of the overall context of the analysis. Such a person is likely to be an experienced analyst or someone specifically trained in sampling. Where it is not practical to use such skilled people to take the samples, the laboratory is encouraged to liaise with the customer to provide advice and possibly practical assistance, in order to ensure the sampling is sufficiently representative of the sampling target (i.e. the portion of material, at a particular time, that the sample is intended to represent, [40]).

18.8 NABs have their own procedures for the accreditation of sampling and can accredit sampling as a stand-alone activity.

18.9 The sampling procedure should be sufficiently detailed to allow sampling to be carried out reliably and consistently. It should include details of the sampling plan, how sampling sites and samples are to be selected, how the samples should be taken and any particular storage or sample treatment requirements. It is important when documenting a sampling procedure to ensure that the terms used are clearly defined, so that the procedure will be clear to other users. Similarly it is important to ensure when comparing two separate procedures that the terminology used is consistent. For example, care should be taken in the use of the word ‘bulk’ since this can refer to either the combining of individual

samples, or an undifferentiated mass. Similarly, the word 'sample' has been applied to material at many different stages in the measurement process, so much more specific terms are required to avoid confusion (e.g. primary sample, sub-sample, laboratory sample, test sample, test portion and test solution [40]).

18.10 A useful treatment of sampling terminology is given in recommendations published by IUPAC [43], which describes the terms used in the sampling of bulk goods or packaged goods. IUPAC have also published separate guidance on terminology in soil sampling [44]. An overview of terminology relevant to sampling is provided by Eurachem [40].

18.11 In the case of sampling bulk or packaged goods, the sampling procedure reduces the original consignment through lots or batches, increments, primary or gross samples, composite or aggregate samples, subsamples or secondary samples to a laboratory sample. The laboratory sample, if heterogeneous, may be further prepared to produce the test sample. The laboratory sample or the test sample is deemed to be the end of the sampling procedure. Operations within this procedure are likely to be subject to sampling uncertainties. Activities undertaken after this step are generally considered to be 'analytical operations' which do not contribute to the uncertainty associated with sampling.

18.12 For the purposes of the guidance given below the following definitions, based on those proposed by IUPAC [43], have been used:

Sample: A portion of material selected to represent a larger body of material.

Sampling plan: A predetermined procedure for the selection, withdrawal, preservation, and preparation of the portions to be removed from a population as samples.

Primary sample: The collection of one or more increments or units initially taken from a population.

Subsample: This term may refer to: a portion of the sample obtained by selection or division; an individual unit of the lot taken as part of the sample or; the final unit of multistage sampling.

Laboratory sample: The sample or subsample delivered to the laboratory.

Test sample: The sample, prepared from the laboratory sample, from which test portions are removed for analysis.

Sample preparation: Procedures followed to select the test portion from the laboratory sample. They include: in-laboratory processing; mixing; reducing; coning and quartering; riffling; and milling and grinding.

Test portion: This refers to the actual portion of material removed from the test sample for the analysis.

Sample handling: Although not defined by IUPAC, this term is frequently used to refer to the manipulation to which samples are exposed after the selection from the original material through to the disposal of all samples and test portions.

18.13 The sampling process should be described in a detailed sampling plan. This should specify the number and size of the portions that need to be taken from the bulk material, and describe how the laboratory sample is to be obtained. The size and number of test samples to be taken from the laboratory sample must also be documented. Sampling plans may be random, systematic or sequential and they may be undertaken to obtain quantitative or qualitative information, or to determine conformance or nonconformance with a specification.

18.14 There are important rules to be followed when designing, adapting, or following a sampling plan.

18.14.1 The sampling plan should be designed in such a way that the resulting data will be representative of the parameters of interest (i.e. contribute an acceptable amount of measurement uncertainty) and allow for all questions, as stated in the analytical requirement, to be answered. The sampling strategy used will depend on whether:

a) the average analyte concentration in the material is required;

b) the analyte profile across the material is required;

c) the material is suspected of contamination by a particular analyte;

d) the contaminant is heterogeneously distributed (occurs in hot spots) in the material;

e) there are other non-analytical factors to consider, including the nature of the area under examination.

18.14.2 Care should be taken in assuming that a material is homogeneous, even when it appears to be. Where a material is clearly in two or more physical phases, the distribution of the analyte may vary within each phase. It may be appropriate to separate the phases and treat them as separate samples. Similarly, it may be appropriate to combine and homogenise the phases to form a

single sample. In solids there may be a considerable variation in analyte concentration if the particle size distribution of the main material varies significantly, and over a period of time the material may settle. Before sampling it may be appropriate, if practical, to mix the material to ensure a sufficiently representative particle size distribution. Similarly analyte concentration may vary across a solid where different parts of the material have been subjected to different stresses. For example, consider the measurement of vinyl chloride monomer (VCM) in the fabric of a PVC bottle. The concentration of VCM varies significantly depending on whether it is measured at the neck of the bottle, the shoulder, the sides or the base.

18.14.3 The properties of the analyte(s) of interest should be taken into account. Volatility, sensitivity to light, thermal stability and chemical reactivity may be important considerations in designing the sampling plan and choosing equipment, packaging and storage conditions. It may be appropriate to add chemicals such as acids, or antioxidants to the sample to stabilise it. Equipment used for sampling, subsampling, sample handling, sample preparation and sample extraction, should be selected in order to avoid unintended changes to the nature of the sample which may influence the final results. This is of particular importance in trace level analysis where there is a danger of adsorption of the analyte onto the storage vessel. The significance of gravimetric or volumetric uncertainties during sampling should be considered and any critical measuring instruments calibrated.

18.14.4 It may be necessary to consider the use and value of the remainder of the original material once a sample has been removed for analysis. Poorly considered sampling, especially if destructive, may render the whole consignment worthless.

18.14.5 Whatever strategy is used for the sampling, it is of vital importance that those performing it keep a clear record of the procedures followed and how the samples were taken. Information to be recorded includes:

- the sampling plan used,
- the date and time the sampling was undertaken,
- sample identification information (e.g. a reference number, amount, name),
- identification of the sampler,
- any specific conditions that could influence how samples have been taken (e.g. environmental conditions).

18.14.6 Where more than one sample is taken from the original material it may be useful to include a diagram as part of the documentation to indicate the pattern of sampling. This will make it easier to repeat the sampling at a later date and also may assist in drawing conclusions from the test results. A typical application where such a scheme would be useful is the sampling of soils over a wide area to monitor fall-out from stack emissions.

18.15 Where the laboratory has not been responsible for the sampling stage, it should state in the report that the samples were analysed as received.

18.16 Once received into the laboratory, the laboratory sample(s) may require further treatment such as removal of extraneous material, subdivision and/or milling and grinding to make it suitable for analysis.

18.17 Unless otherwise specified the test portion taken for analysis must be sufficiently representative of the laboratory sample. To ensure that the test portion is sufficiently homogeneous it may be necessary to reduce the particle size by grinding or milling. However, if the laboratory sample is large it may be necessary to subdivide it first. Care should be taken to ensure that segregation does not occur during subdivision. In some cases it will be necessary to crush or coarsely grind the sample prior to subdivision into test samples. The sample may be subdivided using a variety of mechanisms, including coning and quartering, riffling, or by means of a rotating sample divider or a centrifugal divider. The particle size reduction step may be performed either manually (mortar and pestle) or mechanically using crushers or mills. Care must be taken during these processes to avoid cross contamination of samples, to ensure that the equipment does not contaminate the sample (e.g. metals) and that the composition of the sample is not altered (e.g. loss of moisture). Many standard methods of analysis contain a section that details the preparation of the laboratory sample prior to the removal of the test portion for analysis. In other instances legislation deals with this aspect as a generic issue.

18.18 The analytical operations begin with the removal of a known amount (test portion) from the laboratory sample or the test sample, then proceed through various operations to the final measurement.

18.19 To fully evaluate an analytical result for conformity assessment, or for other purposes, it is important to have knowledge of the sampling plan and its statistical basis. Sampling procedures for inspection by variables [45-49] assume that the characteristic being inspected is measurable and follows the normal distribution. In contrast, sampling for inspection by attributes [50-55] is a method whereby either the unit of product is classified as conforming or nonconforming, or the number of nonconformities in the unit of product is counted with respect to a given set of requirements. In inspection by attributes the risks associated with acceptance/rejection of nonconformities are predetermined by the Acceptable Quality Level and the Rejectable Quality Level, defined using appropriate statistical techniques.

19 Sample handling and storage

19.1 Ensuring the identity and integrity of the sample are maintained is of the utmost importance. Special care shall be taken to avoid deterioration, loss or damage to the item during sampling, handling, transport, storage, preparation and testing.

19.2 If any handling instructions are provided with the sample they shall be followed. For example, when items have to be stored or conditioned under specified environmental conditions, these conditions shall be maintained, monitored and recorded.

19.3 If a sample does not conform to the description provided when received or there is doubt about the suitability of an item, the laboratory shall consult the customer for further instructions before proceeding, and shall record the discussion. When the customer requires the deviating item to be tested or calibrated the laboratory shall include a disclaimer in the report or certificate indicating that the results may be compromised.

19.4 Sample packaging, and equipment used for sample manipulation, should be selected so that all surfaces in contact with the sample are essentially inert. Particular attention should be paid to possible contamination of samples by metals or plasticisers leaching from the container or its stopper into the sample. The packaging should also enable the sample to be handled without causing a chemical, microbiological, or other hazard.

19.5 The laboratory shall have procedures in place for the cleaning of all items used in sampling, including flasks and auxiliary equipment. Records of cleaning processes should be maintained.

19.6 The closure of the packaging should be adequate to ensure there is no leakage of sample from the container, and that the sample itself cannot be contaminated. In some circumstances, for example where samples have been taken for legal purposes, the sample may be sealed so that access to the sample is only possible by breaking the seal. Confirmation of the satisfactory condition of the seals will normally then form part of the analytical report.

19.7 The sample label is an important aspect of documentation and should unambiguously identify the sample to related plans or notes. The identification shall be retained while the item is under the responsibility of the laboratory. Labelling is particularly important later in the analytical process, when the sample may have been divided, subsampled, or modified in some way. In such circumstances, additional information may be appropriate, such as references to the main sample, and to any processes used to extract or subsample the sample. Labelling must be firmly attached to the sample packaging and, where appropriate, be resistant to fading, autoclaving, sample or reagent spillage, and reasonable changes in temperature and humidity. In many laboratories, in particular those handling high sample numbers, samples are identified by means of barcodes linked to a Laboratory Information Management System (LIMS).

19.8 Some samples, those involved in litigation for example, may have special labelling and documentation requirements. Labels may be required to identify all those who have been involved with the sample, including the person taking the sample and the analysts involved in the testing. This may be supported by receipts, to testify that one signatory (as identified on the label) has handed the sample to the next signatory, thus proving that sample continuity has been maintained. This is commonly known as ‘chain of custody’.

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20 Method selection and development

20.1 It is the laboratory's responsibility to use methods which are appropriate for the required application. Ideally this should also include the procedures use to obtain the primary sample [41]. The laboratory may use its own judgement or select a method in consultation with the customer; in some cases the method may be specified in regulation or by the customer. If methods are provided by the customer, the laboratory shall ensure its capacity to carry them out and to achieve the quality requirements previously agreed with the customer.

20.2 Quality standards often favour the use of standard or collaboratively tested methods wherever possible. Whilst this may be desirable in situations where a method is to be widely used, or defined in regulation, sometimes a laboratory may have a more suitable method of its own. The most important considerations are that the method shall be suitable for the purpose intended, be adequately validated and documented, and provide results that are traceable to stated references with an appropriate level of measurement uncertainty.

20.3 The validation of standard or collaboratively tested methods should not be taken for granted. The laboratory shall make sure that the method validation is adequate for the required purpose and that the laboratory personnel can achieve the stated performance criteria. Guidance on the topic of verifying the performance of a standard method is given in the Eurachem Guide on method validation [15].

20.4 Methods developed in-house shall be adequately validated, documented, and authorised before use. Estimation of measurement uncertainty shall form part of this validation process. Advice on method validation and measurement uncertainty is given in Sections 21 and 24, respectively.

20.5 Documentation of methods shall include:

- information on the scope of the method and any limitations;
- values for key performance characteristics such as repeatability, bias and LOD;
- procedures for calibration and QC.

20.6 Information on how the result shall be reported, including the statement of its measurement uncertainty, shall also be included along with instructions on how to deal with failures or out-of-specification test results. Guidance on investigating and reporting out-of-specification results is provided by IUPAC/CITAC [56]. A laboratory documenting methods may find it convenient to adopt a common format, such as the useful model provided in ISO 78-2 [57]. The documentation of methods is also discussed in the Eurachem Guide on method validation [15]. In addition, advice is available from other sources such as national standardisation bodies and accreditation bodies.

20.7 Developments in methodology and techniques will require methods to be changed from time to time. Modification of methods may also be necessary as a result of investigations following poor performance in PTs, or failure to meet IQC criteria. Method documentation must therefore be subject to adequate document control. Where hard copies of the methods are issued, each copy of the method shall show the issue number, date, issuing authority, and copy number. It must be possible to determine from records the most up-to-date version of each method which is authorised for use.

20.8 Obsolete methods shall be withdrawn but must be retained for archive purposes and clearly labelled as obsolete. The difference in performance between revised and obsolete methods should be established so that it is possible to compare new and old data.

20.9 When methods are modified, consideration needs to be given as to whether the validation also needs to be updated. This will depend on the extent and significance of the modification. The modification may be of a minor nature, involving different sample sizes, different reagents etc. Alternatively, it may involve significant changes, such as the use of different technology or methodology. Revalidation shall also be considered following changes in premises or instrumentation. The extent of revalidation will depend on the nature of the change. The laboratory, taking into account the nature of their tests, shall establish rules regarding the extent of revalidation required.

20.10 Regular (though not necessarily frequent) review of the performance is required to ensure that methods are still fit-for-purpose. This may be carried out by an overall review of the outcomes of QC activities, such as results from IQC and PT data.

21 Method validation and verification

21.1 Laboratories shall use appropriate methods for carrying out tests, and ideally these should also include the procedures used to take the primary samples [41]. Selection and development of methods is discussed in Section 20; broadly, laboratories have the following options when selecting a method to meet a particular analytical requirement:

- standard methods published by an international, regional or national body, or by a reputable technical organisation;
- methods published in scientific journals or specified by instrument manufacturers;
- standard or other published methods modified by the laboratory;
- methods developed by the laboratory (often referred to as 'in-house' methods).

21.2 Regardless of the source of the method, checks need to be carried out to ensure that the performance characteristics of a method are understood, and to demonstrate that the method is scientifically sound under the conditions in which it is to be applied before it is put into routine use. The definitions of verification and validation are given in 3.20 and 3.21, respectively. ISO/IEC 17025 [2] requires a laboratory to verify that it can properly perform methods and achieve the required performance before putting them into use. In addition, validation is required for non-standard methods, methods developed in-house by the laboratory and for standard methods that have been modified or are being used outside of their original stated scope. Validation of a method establishes, by systematic laboratory studies, that the method is fit-for-purpose, i.e. its performance characteristics are capable of producing results in line with the needs of the customer. A method validation study starts with clear, sufficiently detailed and unambiguous descriptions of both the measurand and the method. Guidance on how to achieve this is provided by Eurachem [12, 15]. The next step is a statement of the criteria to be met, in terms of analytical performance. In some cases they may be clearly stated in regulations (see, for example, Commission Regulation (EC) 333/2007 [42]), but usually it is the task of the laboratory to translate the customer's needs into analytical requirements. The performance characteristics usually included in a validation study are:

- selectivity (dealing with potential interference problems);
- working range and linearity;
- LOD/LOQ;
- precision (single laboratory: repeatability, intermediate precision);
- trueness (dealing with bias and recovery issues);
- robustness/ruggedness.

21.3 Good practice in method validation is described in a Eurachem Guide [15] to which the reader is referred for more detailed explanation and guidance on this topic. Note that while meanings of the above terms are generally well understood across different sectors, there are differences in the conventions used in their determination. Thus when reporting validation data, any conventions followed should be stated.

21.4 The extent of validation must be clearly stated in the documented method so that the users can assess the suitability of the method for their particular needs. This may be done with an appropriate summary of the results and reference to a separate validation report.

21.5 Standard methods are normally developed and validated collaboratively by a group of experts [58-63]. This development should include consideration of all of the necessary aspects of validation and related measurement uncertainty. However, the responsibility remains firmly with the user to ensure that the validation documented in the method is sufficiently complete to fully meet their needs. This implies that any factors likely to influence the measurement results within the stated scope of the method, but not adequately covered by the collaborative study, should be identified and evaluated in terms of their contribution to the parameters subject to validation and in particular to the estimate of measurement uncertainty. Even if the validation is complete, as mentioned above, the user will still need to verify that the documented performance characteristics (e.g. trueness and precision) can be met in their own laboratory and that they are fit-for-purpose.

21.6 The following explanations supplement those in other parts of this Guide, a more detailed explanation is given in the Eurachem Guide [15]. For further information on the terminology related to method validation and verification see the VIM [11] and the Eurachem Guide [12]. The following parameters are mostly related to quantitative methods. Information on establishing the

performance of qualitative methods can be found in the Eurachem/CITAC Guide [64].

21.7 ***Selectivity*** of a method refers to the extent to which the method can be used to determine particular analytes in mixtures or matrices without interferences from other components with similar characteristics. The applicability of the method should be studied using various samples, ranging from pure measurement standards to mixtures with complex matrices. In each case the recovery of the analyte(s) of interest should be determined and the influences of suspected interferences duly stated. Any restrictions on the applicability of the method should be recorded in the method documentation.

21.8 ***Confirmation (of identity)*** requires the measurement to be performed by more than one technique, where the techniques are based on different physico-chemical principles. For mass spectrometry techniques, special criteria and identification points can be used to confirm identity (for example, criteria defined by CODEX for the determination of pesticide residues [65]). Confirmation increases confidence in the result obtained. In some applications, for example the analysis of unknown organic compounds by gas chromatography, the use of confirmatory techniques is essential.

21.9 ***Working range and linear range:*** The 'working range' is the interval over which the method provides results with an acceptable uncertainty. The lower end of the working range is bounded by the LOQ. The upper end of the working range is defined by concentrations at which significant anomalies in the analytical sensitivity are observed. For quantitative analysis, the working range for a method is determined by examining materials with known analyte concentrations and determining the concentration range for which acceptable measurement uncertainty can be achieved. A prerequisite for carrying out quantification is to establish a calibration function for the final measuring instrument. For that reason, it may be relevant to consider separately the method working range and the instrument working range. The linear range is determined by the analysis of a number of measurement standards of varying analyte concentrations and calculating the regression statistics from the results, usually using the method of least squares. For the instrument working range the relationship of analyte response to concentration does not have to be perfectly linear for a method to be effective. Where linearity is unattainable for a particular procedure, a suitable algorithm for calibration should be determined. For some measuring instruments and methods, the working range may be more extensive than the linear range. The working range needs to be established for each matrix covered in the method scope.

21.10 The ***limit of detection (LOD)*** is the lowest amount of the analyte that can be detected by the method at a specified level of confidence. Its value is likely to be different for different types of sample. LOD is a complex parameter which is particularly important in trace level analysis. For more detailed explanation and guidance refer to the Eurachem Guide [15].

21.11 The ***limit of quantification (LOQ)*** is the lowest concentration of analyte that can be determined with an acceptable level of measurement uncertainty and can, therefore, be set arbitrarily as the required lower end of the method working range. For more detailed explanation and guidance refer to the Eurachem Guide [15].

21.12 ***Precision*** is a measure of the closeness of agreement between mutually independent measurement results obtained by replicate measurements on the same or similar objects under specified conditions. It is usually expressed by statistical parameters which describe the spread of results, typically a standard deviation. Precision is generally dependent on analyte concentration, and this dependence should be determined and documented. Deciding on the 'specified conditions' is an important aspect of evaluating measurement precision. *Repeatability* is a type of precision expected to represent the smallest variation in results. It is a measure of variability in results when measurements are performed on the same material by a single analyst using the same method and equipment over a short timescale. *Intermediate precision* gives an estimate of the variation in results when measurements on the same material are made in a single laboratory using the same method over an extended timescale, and therefore under conditions that are more variable than repeatability conditions. Other parameters can be varied during the period of the study (e.g. analyst, reagents, equipment) and it is important for these to be documented. Reproducibility, expected to represent the largest variation in results, is a measure of the variability in results when measurements are made in different laboratories.

21.13 ***Trueness*** of a method is generally estimated as bias, i.e. the systematic error. Three approaches are commonly used during validation for the determination of bias: a) analysis of RMs, b) recovery experiments using spiked samples, and c)

comparison with results obtained using another method.

21.14 ***Ruggedness*** (sometimes also called ***robustness***) provides an indication of a method's reliability during normal use. A ruggedness study evaluates a method's capacity to remain unaffected by small variations in method parameters. It involves deliberately introducing small changes to the method and examining the consequences. A large number of factors may need to be considered, but because most of these will have a negligible effect, it will normally be possible to vary several at once, particularly if experimental design tools are used. A commonly applied approach is described by AOAC International [66] and a practical example of its application in the area of testing for drug residues in food of animal origin is given in Commission Decision 657/2002/EC [67]. Ruggedness should be established for methods developed in-house. However, it is not generally necessary for an individual laboratory to carry out ruggedness testing when implementing a standard method being used within in its scope, as ruggedness should have been established prior to publication of the method.

22 Metrological traceability

22.1 The formal definition of metrological traceability is given in 3.17. Practical guidance is provided by Eurachem/CITAC [13] and IUPAC [68]. In addition, ISO/IEC 17025:2017 [2] includes a new informative Annex which provides additional information on metrological traceability. Metrological traceability is essential because it provides the linkage that ensures that measurement results obtained in different laboratories or at different times are comparable. To achieve this it is necessary to link all the individual measurement results to some common, stable reference. According to VIM 3 [11] such reference points can be a measurement unit through its practical realisation (preferably those included in the International System of Units, the SI), a measurement standard (etalon) or a measurement procedure including the measurement unit (e.g. a reference measurement procedure). A complete traceability chain is achieved through a calibration hierarchy consisting of primary measurement standards (or other high level measurement standards) which are used to establish secondary measurement standards that can be used to calibrate working level standards and related measuring systems. Laboratories normally purchase their measurement standards from commercial producers. These are supplied with certificates demonstrating their metrological traceability to higher level measurement standards. ILAC document P10 [69] describes the ILAC policy with regard to metrological traceability requirements and supports the implementation of ISO/IEC 17025 and ISO 15189 [3], providing laboratories with guidance on how to address the metrological traceability issue. It has to be noted that every step in the traceability chain adds additional measurement uncertainty.

22.2 Whenever possible, metrological traceability to SI units through suitable measurement standards should be documented, in order to support the comparability of measurement results across space and time. According to ISO/IEC 17025 [2], this can be achieved through:

- calibration provided by a competent laboratory (those fulfilling the requirements of ISO/IEC 17025 are considered to be competent); or
- certified values of CRMs provided by a competent producer with stated metrological traceability to the SI (RM producers fulfilling the requirements of ISO 17034 [20] are considered to be competent); or
- direct realisation of the SI units ensured by comparison, directly or indirectly, with national or international standards.

22.3 It is acknowledged that some measurement results (e.g. pH, concentration of some biological substances, hardness) have no SI units but even these can be defined. Such measurement results should be traceable to internationally agreed measurement references (e.g. pH scale [70], WHO RMs or Mohs scale). Therefore although traceability to SI is the ideal, it is not the only option for the start of a traceability chain.

22.4 The results from chemical measurements are generally obtained by calculating the value of the measurand from a measurement model (or measurement function) that involves the values of other quantities, such as mass, volume, composition of measurement standards etc. This measurement model should be established during method development. Other quantities not present in the measurement model, such as pH, temperature etc. may also significantly affect the result. In addition to the measurement model, the method should also identify these 'specified conditions'. Method validation (see Section 21) demonstrates that the measurement model and specified conditions are sufficient to produce results that are fit-for-purpose. For the measurement results to be traceable, all the quantity values in the measurement model and the values of the specified conditions must also be traceable to appropriate references. This is achieved by calibration using appropriate measurement standards.

22.5 For some measurements, the measurand can only be defined with reference to an agreed method (e.g. mass fraction of fat in food or mass concentration of lead extracted from the paint on a toy following the measurement procedure described in European Standard EN 71-3 'Safety of Toys. Migration of certain elements' [71]). Such measurands are sometimes referred to as 'operationally defined measurands' [20] and the methods used to determine them as 'empirical methods'. In such cases comparability of measurement results can only be achieved by the use of relevant agreed methods and metrological traceability is established as described in Section 22.7.

22.6 As mentioned in Section 22.4 results from chemical measurements generally require the determination of a number of quantities (such as

mass and volume) in addition to the measurement of the analyte of interest. Calibration is therefore usually applied to different parts of the measuring system. Establishing the metrological traceability of physical quantities such as mass and volume is readily achieved, at the level of uncertainty needed for analytical measurements, by calibration of the relevant equipment according to well established procedures. The problem areas for analysts often relate to the calibration of measuring instruments such as chromatographs or spectrometers used in the determination of analytes. Calibration is generally based on the repeated measurement of suitable measurement standards having values with demonstrable metrological traceability (e.g. pure substances or solutions of pure substances). Identity and purity of the chosen RMs are important issues, the former being more of a problem in organic chemistry, where much higher levels of structural detail are often required and confusion with similar components can readily occur. However, only in the case of some organic materials, where purity and stability problems can be severe, or where low measurement uncertainty is required, will purity be a significant problem. A major issue in chemical analysis is the different analytical behaviour of atoms and molecules depending on their surrounding environment, i.e. a substance in pure water will behave differently from the same substance in a sample of food, waste water or blood. This is known as 'matrix effect'. Therefore, as mentioned in 22.4, in addition to calibration of measuring equipment, the metrological traceability of measurement results in analytical sciences also relies on method validation, to establish that the method actually measures what it is intended to measure (e.g. the mass fraction of methyl mercury in fish) and confirmation that the measurement model used to calculate the results, including appropriate 'recovery' factors, if necessary, is valid. The Eurachem/CITAC Guide [13] contains a detailed discussion and illustrative examples addressing the issues associated with establishing the metrological traceability of results from chemical analysis.

22.7 Most measurement results from chemical analysis can, in principle, be made traceable to the mole. However, when the measurand is defined in operational terms, such as extractable fat or protein based on a nitrogen determination, then establishing metrological traceability of these measurement results to the mole is not feasible. In such cases the measurand is defined by the method and variations in the protocol (e.g. a different solvent or a different conversion factor) lead to a different measurand. When using such 'empirical' methods metrological traceability is to the agreed method (e.g. standard method), which shall be followed exactly, as well as to the corresponding SI units for the quantities used to calculate the result, e.g. mass and volume, the values produced by the method and/or the values carried by a RM.

23 Calibration

23.1 ISO/IEC 17025 [2] is used for accreditation of both calibration and testing laboratories. Thus testing laboratories can use services of calibration laboratories (so called external calibration) to calibrate some of their equipment such as piston pipettes or weights for checking their balances. If a testing laboratory intends to perform calibration of its equipment internally (so called in-house calibration), it should comply with the same technical requirements as a calibration laboratory. Calibration should be carried out according to documented calibration procedures and should demonstrate the ability to estimate uncertainty and the competence of the personnel performing the calibration [69].

23.2 As discussed in Section 22, calibration is the fundamental process in establishing metrological traceability. It is the process of establishing the relationship between values shown by a measuring instrument and the values provided by measurement standards (see 3.18 for the formal definition). A discussion of the concept of calibration can be found in Eurachem Guides [12, 13]. Calibration is usually applied to different parts of a measuring system (e.g. equipment such as pipettes and analytical balances, as well as instruments such as HPLC or GC systems used to determine the concentration of the analyte). ISO/IEC 17025 [2] requires equipment to be calibrated when the measurement accuracy/uncertainty affects the validity of the reported results and where it is required to establish the metrological traceability of results.

23.3 The overall programme for calibration in the laboratory shall be designed to ensure that all measurements that have a significant effect on results are traceable to a suitable common stable reference (see Section 22). For chemical measurements, it is often possible to purchase suitable CRMs for calibration. Because the values are traceable to national or international standards, their use is recommended where practicable. Where appropriate CRMs are not available, alternative materials with suitable properties, homogeneity and stability shall be selected. More detailed information on RMs is given in Section 13. Information on the selection of suitable measurement standards for calibration is given in the Eurachem/CITAC Guide on metrological traceability [13]. Guidance on linear calibration using RMs is given in ISO 11095 [72].

23.4 Individual calibration programmes shall be established depending on the specific requirements of the analytical method. Items such as balances and thermometers are calibrated less frequently because they are relatively stable, whereas the responses of measuring instruments such as chromatographs or spectrometers tend to vary with time much more and are typically calibrated much more frequently. In some cases, frequent drift checks and recalibration during the course of a single measurement session may be required. It is recommended to check the calibration of any relevant instrument after any shutdown and following service or other substantial maintenance. The level and frequency of calibration shall be based on previous experience and shall be at least that recommended by the manufacturer. Guidance on calibration is given in Annex B which includes typical calibration intervals for various types of simple instruments and indicates the parameters which may require calibration when using more complex analytical instruments. The frequency of calibration required will depend on the stability of the measuring system, the level of measurement uncertainty required and the criticality of the work. Additional guidance on how to establish suitable calibration intervals is given by OIML and ILAC [73].

23.5 Analytical tests may be grouped depending on the type of calibration required.

23.5.1 Some analytical tests depend critically on the measurement of physical properties, such as weight measurement in gravimetry and volume measurement in titrimetry. Since these measurements have a significant effect on the results of the test, a suitable calibration programme for these quantities is essential. The requirements and methods for the calibration and control of balances are described in a Euramet Guide [74], while procedures for the calibration of volumetric devices, such as piston pipettes and burettes, are described in ISO 8655 Parts 1-7 [75-81]. In addition, the calibration of measuring devices used to establish the purity or concentration of all the chemical standards used needs to be considered.

23.5.2 Where a test is used to measure an operationally defined property of a sample, such as flashpoint, equipment is often defined in a national or international standard method. RMs with metrologically traceable values should, where available, be used for calibration purposes. Calibration of measuring instruments used in the method shall be carried out for each measurement tool in the test (for example, thermometer and

barometer for flashpoint). New or newly acquired equipment must be checked by the laboratory before use to ensure conformity with the specified design, dimensions and performance requirements.

23.5.3 Measuring instruments which require calibration as part of their normal operation, such as spectrometers or chromatographs, should be calibrated using RMs of known composition (usually solutions of pure chemicals). For further information see the Eurachem/CITAC Guide [13] and, e.g. OIML Recommendation 135 [82].

23.5.4 In some cases, calibration of the whole analytical process can be carried out by comparing the measurement output from a sample with the output produced by a suitable RM that has been subjected to the same full analytical process as the sample (e.g. through the use of an internal standard). The RM may be either a synthetic mixture prepared in the laboratory from materials of known (and preferably certified) purity, or a purchased certified matrix RM. However, in such cases, a close match between the test sample and the matrix RM, in terms of the nature of the matrix and the concentration of the analyte, has to be assured. ISO 33403 provides guidance on the use of RMs [35].

23.6 Procedures for performing calibrations shall be adequately documented, either as part of a specific analytical method or as a general calibration document. The documentation shall include:

- how to perform the calibration and intermediate checks of calibration status;
- how to determine the uncertainty of the calibration;
- how frequently calibration and checks are required;
- action to be taken in the event of calibration failure.

23.7 A description of how to estimate the uncertainties associated with a linear least squares calibration curve is given in the Eurachem/CITAC Guide [14]). Frequency intervals for the calibration of physical measurement standards shall also be indicated and, where feasible, procedures and plans for intermediate checks of their calibration status should be in place.

23.8 Calibration information (including calibration intervals) shall be marked on a label or otherwise identified so that the user of a measuring instrument can easily monitor the status of its calibration.

23.9 The calibration of volumetric glassware is primarily performed indirectly by mass determination of a specific volume of water of known density at a given temperature [83]. If the glassware is subsequently used with liquids having properties that are very different from water (wetting characteristics, surface tension etc.) the uncertainty in the measured volume would be expected to increase. This is particularly pertinent for volumetric glassware calibrated to deliver a fixed volume. Where small uncertainties are required for test results, it is recommended that the volume is determined indirectly through mass and density of the particular liquid(s).

24 Measurement uncertainty

24.1 Measurement uncertainty is formally defined in 3.19. An internationally agreed approach to the evaluation of measurement uncertainty is described in the Guide to the expression of uncertainty in measurement (GUM) [84]. An interpretation for analytical measurements, including a number of worked examples, is given in a Eurachem/CITAC Guide [14]. Measurement uncertainty characterises the range of values attributable to the measurand, at a specified level of confidence. Every measurement result has an uncertainty associated with it, deriving from errors arising in the various stages of sampling and analysis and from imperfect knowledge of factors affecting the result. For measurement results to be of practical value it is necessary to have some knowledge of their uncertainty. A statement of the measurement uncertainty associated with a result conveys to the customer the 'quality' of the result.

24.2 ISO/IEC 17025 [2] requires laboratories to evaluate the measurement uncertainty of their results. There is also a requirement to report measurement uncertainty under specific circumstances, for example, where it is relevant to the interpretation of the test result (which is often the case) or when it is requested by the customer.

24.3 The estimation of measurement uncertainty provides several advantages to both accredited and non-accredited laboratories, including:

- a clear and quantitative statement of the quality of measurement results;
- improved knowledge of the (overall or individual) factors that affect the measurement result. This may provide key information for improving/optimising the method and for identifying efficient and cost-effective corrective measures, when necessary;
- competitive advantage due to the added value the measurement uncertainty estimation can provide for customers, particularly when assessing compliance with specifications;
- less stringent control on influence quantities (e.g. environmental temperature, pH value of the sample) shown by the uncertainty evaluation to provide a negligible contribution to the overall uncertainty of the measurement result.

24.4 A wide variety of factors affect the result obtained from an analytical measurement. For example, temperature effects on volumetric measurements, interferences from matrix components, an individual analyst's interpretation of the method and incomplete extraction of the analyte, all potentially influence the result. As far as reasonably possible such errors must be minimised by external control, or corrected for by applying a suitable correction factor. The exact effect on a single measurement result is, however, impossible to obtain. This is because the different factors vary from measurement to measurement, and because the effect of each factor on the result is never known exactly. The likely range of deviation must therefore be estimated.

24.5 Each step of the measurement process – such as sample preparation, extraction, clean-up, pre-concentration or dilution, measuring instrument calibration (including RM preparation), instrumental analysis and raw data processing – will contribute to the measurement uncertainty. ISO/IEC 17025 [2] requires laboratories to identify the contributions to measurement uncertainty, and to take into account all contributions that are of significance. The separate contributions must be appropriately combined in order to give an overall value (see [14] for guidance). A record should be kept of the sources of uncertainty included in the uncertainty estimate, the value of each contribution, and the source of the value (for example, repeated measurements, literature reference, CRM data).

24.6 The component uncertainties can be evaluated individually or in convenient groups [85, 86]. For example, data from a precision study during method validation may provide an estimate of the total contribution of random variability, due to a number of steps in a measurement process. Similarly, an estimate of overall bias and its uncertainty may be derived from the analysis of matrix matched CRMs and spiking studies.

24.7 Where uncertainty contributions are estimated in groups, it is nonetheless important to record the sources of uncertainty which are considered to be included in each group.

24.8 If information from interlaboratory trials is used, it is essential to consider uncertainties arising outside the scope of such studies. Further guidance on this issue can be found in ISO 21748 [87].

24.9 The uncertainty contributions for each source must all be expressed as standard deviations or relative standard deviations [84]. In some cases, this will require conversion of data. An uncertainty expressed as a standard deviation is known as a

'standard uncertainty' and has the symbol *u*. Details of how to calculate standard uncertainties from different types of data can be found in the Eurachem/CITAC Guide [14]. The summation of the components to obtain a combined standard uncertainty is also explained.

24.10 In order to express the measurement uncertainty of a result with a particular level of confidence the overall measurement uncertainty should be expressed as a multiple of the calculated combined standard measurement uncertainty (this multiple is known as the expanded measurement uncertainty, *U*). The recommended multiplier (coverage factor, *k*) is 2, that is, the expanded uncertainty is equal to 2*u*. Where the uncertainty contributions have been estimated with sufficient degrees of freedom and arise from close to normally distributed errors, this value will correspond approximately to a 95% confidence interval.

24.11 It is often not necessary to evaluate uncertainties for every test and sample type. It will normally be sufficient to investigate the measurement uncertainty over the scope of the method, and to use the information to estimate the measurement uncertainty for the results obtained with that method during routine use.

24.12 The uncertainty of a measurement result should be reported in such a way as to allow customers to interpret results unambiguously, taking into account the level of confidence that can be placed in them. A measurement result is therefore usually reported as $y \pm U$, with an indication of the coverage factor (k) used, the expected confidence level and a description or a reference to the procedure applied for the evaluation of the measurement uncertainty.

24.13 The significant figures used to report the measurement result and its uncertainty should be consistent with the measurement capability. Therefore, in most analytical measurements, values for the expanded measurement uncertainty should be reported with no more than two significant digits. The measurement result should be rounded [88] to be consistent with the stated measurement uncertainty. For example, given a result of 215.342 mg kg^{-1} with an estimated combined standard measurement uncertainty of 5.12 mg kg^{-1}, which corresponds to an expanded measurement uncertainty of 10.24 mg kg^{-1}, the reported result should be: 215 mg kg^{-1} ± 10 mg kg^{-1} ($k = 2$, 95% confidence level).

24.14 When the laboratory performs sampling activities, contributions arising from sampling shall be taken into account using appropriate methods of analysis [40].

25 Reporting results

25.1 Results shall be provided accurately, clearly, unambiguously and objectively, usually in a report. The report shall include all the information agreed with the customer and any information necessary for the interpretation of the results. ISO/IEC 17025 [2] includes a list of the information to be included in the report. Where the laboratory is involved in sampling, information relating to the sampling shall be included in the report (i.e. date of sampling, sampling plan, sampling method, location of sampling, environmental conditions etc). When the laboratory reports a statement of conformity, it shall document the decision rule employed and the level of risk associated with the decision rule (see Section 26).

25.2 All results shall be reviewed and authorised by appropriate personnel before they are released to the customer.

26 Decision rules and statements of conformity

26.1 The 2017 version of ISO/IEC 17025 [2] includes the concept of a 'decision rule' (see definition at 3.23) in relation to statements of conformity (e.g. statements on whether a regulatory limit has been exceeded or whether the composition of a material meets a certain specification). In order to utilise a result to decide whether it indicates compliance or non-compliance with a specification, it is necessary to take into account the measurement uncertainty. A decision rule gives a prescription for the acceptance or rejection of an item based on the measured value, its uncertainty and the specification limit or limits, taking into account the acceptable level of the probability of making a wrong decision. On the basis of a decision rule, an 'acceptance zone' and a 'rejection zone' can be determined, such that if the measurement result lies in the acceptance zone the item is declared compliant and if in the rejection zone it is declared noncompliant.

26.2 When a customer requests a statement of conformity, the specification and the decision rule used must be clearly defined and agreed with the customer. The decision rule used shall be documented, taking into account the level of risk associated with the rule (e.g. the risk associated with false acceptance or rejection).

26.3 On the statement of conformity the laboratory shall clearly identify to which results the statement applies, which specifications are met/not met and the decision rule applied.

26.4 Further information on decision rules and the role of measurement uncertainty in conformity assessment is available in guidance published by Eurachem/CITAC, ILAC and JCGM [16, 89, 90].

27 Opinions and interpretations

27.1 The expression of opinions and interpretations requires the involvement of authorised personnel. There is a need to distinguish opinions and interpretations from statements of inspections (ISO/IEC 17020 [91]) and product certifications (ISO/IEC 17065 [92]), and from statements of conformity (see Section 26). Opinions and interpretations shall be based on the results obtained only from the tested or calibrated item. The basis on which opinions and interpretations were made shall be documented and records of the communication with the customer shall be retained.

28 Quality control and quality assurance

28.1 'Quality control' (QC) and 'Quality assurance' (QA) are both part of quality management. Although they have distinct definitions, QC is often considered to be a subset of QA. According to ISO 9000 [10], QA addresses the activities the laboratory undertakes to provide confidence that quality requirements will be fulfilled, whereas QC describes the individual measures which are used to actually fulfil the requirements. QA is proactive with a focus on preventing problems and mistakes that impact on quality. It can therefore be considered as being process orientated. In contrast, QC is reactive and focusses on identifying problems that impact on quality and correcting them. QC can therefore be considered as being product orientated. In the context of a laboratory the 'product' is the results provided to the customer along with any associated opinions or interpretations.

28.2 Once method performance criteria have been set and method validation completed successfully, as part of a laboratory's QMS, specific controls need to be applied to the method to verify that it remains in control during routine use, i.e. its performance continues to be fit-for-purpose. Details about how to validate analytical methods are given in a Eurachem Guide [15]. During the validation stage the method is largely applied to samples of known content. Once the method is in routine use it is used for samples of unknown content. Therefore, suitable QC should be planned and implemented to allow ongoing monitoring of day-to-day and batch-to-batch analytical performance. The level and type of QC will depend on the nature, criticality and frequency of the analysis, batch size, degree of automation and test difficulty, and also on the lessons learnt during development and validation processes. QC can take a variety of forms. This Section of the Guide is concerned with IQC. However, laboratories should also seek to obtain an independent check of their performance through external activities such as participation in PT or other ILCs (see Section 29). The extent of QC should be decided based on risk considerations for reporting wrong results. The higher the risk, the more QC will be needed.

28.3 IQC refers to procedures undertaken by laboratory personnel for the continuous monitoring of operations and measurement results in order to decide whether results are reliable enough to be released [93-95]. This includes analysis of QC materials, analysis of test samples in duplicate within the same run to monitor repeatability and analysis of blind samples (a sample where the composition and identity is unknown to the analyst). IUPAC identifies a range of materials that can be used as QC materials, including blank materials, analytical samples, RMs and CRMs [94]. ISO/TR 33402 [37] provides guidance on the preparation of QC materials.

28.3.1 Different types of QC materials may be used to monitor different types of variation within the process. Standard solutions, analysed at intervals in a batch of analyses will indicate drift in the system; use of various types of blank materials will indicate any contribution to the measuring instrument signal from sources other than the analyte; duplicate analyses of routine test samples will give a check of repeatability and cross-contamination.

28.3.2 To monitor the performance of the entire method, the analysis of QC materials with composition similar to test samples is required. As long as the results for the QC material are acceptable it is likely that results from samples in the same batch as the QC material can be taken as reliable. Where practical, the materials should be sufficiently stable, homogeneous and available in sufficient quantity to allow repeated analysis over time. The use of control charts is recommended for both an immediate assessment of whether the result from the QC material is acceptable and for longer term monitoring of method performance [96-100]. A frequently used control chart (known as an x-chart or Shewhart chart) consists of a central line representing the mean value for the QC material and two other lines described as warning limits and action limits. These limits are set at $\pm 2s$ and $\pm 3s$ about the mean value respectively (where s is an experimentally obtained estimate of the standard deviation or a target standard deviation based on a requirement). Detailed criteria for assessing QC results against the limits are required to enable the laboratory to make best use of the QC results and take appropriate action when necessary [94,95,97]. In order to set realistic limits on the control chart, the initial measurements made on the QC material to estimate the standard deviation must reflect the way the method is actually intended to be used on a day to-day basis. If this is not done, then the experimentally obtained standard deviation will be unrealistically small, resulting in limits being set on the chart which cannot possibly be complied with in normal use. Since the initial estimate of s is often based on a relatively small dataset, it is generally advisable to reassess the

limits after one year or when sufficient results have been collected [95]. Over this period, the standard deviation obtained from the results from the analysis of the QC material provides a reliable estimate of the intermediate precision of the method. As an alternative to the statistical definition of the warning and action limits, target value control charts are increasingly being used, in which the action limits are derived from the analytical requirements.

28.3.3 The analysis of various types of blanks enables the analyst to check for contamination or carryover and also to ensure that results obtained for test samples can be suitably corrected (if required) to remove any contributions to the response which are not attributable to the analyte. Different types of blank are discussed in a Eurachem supplement [101].

28.3.4 Replicate analysis of routine test samples provides a means of checking for changes in precision in an analytical process, which could adversely affect the result [102]. Analysis of replicates of test samples in the same run can be used to check repeatability. Repeatability can also be checked through the analysis of blind samples. This involves analysis of replicates where the analyst is unaware of the identity of the test portions or that they are replicates. Thus the analyst has no preconceived ideas that the particular results should be related. Standards or materials similar to those used for calibration, placed at intervals in an analytical batch, enable checks to be made that the response of the analytical process to the analyte is stable.

28.3.5 It is the responsibility of the laboratory management to set and justify an appropriate level of QC, based on risk assessment, taking into account the reliability of the method, the criticality of the work, and the feasibility of repeating the analysis if the results for the QC material are unacceptable. The level of QC adopted must be demonstrably sufficient to ensure the validity of the results. It is widely accepted that for routine analysis, a level of IQC of 5% is sufficient, i.e. 1 in every 20 samples analysed should be a QC material. However, for robust routine methods with high sample throughput, a lower level of IQC may be reasonable. For more complex procedures, a level of 20% is not unusual and on occasions even 50% may be required. In some sectors, for example water analysis, guidance is available on the level of IQC required [103]. For analyses performed infrequently, a system validation should be performed on each occasion. This may typically involve the analysis of a suitable RM or CRM, followed by replicate analyses of the sample and a spiked sample (a sample to which a known amount of the analyte has been deliberately added). Analyses performed more frequently should be subject to systematic QC procedures incorporating the use of control charts.

28.4 ISO/IEC 17025 [2] does not refer specifically to the term QC as a measure in itself to be implemented in the laboratory (only indirectly in terms of reference to ‘Quality Control Materials’). The activities discussed in this section are covered in clause 7.7 of the standard, ‘Ensuring the validity of results’. The standard requires that data generated from monitoring the validity of results shall be analysed and, where they are found to be outside pre-defined criteria, planned action shall be taken to correct the problem and to prevent incorrect results from being reported. Therefore, the data obtained from QC activities should be checked and interpreted against predetermined criteria immediately. Moreover, it is recommended to plot results and review trends in the data obtained from QC. The laboratory’s QMS should include procedure(s) for identifying nonconforming work in relation to QC results, and procedures for identifying and implementing appropriate corrective actions.

29 Proficiency testing

29.1 A regular independent assessment of the technical performance of a laboratory is necessary to assure the validity of results, and should be part of a laboratory's overall quality strategy. A common approach to obtaining this independent assessment is through participation in PT schemes. ISO/IEC 17025 [2] requires laboratories to monitor their performance through participation in comparisons with other laboratories, where available and appropriate. This monitoring of performance can be achieved by participation in PT schemes and/or other ILCs.

29.2 The value of PT is of course only as good as the schemes themselves. Requirements for the competence of PT providers are described in the standard ISO/IEC 17043 [21]. The statistical aspects of PT schemes are described in ISO 13528 [104]. Practical information on how to select, use and interpret PT schemes is presented in a Eurachem Guide [17]. Information about a large number of schemes can be found in the EPTIS database (www.eptis.org). However, for emerging fields of analysis or rare applications in particular, there may be no scheme available that is fully appropriate. These, and other limitations, are considered in an EA guidance document on the level and frequency of participation in PT [105] and guidance from IUPAC/CITAC on the selection and use of PT schemes for a limited number of participants [106].

30 Computers & computer controlled systems

30.1 In the laboratory, computers and the associated software have a wide variety of uses, including:

- control of critical environmental conditions;
- monitoring and control of inventories;
- calibration and maintenance schedules;
- stock control of reagents and measurement standards;
- experimental design;
- statistical analysis of data;
- scheduling of samples and monitoring of work throughput;
- control chart generation;
- monitoring of test procedures;
- control of automated instrumentation;
- capture, storage, retrieval, processing of data, manually or automatically;
- data transfer;
- on-board instrumental data processing;
- matching of sample and library data (e.g. comparing mass spectra);
- sample tracking;
- generation of test reports;
- word processing;
- communication;
- LIMS.

30.2 Guidance on the management of computers and software in laboratories in the context of ISO/IEC 17025 [2] accreditation has been produced by Eurolab [107].

30.3 The chemical testing environment creates particular hazards for the operation of computers and storage of electronic media. Advice can usually be found in the operating manuals, however particular care should be taken to avoid damage due to chemical, microbiological or dust contamination, heat, damp, and magnetic fields.

30.4 Initial checking shall verify as many aspects of a computer's operation as possible. Similar checks shall also be carried out if the computer's use is changed, or after maintenance, or revision of software. Where a computer is used to gather and process data associated with chemical testing and in order to validate that function, it is usually sufficient to consider correct operation if the computer produces expected answers when input is made with known parameters. Computer programmes performing calculations can be validated by comparison with manually generated results. It should be noted that some faults will occur only when a particular set of parameters is input. For this reason, it is necessary to ensure that the dataset to be used for validation provides all the variables that may occur during the expected use. At least three sets of data are recommended for the validation. If commercial software is used, the validation can be replaced by the certification provided by the manufacturer. ISO/IEC 17025 [2] notes that commercial off-the-shelf software in general use within its designated application range can be considered to be sufficiently validated. In all cases the software must be verified before use. Suitable checks on the data gathering and handling functions could be made using a CRM for the initial verification, with a secondary measurement standard such as a QC material used for regular repeat checks. Any recommendations made by the manufacturer shall be taken into consideration. The validation procedure used for a particular system and any data recorded during validation shall be documented. It may be difficult to validate these systems in isolation from the measuring instrument producing the original signal. Usually the whole system is validated in one go, by using chemical measurement standards. Such validation is normally acceptable. The validation required in particular cases is discussed in Sections 30.4.1-30.4.9.

30.4.1 ***Word processing packages*** are widely used in laboratories to generate a variety of documentation. The laboratory should ensure that the use of word processing packages is controlled sufficiently to prevent the production of unauthorised reports or other documents. In the most simple cases, where the computer acts as little more than an electronic typewriter, validation is achieved by manually checking and approving hard or soft copies. More sophisticated systems read and process data to automatically produce reports in predetermined formats. Such systems will require additional checks.

30.4.2 ***Spreadsheet packages*** are commonly used in laboratories to store, collate, summarise and present data, to calculate measurement results from measuring instrument outputs, to plot charts

and to carry out statistical analysis. For certain applications (particularly statistical analysis) in-built functions may be used rather than entering the relevant equations manually. In either case, spreadsheets should be validated to confirm that any equations/in-built functions used return the correct value. It is particularly important to establish that the correct input data are being referenced. Spreadsheets can be validated by using a test dataset and comparing the results with manual calculations. Procedures should be put in place to minimise the risk of incorrect data entry/transfer and to ensure that any calculations cannot be edited (either intentionally or accidentally) after the spreadsheet has been validated.

30.4.3 ***Computer controlled measuring instruments*** will normally have a self-checking routine which is activated when the measuring instrument is switched on, and will include the recognition and checking of all peripheral equipment. Often the software is not accessible. Under most circumstances validation can be performed by testing the various aspects of instrument function using known parameters, e.g. by testing RMs, physical or chemical measurement standards or other QC materials.

30.4.4 ***Data handling, processing or integration systems.*** The output from measuring instruments will usually need to be converted to a digital signal using an analogue/digital converter, before it can be processed. The digitised data are then translated into a recognisable signal (numbers, peaks, spectra according to the system) by the software algorithm. Programmed instructions are provided by the algorithm for a number of factors, e.g. deciding where peaks start and finish, whether a number should be rounded up or down. The algorithm is a common source of unexpected performance and validation should test the logic behind the decisions made by the algorithm.

30.4.5 ***Computer controlled automated system.*** This may embrace one or more of the foregoing examples, operated either simultaneously or in a controlled time sequence. Such systems, when operated according to the specification, will normally be verified by checking for satisfactory operation (including performance under extreme circumstances) and establishing the reliability of the system before it is allowed to run unattended. The verification shall consist of a verification of individual components, plus an overall check on the dialogue between individual components and the controlling computer. An assessment should be made of the likely causes of system malfunction. The use of QC materials and standards run at intervals in the sample batches should be sufficient to monitor correct performance on a day-to-day basis. Calculation routines can be checked by testing with known parameter values. Electronic transfer of data shall be checked to ensure that no corruption has occurred during transmission.

30.4.6 ***Laboratory Information Management Systems (LIMS)*** are widely used as a means to manage laboratory activities. A LIMS is a computer based system with software which allows the electronic collation, calculation and dissemination of data, often received directly from measuring instruments. It incorporates word-processing, database, spreadsheet, and data processing capabilities and can perform a variety of functions, including:

- sample registration and tracking;
- test assignment and allocation;
- worksheet generation;
- processing captured data;
- QC;
- financial control; and
- report generation.

30.4.7 The operation of the LIMS may be confined to the laboratory itself or it may form part of a company-wide computer system. Information may be input manually or downloaded directly from measuring instruments or other electronic devices such as bar-code readers. Information can be output either electronically or as hard-copies. Electronic outputs could consist of raw or processed data written to other computers either within the organisation, or remotely. Similarly the information could be downloaded to an external storage device. Where data cross from one system to another there may be a risk of data corruption through system incompatibility or the need to reformat the information. A well designed system enables high levels of QA to be achieved, right from the point of sample receipt to the production of the final report. Particular validation requirements include management of access to the various functions, and audit trails to catalogue alterations and file management. Where data are transmitted electronically it will be necessary to

build in safety checks to guard against data corruption and unauthorised access.

30.4.8 It is noted that according to ISO/IEC 17025 [2]:

- LIMS includes the management of data and information in both computerised and non-computerised systems.
- where a LIMS is managed and maintained off-site or through an external provider, the laboratory shall ensure that the provider or operator of the system complies with all applicable requirements of ISO/IEC 17025.

30.4.9 In addition, the LIMS must be validated before it is introduced and verified after any changes, and instructions, manuals and reference data relevant to the LIMS should be made available to personnel.

31 Data handling and control

31.1 ISO/IEC 17025 [2] has specific requirements in relation to the control of documents, records, data and information management. Any electronic system used for the generation and management of documents/records shall therefore meet these requirements. In many respects, electronic systems can simplify document management and control. However, a number of key aspects still need to be considered. These include:

- accessibility;
- security, in particular controls to prevent unauthorised modification;
- retrieval – will the documents/records still be accessible after future hardware/software upgrades?

31.2 The standard specifies requirements regarding the access of the laboratory to the data and information needed to perform its activities. Furthermore, requirements are set for the collection, processing, recording, storage, and retrieval of data. All such activities should be validated for their functionality and operate within a described framework. Requirements specific to LIMS are discussed in Section 30.4.6.

32 Audit and review

32.1 See paragraphs 3.10 and 3.11 for terminology.

32.2 An important aspect of quality management is the periodic re-examination of all aspects of the QMS by the laboratory, according to a defined schedule. The system should be examined in two ways:

1) To ensure that it is sufficiently well documented to enable adequate and consistent implementation, and that personnel are following the procedures described. This examination is commonly known as an internal audit (as opposed to the external assessment carried out by an accreditation body). ISO 19011 [108] provides guidance on the auditing of management systems.
2) To determine whether it meets the requirements of the laboratory, its customers and, if appropriate, the quality management standard. Over a period of time the needs of the laboratory and its customers will change and the QMS should evolve to continue to fulfil its purpose. This type of examination is commonly known as management review.

32.3 The programme of internal audits is normally delegated by the management of the laboratory to qualified personnel, who are responsible for ensuring that auditors have the correct technical knowledge, training, guidance, independence, and authority necessary for their work. Note that although ISO/IEC 17025 [2] does not require a laboratory to have a designated quality manager, it may be the case that this role appears in the organisation of a laboratory. The laboratory must draw-up a programme for a specific time frame, regarding the internal audits of specific areas, including the audit scopes, criteria, frequency, audit methods, responsibilities and the personnel involved. The audit programme must take into consideration the risks and opportunities related to the activities to be audited. The results are reported at the management review (see 32.6). Internal audits are normally carried out by qualified laboratory personnel who work outside of the area they are examining. This may not always be possible where the number of personnel is small. Sometimes it is necessary to ask a person external to the organisation, or another qualified person to carry out the audit alone or assisted by a qualified person working in the area. ISO/IEC 17025 makes no reference to the duration of the cycle for internal audits. It is up to the laboratory to specify and justify the duration of the auditing cycle, taking into account the importance and risks associated with the activities to be audited, the results from previous audits, and the nature and impact of any changes affecting the laboratory.

32.4 Audits may be carried out in two basic ways:

1) In a horizontal internal audit, the auditor will examine in detail single aspects of the QMS, for example calibration, training procedures and records, or reports. This methodology will help the auditor to evaluate the consistency of operation for a specific activity.
2) In a vertical internal audit, which is a detailed check that all elements associated with a particular test are implemented, the auditor will typically select a sample and follow its progress from sampling (or receipt of the sample) through to reporting of result(s) and sample disposal. During the audit, all aspects of the QMS relating to testing of the sample (calibration, results from participation in PT, IQC, control of measuring instruments, etc.) are examined. In this way, the auditor will be able to evaluate the coherence of compliance of different requirements by the laboratory.

32.5 A check list, with examples, of aspects of a chemical laboratory which could be relevant for examination during an internal audit is shown in Annex A of this Guide. It is a requirement that all points of the relevant ISO standard are covered and controlled over the internal audit period. On completion of the audit, the auditor prepares a report documenting the noncompliances and shortcomings, and the timescale of the required implementation of corrections and improvements to the QMS. It is a requirement that these points are followed up and closed in a specific period of time. The laboratory should also monitor and demonstrate the effectiveness of the actions taken.

32.6 The management review is carried out by the laboratory management and draws on information from a number of sources. These include: feedback on changes in internal and external factors that are relevant to the laboratory; results of risk identification exercises; results from internal audits, external assessments, performance in PT schemes and IQC; revision of procedures; market trends; customer complaints and compliments; feedback from the laboratory's personnel, etc. The management review should be carried out at planned intervals but ISO/IEC 17025 does not specify the duration of the intervals. For many laboratories, once a year is normally sufficient although, for laboratories with extensive scopes of accreditation, it

may be necessary to split the management review into discrete modules that can be examined over a specified time period. The laboratory should establish a procedure for planning, performing and reporting of management reviews and follow up – including a fixed agenda.

32.7 All the actions and decisions related to the effectiveness of the management system; the improvement of the laboratory activities; the fulfilment of the ISO 17025 [2] requirements; the provision of required resources or any need for change must be recorded and followed-up.

Annex A – Quality audit: Areas of particular importance to a chemistry laboratory

A1 Personnel

i) The laboratory has defined the minimum requirements of competence for each function influencing the results of laboratory activities.

ii) The duties, responsibilities and authorities are defined and communicated to the personnel by the laboratory management.

iii) Personnel who operate specific equipment, perform tests and/or calibrations, develop and validate methods, evaluate results, sign test reports and calibration certificates, provide statements of conformity, and/or provide opinions and interpretations are qualified on the basis of appropriate education, training, experience and/or demonstrated skills.

iv) On-the-job training is carried out by authorised personnel against established criteria, which are relevant to the present and anticipated tasks of the laboratory. Up-to-date records of the training are maintained.

v) Tests and calibrations are carried out only by authorised analysts. Personnel undergoing training have appropriate supervision.

vi) The performance of personnel carrying out analyses is observed by the auditor.

vii) The performance of authorised personnel is continuously monitored.

A2 Accommodation and environmental conditions

i) The laboratory environment is suitable for the work carried out.

ii) The laboratory services and facilities are adequate for the work carried out.

iii) There is adequate separation of potentially conflicting work.

iv) The laboratory areas are sufficiently clean and tidy to ensure the quality of the work carried out is not compromised.

v) There is adequate separation of sample reception, preparation, clean-up, and measurement areas, to ensure the quality of the work carried out is not compromised. In the case of small laboratories where management of space is not feasible, management of time (i.e. effective scheduling of different aspects of the work) is required.

vi) Adherence to health and safety regulations is consistent with the requirements of the QMS.

vii) Environmental conditions are monitored and recorded when specified in methods or procedures, or where they influence the quality of the results. Tests and calibrations are stopped when the environmental conditions jeopardise the results of the tests and/or calibrations.

viii) Access to, and use of, areas affecting the quality of the tests and/or calibrations is maintained under appropriate control.

ix) Measures are taken to ensure good housekeeping in the laboratory. Special procedures are implemented where necessary, for example where particular cleaning protocols are required to ensure the quality of results.

x) Measures to control facilities are periodically reviewed to ensure their appropriateness.

xi) All requirements mentioned above for accommodation and environmental conditions are met when the laboratory activities are performed at sites or facilities outside its permanent control.

A3 Equipment – General

i) The laboratory has available all equipment required for the correct performance of the tests, calibrations and/or sampling (including, among others, measuring instruments, software, measurement standards, RMs, reference data, reagents, consumables or auxiliary apparatus). The equipment in use (and any associated software) is suitable for its intended purpose.

ii) Appropriate instructions for handling, transport, storage, use and maintenance of equipment (including manuals) are available.

iii) Equipment is used by authorised personnel.

iv) Major measuring instruments are correctly maintained and records of this maintenance are kept.

v) Measuring instruments with an effect on the validity of test results are calibrated or checked before use.

vi) Programmes for the metrological control of measuring instruments are established, reviewed, and adjusted when necessary.

vii) Critical measuring instruments (e.g. balances, thermometers, glassware, timepieces, pipettes) are uniquely identified, appropriately calibrated (with suitable metrological traceability), and the corresponding certificates or other records demonstrating metrological traceability to an appropriate reference (preferably to International System of Units) are available.

viii) Calibrated measuring instruments are appropriately labelled or otherwise identified to ensure that they are not confused with uncalibrated instruments and to ensure that the calibration status is clear to the user (including the date when last calibrated and the date or criteria when recalibration is due).

ix) Measuring instrument calibration procedures and performance checks are documented and available to users. These procedures should include acceptance criteria, even when the metrological control is outsourced.

x) Measuring instrument performance checks and calibration procedures are carried out at appropriate intervals and show that calibration is maintained, and day-to-day performance is acceptable. Appropriate corrective action is taken where necessary.

xi) Intermediate checks needed to maintain confidence in the calibration status of measuring instruments are carried out according to defined procedures.

xii) Test, calibration and sampling equipment, including both hardware and software, is safeguarded from adjustments which would invalidate the test, calibration and/or sampling results.

xiii) Where calibrations give rise to a set of correction factors, the laboratory has procedures to ensure that copies (e.g. in instrument software/spreadsheets) are correctly updated.

xiv) Records of calibration, performance checks and corrective actions are maintained.

xv) When the laboratory uses measuring instruments out of its permanent control, adequate measures to ensure the above requirements for equipment are met.

A4 Equipment – Reagents and measurement standards (including reference materials)

i) The laboratory has a programme and procedure for the calibration of its measurement standards. The procedures should include acceptance criteria.

ii) Measurement standards are calibrated by a body that can provide metrological traceability.

iii) A measurement standard is used for only one purpose (e.g. calibration or performance checks).

iv) Measurement standards are calibrated before and after any adjustment.

v) Checks needed to maintain confidence in the calibration status of reference, primary, transfer or working standards and RMs are carried out according to defined procedures and schedules.

vi) The measurement standards required for the tests are readily available.

vii) The measurement standards are certified by a competent producer. RM producers fulfilling the requirements of ISO 17034 [20] are considered to be competent.

viii) The preparation of working measurement standards and reagents is documented.

ix) Property values of RMs are traceable to SI units of measurement where possible, or to property values of appropriate CRMs. RMs prepared in-house are checked as far as is technically and economically practicable.

x) Measurement standards, RMs and reagents are properly labelled and correctly stored. Where appropriate 'opening' and 'use-by' dates are shown on the label.

xi) New batches of measurement standards and reagents critical to the performance of the method are compared against old batches before use.

xii) The correct grade of each material is being used in the tests.

xiii) Where measurement standards are certified, copies of the certificate are available for inspection.

A5 Test methods and method validation

i) Laboratory developed methods are appropriate for the intended use, fully documented, appropriately validated and authorised for use.

ii) The introduction of test, calibration and sampling methods developed by the laboratory is a planned activity and is assigned to qualified personnel.

iii) The laboratory demonstrates and documents, that standard (published/official) methods are fit-for-purpose, and that published performance levels can be achieved.

iv) Alterations to methods are documented, technically justified, authorised, and accepted by the customer.

v) Authorised copies of published and official methods are available.

vi) The most up-to-date version of the method is available to the analyst.

vii) Analysts are (observed to be) following the methods specified.

viii) Laboratory developed methods contain at least the following information:

a) appropriate identification;

b) scope;

c) description of the type of item to be tested, calibrated or sampled;

d) parameters or quantities and ranges to be determined;

e) apparatus and equipment, including technical performance requirements;

f) chemicals, measurement standards (including RMs) required, with specifications for purity;

g) environmental conditions required and any stabilisation/equilibration period needed;

h) description of the procedure, including:

- affixing of identification marks, handling, transporting, storing and preparation of items,
- checks to be made before the work is started,
- checks that the measuring instruments are working properly and, where required, calibration and adjustment of the instrument before each use,
- the method of recording the observations and results,
- any safety measures to be observed.

i) criteria and/or requirements for approval/rejection;

j) data to be recorded and method of analysis and presentation;

k) the measurement uncertainty or the procedure for estimating uncertainty.

ix) Methods developed by the laboratory include a specified timescale for review.

A6 Quality control – Ensuring the validity of results

i) There is an appropriate level of QC for each method to monitor the validity of its results.

ii) QC materials are being tested by the defined procedures, at the required frequency and there is an up-to-date record of the results and actions taken where results have exceeded action limits. This monitoring is reviewed by the laboratory.

iii) The laboratory has means to detect trends and when possible applies statistical tools to review the results. Where control charts are used, performance has been maintained within specified acceptance criteria.

iv) Results from the random re-analysis of samples show an acceptable measure of agreement with the original analyses.

v) QC data are analysed and, where they are found to be outside pre-defined criteria, planned action is taken to correct the problem and to prevent incorrect results from being reported.

vi) The laboratory participates in fit for purpose PT schemes and/or other ILCs at an appropriate frequency, monitoring their performance using appropriate statistical tools. Where results indicate problems or potential problems a record of the actions taken and subsequent effectiveness checks is available.

vii) There is an effective system for linking PT and/or other ILC performance into day-to-day IQC.

A7 Handling of test items

i) There is an effective documented system for transporting, receiving, and unambiguously identifying test items against requests for analysis, showing progress of analysis, issuing reports, and tracking the fate of test items.

ii) Test items, including any sub-divisions, are properly labelled and stored.

iii) Upon receipt, records are kept of abnormalities, or departures from normal or specified conditions, as described in the test method. In such cases, the laboratory keeps records of the consultation with the customer and any issued report includes a disclaimer indicating which results may be affected by the deviation.

iv) The laboratory has procedures and appropriate facilities for avoiding deterioration, loss or damage to the test item during storage, handling and preparation.

v) Storage conditions of test items are monitored and recorded if needed.

A8 Records

i) Notebooks/worksheets or other records show the date of test, analyst, analyte(s), sample details, test observations, QC, all rough calculations, any relevant measuring instrument output (e.g. chromatograms), raw data, relevant calibration data (the auditor should use a vertical audit to verify compliance with this requirement).

ii) Notebooks/worksheets are indelible and mistakes are crossed out rather than erased or obliterated. Where a mistake is corrected the alteration is traceable to the person making the change.

iii) Records identify the person responsible for the action recorded, including the individual responsible for checking data and results.

iv) The laboratory has procedures for checking data transfers and calculations and is using them.

v) Observations, data, and calculations are recorded at the time they are made.

vi) In the case of records stored electronically, the laboratory adopts adequate measures to avoid loss of or change to the original data.

A9 Test reports

i) The test report provides information about the measurement result(s) in a clear, accurate, concise and unambiguous manner.

ii) The information given in reports is consistent with the requirements of the standard and the customer, and reflects any provisions made in the documented method.

iii) The test report includes the following information:

- a) title;
- b) the name and address of the laboratory;
- c) the location of performance of the laboratory activities;
- d) unique identification of the test report and on each page an identification and a clear identification of the end of the test report or calibration certificate;
- e) the name and contact information of the customer;
- f) identification of the method used and, where appropriate, reference to an International Standard;
- g) a description of the condition of, and unambiguous identification of, the item(s) tested;
- h) the date of receipt of the test item, date of sampling, the date of performance of the test, and the date of issue of the report;
- i) reference to the sampling plan or sample taking procedure clarifying whether sampling was carried out by the laboratory or other body;
- j) the test results with the correct number of significant figures and, where appropriate, the units of measurement and the uncertainty of the measurement;
- k) the name and function of the person authorising the test report;
- l) where relevant, a statement to the effect that the results relate only to the items tested or sampled.
- m) information on specific test conditions, e.g. environmental conditions.

iv) Where relevant, the test report contains a statement of conformity with requirements or specifications. In such a case, the laboratory shall document the decision rule and apply it [16]. The decision rule shall take into account the level of risk associated with assessments of conformity (if the decision rule is prescribed by the customer, regulations or normative documents no further consideration of the level of risk is necessary). It shall also be clear in the report to which results the statement of conformity applies, and which specification or standard the assessment is being made against.

v) Where applicable, the test report also contains a statement of the estimated measurement uncertainty of the results as well as any other additional information which may be required by specific methods, customers or groups of customers.

vi) Where applicable, the test report contains opinions and interpretations; in such a case the laboratory shall ensure that only personnel authorised for this task release the respective statement and document the basis upon which it has been made. These opinions and interpretations are based on the results obtained from the tested item and are clearly identified as such.

vii) When the test report contains results of tests performed by subcontractors, these results are clearly identified.

viii) When the test report contains results from accredited methods the appropriate accreditation mark is included. Where the test report contains results from both accredited and non-accredited methods this is clearly indicated.

ix) Where the laboratory is responsible for the sampling activity, the test report contains relevant information (date and location, environmental conditions, information required to evaluate the subsequent testing).

x) Data provided by a customer shall be clearly identified and a disclaimer added to the report if it would affect the validity of the results.

xi) Any change of information in an amended, changed or re-issued report shall be clearly identified and, where appropriate, the reason for the change included in the report. Amendments to issued reports must be made in the form of a new document (containing either just the amended information or the complete report), clearly traceable to the original document.

A10 Miscellaneous

i) The QMS documentation is up-to-date, and is accessible to all relevant personnel in the area where the activities take place.

ii) Documented procedures are in operation to handle queries, complaints and system failures.

iii) There is adequate evidence of corrective action (in the case of system failures) and evaluation of effectiveness.

iv) Actions to address risks and opportunities are planned, implemented and their effectiveness evaluated.

v) There are documented procedures for subcontracting work, including verification of the suitability of subcontractors.

vi) Vertical audits on random samples (i.e. checks made on a sample, examining all procedures associated with its testing from receipt through to the issue of a report, and sample retention and disposal) have not highlighted any problems.

Annex B – Measuring instrument calibration and equipment performance checks

B1 The purpose of periodic calibration is to:

i) Improve the estimate of the deviation between a reference value and a value obtained by using a measuring instrument (correction);

ii) Improve the measurement uncertainty in this deviation, at the time the measuring instrument is used;

iii) Confirm that there has been no alteration of the measuring instrument which could introduce doubt about the results obtained during the period.

B1.1 Before the establishment of calibration periods the laboratory must know:

i) The maximum permissible error (mpe) with which the measuring instrument can perform the measurements;

ii) Factors related to the type of measuring instrument, possible deterioration and drift, and the manufacturer's recommendation;

iii) The extent to which the measuring instrument is used, the severity of the environmental conditions (humidity, temperature) and level of expertise of the personnel using the measuring instrument;

iv) The trend of the data obtained from previous calibration records;

v) Cost-benefit ratio.

B1.2 The frequency of calibration will be justified by experience and risk analysis based, e.g. on need, type, producer's recommendations and previous performance of the equipment. Guidance is given in Table B1 on the calibration of equipment in common use in analytical laboratories and on which the calibration of other measuring instruments may be dependent. Table B2 gives guidance on equipment validation and verification of performance. More comprehensive advice is available in the literature [73] and also in equipment manuals.

Table B1 – Guidance on calibration of laboratory equipment

This information is provided for guidance purposes and the frequency will be based on the need, type and previous performance of the equipment.

Type of equipment	**Requirement**	**Suggested frequency**
Balances	Calibration of the entire range	Annually in the first 3 years, followed by less frequently, based on satisfactory performance
Calibration weights	Calibration	Every 5 years
Barometers	One point calibration	Every 5 years
Gas analysers	Calibration	Annually

Hydrometers (reference)	One point calibration using measurement standard of known specific gravity	Every 5 years
Hydrometers (working)	One point calibration versus reference hydrometer	Annually
pH meters	Calibration with traceable standard buffer solutions	Annually or more frequently if required
Pipettors/pipettes	Calibration	Annually
Volumetric glassware	Gravimetric calibration to required tolerance unless accompanied by appropriate certificates	Annually
Thermometers (liquid-in-glass) (reference)	Calibration	Every 5 years
Thermocouples (reference)	Calibration	Every 3 years
Thermometers and thermocouples (working)	Calibration	Annually in the first 3 years, followed by less frequently, based on satisfactory performance
Temperature and pressure sensors of temperature/pressure-controlled equipment	Calibration	Annually

Note: Some measuring instruments will normally be calibrated in an accredited calibration laboratory, and should at least provide results traceable to national measurement standards.

Table B2 – Guidance on performance checks of laboratory equipment

This information is provided for guidance purposes and the frequency will be based on the need, type and previous performance of the equipment.

Type of measuring instrument	**Requirement**	**Suggested frequency**
Balances	Check zero, and reading against check weight	Daily/each use
Check weight(s)	Check against calibrated weight or check on balance immediately following traceable calibration	Every 3 years
Centrifuges	Check speed against a calibrated tachometer	Annually
pH meters	Check the calibration with buffer solution not used for calibration	Daily/each use

Pipettors/pipettes	Check trueness and precision of volume dispensed by gravimetric method	Regularly (to be defined by taking account of the frequency and nature of use)
Thermometers (liquid-in-glass) (reference)	Single point (e.g. ice-point check)	Annually
Thermocouples (reference)	Check against reference thermometer	Annually
Thermometers and thermocouples (working)	Check against reference thermometer at ice-point and/or working temperature range	Annually
Temperature controlled equipment	(a) Establish stability and uniformity of temperature (b) Monitor temperature	(a) Initially, periodically, at documented frequency, and after repair/modification (b) Daily/each use
Atmosphere controlled equipment	(a) Define acceptability limits for stability and homogeneity of atmosphere composition (usually, humidity and CO_2 content) (b) Determine the stability and homogeneity of atmosphere composition and compare with acceptability limits (c) Define/confirm the operating range and the corresponding alarm limits (d) Monitor atmosphere composition	(a) Initially (b) Initially, and after any repair/modification /change of location, that may have an effect on the temperature control (c) Initially and at each further occasion of evaluation (d) At least daily/at each use or by continuous monitoring and recording during the time of use
Timers	Check if critical	Annually

B2 The following aspects of the measuring instruments listed below may need to be checked, depending on the method:

B2.1 *Chromatographic instruments:*

i) Overall system checks, precision of repeat sample injections, carry-over;

ii) Column performance (capacity, resolution, retention);

iii) Detector performance (output, response, noise, drift, selectivity, linearity);

iv) System heating/thermostatting (trueness, precision, stability, ramping characteristics);

v) Autosampler (trueness and precision of time routines).

B2.2 *Liquid and ion chromatographs:*

i) Composition of mobile phase;

ii) Mobile phase delivery system (pressure, precision, trueness, pulse-free).

B2.3 *Electrode/meter systems, including conductivity, pH and ion-selective:*

i) Electrode drift or reduced response;

ii) Fixed point and slope checks using chemical measurement standards.

B2.4 *Heating/cooling apparatus, including freeze dryers, freezers, furnaces, hot air sterilisers, incubators, melting and boiling point apparatus, oil baths, ovens, steam sterilisers and water baths:*

i) Periodic calibration of temperature sensing system using the appropriate calibrated thermometer or pyroprobe;

ii) Thermal stability;

iii) Heating/cooling rates and cycles;

iv) Temperature gradients in ovens and furnaces;

v) Ability to achieve and sustain pressure or vacuum.

B2.5 *Spectrometers and spectrophotometers, including atomic absorption, fluorimetric, inductively coupled plasma-optical emission, infra-red, luminescence, mass, nuclear magnetic resonance, UV/visible and X-ray fluorescence:*

i) Selected wavelength trueness, precision, stability;

ii) Source stability;

iii) Detector performance (resolution, selectivity, stability, linearity, trueness, precision);

iv) Signal to noise ratio;

v) Detector calibration (mass, wavelength, frequency, absorbance, transmittance, bandwidth, intensity etc.);

vi) Internal temperature controllers and indicators where applicable.

B2.6 *Microscopes:*

i) Resolving power;

ii) Performance under various lighting conditions (fluorescence, polarisation, etc.);

iii) Graticule calibration (for length measurement).

B2.7 *Autosamplers:*

i) Trueness and precision of timing systems;

ii) Reliability of sequencing programmes;

iii) Trueness and precision of sample delivery systems.

Bibliography

For a list of current references relating to quality in analytical measurement, please refer to the Eurachem *Reading List* available under the *Publications* section of the Eurachem website, www.eurachem.org.

1. Eurachem/CITAC Guide CG2: Quality assurance for research and development and non-routine analysis (1998). Available from www.eurachem.org.
2. ISO/IEC 17025:2017, General requirements for the competence of testing and calibration laboratories, ISO, Geneva (2017).
3. ISO 15189:2022, Medical laboratories – Requirements for quality and competence, ISO, Geneva (2022).
4. ISO 15195:2018, Laboratory medicine – Requirements for the competence of calibration laboratories using reference measurement procedures, ISO, Geneva (2018).
5. ISO 9001:2015, Quality management systems – Requirements, ISO, Geneva (2015).
6. Directive 2004/10/EC of the European Parliament and of the Council of 11 February 2004 on the harmonisation of laws, regulations and administrative provisions relating to the application of the principles of good laboratory practice and the verification of their applications for tests on chemical substances (codified version), Official Journal of the European Union, L 50/44, 20.2.2004.
7. Commission Directive (EU) 2017/1572 of 15 September 2017 supplementing Directive 2001/83/EC of the European Parliament and of the Council as regards the principles and guidelines of good manufacturing practice for medicinal products for human use, Official Journal of the European Union, L 238/44, 16.9.2017.
8. Quality management for organizational excellence: Introduction to total quality, D. Goetsch and Stanley Davis, Pearson (8th ed. 2015). ISBN 978-0133791853.
9. ISO/IEC 17000:2020, Conformity assessment – Vocabulary and general principles, ISO, Geneva (2020).
10. ISO 9000:2015, Quality management systems – Fundamentals and vocabulary, ISO, Geneva (2015).
11. International vocabulary of metrology – Basic and general concepts and associated terms (VIM), JCGM 200:2012, www.bipm.org. A previous version is published as ISO/IEC Guide 99:2007, ISO, Geneva (2007).
12. V. J. Barwick (Ed.) Eurachem Guide: Terminology in analytical measurement – Introduction to VIM 3 (2nd ed. 2023). ISBN 978-0-948926-40-2. Available from www.eurachem.org.
13. S. L. R. Ellison and A. Williams (Eds.), Eurachem/CITAC Guide: Metrological traceability in analytical measurement (2nd ed. 2019). ISBN 978-0-948926-34-1. Available from www.eurachem.org.
14 S. L. R. Ellison, A. Williams (Eds.), Eurachem/CITAC Guide CG4: Quantifying uncertainty in analytical measurement (3rd ed. 2012). ISBN 978-0-948926-30-3. Available from www.eurachem.org.
15. H. Cantwell (Ed.), Eurachem Guide: The fitness for purpose of analytical methods – A laboratory guide to method validation and related topics (3rd ed. 2025). Available from www.eurachem.org.
16. A. Williams and B. Magnusson (eds.) Eurachem/CITAC Guide: Use of uncertainty information in compliance assessment (2nd ed. 2021). ISBN 978-0-948926-38-9. Available from www.eurachem.org.
17. B. Brookman and I. Mann, (Eds.), Eurachem Guide: Selection, use and interpretation of proficiency testing (PT) schemes (3rd ed. 2021). Available from www.eurachem.org.
18. Regulation (EC) No 765/2008 of the European Parliament and of the Council of 9 July 2008 setting out the requirements for accreditation and market surveillance relating to the marketing of products

and repealing Regulation (EEC) No 339/93, Official Journal of the European Union, L 218/30, 13.8.2008.

19. ISO/IEC 17011:2017, Conformity assessment – Requirements for accreditation bodies accrediting conformity assessment bodies, ISO, Geneva (2017).
20. ISO 17034:2016, General requirements for the competence of reference material producers, ISO, Geneva (2016).
21. ISO/IEC 17043:2023, Conformity assessment – General requirements for the competence of proficiency testing providers, ISO Geneva, (2023).
22. ISO/IEC 17025:2005, General requirements for the competence of testing and calibration laboratories, ISO, Geneva (2005).
23. ILAC G18:04/2024, Guideline for describing scopes of accreditation, ILAC (2024). Available from www.ilac.org.
24. Gen 4, UKAS policy and general guidance for the implementation and management of flexible scopes of accreditation, UKAS (Edition 2 2024). Available from www.ukas.com.
25. EA-2/15 M:2023, EA Requirements for the accreditation of flexible scopes, EA (2023). Available from www.european-accreditation.org.
26. ISO 31000:2018, Risk management – Guidelines, ISO, Geneva (2018).
27. ISO 31073:2022, Risk management – Vocabulary, ISO, Geneva (2022).
28. ISO 31010:2019 Risk management – Risk assessment techniques, ISO, Geneva (2019).
29. P. Bedson, M. Sargent, The development and application of guidance on equipment qualification of analytical instruments, Accred. Qual. Assur., 1, 265–274 (1996). https://doi.org/10.1007/s007690050083.
30. General European OMCL Network (GEON) Quality Management Document. Qualification of equipment, Core document, PA/PH/OMCL (08) 73 R7. Date of entry into force of revised document 15 Nov 2023. Available from www.edqm.org.
31. ISO 10012:2003, Measurement management systems – Requirements for measurement processes and measuring equipment, ISO, Geneva (2003).
32. OIML R 111-1, Weights of classes E1, E2, F1, F2, M1, M1–2, M2, M2–3 and M3 Part 1: Metrological and technical requirements (2004). Available from www.oiml.org.
33. ISO Guide 30:2015, Reference materials – Selected terms and definitions, ISO, Geneva (2015).
34. ISO 33401:2024, Reference materials – Contents of certificates, labels and accompanying documentation, ISO, Geneva (2024).
35. ISO 33403:2024, Reference materials – Requirements and recommendations for use, ISO, Geneva (2024).
36. ISO 33405:2024 Reference materials – Approaches for characterization and assessment of homogeneity and stability, ISO, Geneva (2024).
37. ISO/TR 33402:2025, Good practice in reference material preparation, ISO, Geneva (2025).
38. CLSI. Characterization and qualification of commutable reference materials for laboratory medicine, 2nd ed., CLSI document EP30, Clinical and Laboratory Standards Institute (2024). ISBN 978-1-68440-243-4.

39. R. Bettencourt da Silva, A. Williams (Eds), Eurachem/CITAC Guide: Setting and using target uncertainty in chemical measurement (1st ed. 2015). ISBN: 978-989-98723-7-0. Available from www.eurachem.org.

40. M. H. Ramsey, S. L. R. Ellison, P. Rostron (Eds.), Eurachem/EUROLAB/CITAC/Nordtest/AMC Guide: Measurement uncertainty arising from sampling: a guide to methods and approaches, Eurachem (2nd ed., 2019). ISBN 978-0-948926-35-8. Available from www.eurachem.org.

41. M. H. Ramsey, P. D. Rostron, F. C. Raposo (Eds), Eurachem/EUROLAB/CITAC/Nordtest/AMC Guide: Validation of measurement procedures that include sampling, Eurachem (2024). Available from www.eurachem.org.

42. Commission Regulation (EC) No 333/2007 of 28 March 2007 laying down the methods of sampling and analysis for the official control of the levels of lead, cadmium, mercury, inorganic tin, 3-MCPD and benzo(a)pyrene in foodstuffs, Official Journal of the European Union, L 88/29, 29.3.2007.

43. W. Horwitz, Nomenclature for sampling in analytical chemistry (IUPAC Recommendations 1990), Pure Appl. Chem., 62(6), 1193-1208 (1990).

44. P. de Zorzi, S. Barbizzi, M. Belli, G. Ciceri, A. Fajgelj, D. Moore, U. Sansone, M. van der Perk, Terminology in soil sampling (IUPAC Recommendations 2005), Pure Appl. Chem., 77(5), 827-841 (2005).

45. ISO 3951-1:2022, Sampling procedures for inspection by variables – Part 1: Specification for single sampling plans indexed by acceptance quality limit (AQL) for lot-by-lot inspection for a single quality characteristic and a single AQL, ISO, Geneva (2022).

46. ISO 3951-2:2013, Sampling procedures for inspection by variables – Part 2: General specification for single sampling plans indexed by acceptance quality limit (AQL) for lot-by-lot inspection of independent quality characteristics, ISO, Geneva (2013).

47. ISO 3951-3:2007, Sampling procedures for inspection by variables – Part 3: Double sampling schemes indexed by acceptance quality limit (AQL) for lot-by-lot inspection, ISO, Geneva (2007).

48. ISO 3951-4:2011, Sampling procedures for inspection by variables – Part 4: Procedures for assessment of declared quality levels, ISO, Geneva (2011).

49. ISO 3951-5:2006, Sampling procedures for inspection by variables – Part 5: Sequential sampling plans indexed by acceptance quality limit (AQL) for inspection by variables (known standard deviation), ISO, Geneva (2006).

50. ISO 2859-1:2026, Sampling procedures for inspection by attributes – Part 1: Sampling schemes indexed by acceptance quality limit (AQL) for lot-by-lot inspection, ISO, Geneva (2026).

51. ISO 2859-2:2020, Sampling procedures for inspection by attributes – Part 2: Sampling plans indexed by limiting quality (LQ) for isolated lot inspection, ISO, Geneva (2020).

52. ISO 2859-3:2005, Sampling procedures for inspection by attributes – Part 3: Skip-lot sampling procedures, ISO, Geneva (2005).

53. ISO 2859-4:2020, Sampling procedures for inspection by attributes – Part 4: Procedures for assessment of declared quality, ISO, Geneva (2020).

54. ISO 2859-5:2005, Sampling procedures for inspection by attributes – Part 5: System of sequential sampling plans indexed by acceptance quality limit (AQL) for lot-by-lot inspection, ISO, Geneva (2005).

55. ISO 28590:2017, Sampling procedures for inspection by attributes – Introduction to the ISO 2859 series of standards for sampling for inspection by attributes, ISO, Geneva (2017).

56. I. Kuselman, F. Pennecchi, C. Burns, A. Fajgelj, P. de Zorzi, IUPAC/CITAC Guide: Investigating out-of-specification test results of chemical composition based on metrological concepts (IUPAC Technical Report), Pure Appl. Chem., 84(9), 1939-1971 (2012).
57. ISO 78-2:1999, Chemistry – Layouts for standards – Part 2: Methods of chemical analysis, ISO, Geneva (1999).
58. ISO 5725-1:2023, Accuracy (trueness and precision) of measurement methods and results – Part 1: General principles and definitions, ISO, Geneva (2023).
59. ISO 5725-2:2025, Accuracy (trueness and precision) of measurement methods and results – Part 2: Basic method for the determination of repeatability and reproducibility of a standard measurement method, ISO, Geneva (2025).
60. ISO 5725-3:2023, Accuracy (trueness and precision) of measurement methods and results – Part 3: Intermediate precision and alternative designs for collaborative studies, ISO, Geneva (2023).
61. ISO 5725-4:2020, Accuracy (trueness and precision) of measurement methods and results – Part 4: Basic methods for the determination of the trueness of a standard measurement method, ISO, Geneva (2020).
62. ISO 5725-5:2025, Accuracy (trueness and precision) of measurement methods and results – Part 5: Alternative methods for the determination of the precision of a standard measurement method, ISO, Geneva (2025).
63. ISO 5725-6:1994, Accuracy (trueness and precision) of measurement methods and results – Part 6: Use in practice of accuracy values, ISO, Geneva (1994).
64. R. Bettencourt da Silva and S. L. R. Ellison (Eds.), Eurachem/CITAC Guide: Assessment of performance and uncertainty in qualitative chemical analysis (1st ed, 2021). ISBN 978-0-948926-39-6. Available from www.eurachem.org.
65. Guidelines on performance criteria for methods of analysis for the determination of pesticide residues in food and feed CXG 90-2017, CODEX ALIMENTARIUS (2017). Available from https://www.fao.org/fao-who-codexalimentarius/codex-texts/guidelines/en/.
66. W. J. Youden, E. H. Steiner, Statistical Manual of the AOAC, AOAC International (1975). ISBN 0-935584-15-3.
67. Commission Decision of 12 August 2002 implementing Council Directive 96/23/EC concerning the performance of analytical methods and the interpretation of results, Official Journal of the European Union, L221/8, 17.8.2002.
68. P. De Bievre, R. Dybkaer, A. Fajgelj, D. Brynn Hibbert, Metrological traceability of measurement results in chemistry: Concepts and implementation (IUPAC Technical Report), Pure Appl. Chem., 83(10), 1873-1935 (2011).
69. ILAC P10:07/2020, ILAC Policy on metrological traceability of measurement results, ILAC (2020). Available from www.ilac.org.
70. OIML R 54, pH scale for aqueous solutions (1981). Available from www.oiml.org
71. EN 71-3:2019+A1:2021, Safety of toys – Part 3: Migration of certain elements, CEN, Brussels (2021).
72. ISO 11095:1996, Linear calibration using reference materials, ISO, Geneva (1996).
73. OIML D 10/ILAC-G24, 2022, Guidelines for the determination of recalibration intervals of measuring equipment, ILAC (2022). Available from www.ilac.org.
74. Guidelines on the Calibration of Non-Automatic Weighing Instruments, EURAMET Calibration Guide No. 18 Version 4.0 (11/2015).

75. ISO 8655-1:2022, Piston-operated volumetric apparatus – Part 1: Terminology, general requirements and user recommendations, ISO, Geneva (2022).
76. ISO 8655-2:2022, Piston-operated volumetric apparatus – Part 2: Pipettes, ISO, Geneva (2022).
77. ISO 8655-3:2022, Piston-operated volumetric apparatus – Part 3: Burettes, ISO, Geneva (2022).
78. ISO 8655-4:2022, Piston-operated volumetric apparatus – Part 4: Dilutors, ISO, Geneva (2022).
79. ISO 8655-5:2022, Piston-operated volumetric apparatus – Part 5: Dispensers, ISO, Geneva (2022).
80. ISO 8655-6:2022, Piston-operated volumetric apparatus – Part 6: Gravimetric reference measurement procedure for the determination of volume, ISO, Geneva (2022).
81. ISO 8655-7:2022, Piston-operated volumetric apparatus – Part 7: Alternative measurement procedures for the determination of volume, ISO, Geneva (2022).
82. OIML R 135, Spectrophotometers for medical laboratories (2004). Available from www.oiml.org.
83. ISO 4787:2021, Laboratory glass and plastic ware – Volumetric instruments – Methods for testing of capacity and for use, ISO, Geneva (2021).
84. Evaluation of measurement data – Guide to the expression of uncertainty in measurement (GUM), JCGM 100:2008 (corrected version 2010), www.bipm.org. Printed as ISO/IEC Guide 98-3:2008, ISO, Geneva (2008).
85. B. Magnusson, T. Näykki, H. Hovind, M. Krysell, Handbook for calculation of measurement uncertainty in environmental laboratories, NT TR 537 (ed. 4 2017). Available from www.nordtest.info.
86. Measurement uncertainty revisited, Technical Report 1/2007, Eurolab (2007). Available from www.eurolab.org.
87. ISO 21748:2017, Guidance for the use of repeatability, reproducibility and trueness estimates in measurement uncertainty evaluation, ISO, Geneva (2017).
88. ISO 80000-1:2022, Quantities and units – Part 1: General, ISO, Geneva (2022).
89. ILAC G8:2019, Guidelines on Decision Rules and Statements of Conformity. Available from www.ilac.org.
90. Evaluation of measurement data – The role of measurement uncertainty in conformity assessment, JCGM 106:2012, www.bipm.org. Printed as ISO/IEC Guide 98-4:2012, ISO, Geneva (2012).
91. ISO 17020:2012 Conformity assessment – Requirements for the operation of various types of bodies performing inspection, ISO, Geneva (2012)
92. ISO 17065:2012 Conformity assessment – Requirements for bodies certifying products, processes and services, ISO, Geneva (2012).
93. Compendium of terminology in analytical chemistry (Orange Book), 4th edition, D. Brynn Hibbert (Ed), The Royal Society of Chemistry (2023), ISBN (print) 978-1-78262-947-4.
94. M. Thompson, R. Wood, Harmonised guidelines for internal quality control in analytical chemistry laboratories, (IUPAC technical report), Pure Appl. Chem., 67(4), 649-666 (1995).
95. H. Hovind, B. Magnusson, M. Krysell, U. Lund, and I. Mäkinen, Internal quality control – Handbook for chemical laboratories, NT TR 569, (ed 5.1. 2018). Available from www.nordtest.info.
96. ISO 7870-1:2019, Control Charts – Part 1: General guidelines, ISO, Geneva (2019).
97. ISO 7870-2:2023, Control Charts – Part 2: Shewhart control charts, ISO, Geneva (2023).

98. ISO 7870-3:2020, Control Charts – Part 3: Acceptance control charts, ISO, Geneva (2020).

99. ISO 7870-4:2021, Control Charts – Cumulative sum charts, ISO, Geneva (2021).

100. ISO 7870-5:2014, Control Charts – Specialized control charts, ISO, Geneva (2014).

101. H. Cantwell (ed.) Blanks in method validation – Supplement to Eurachem Guide the fitness for purpose of analytical methods, (2nd ed. 2025). Available from www.eurachem.org.

102. AMC technical brief No. 9, Feb 2002, M. Thompson (ed.), A simple fitness-for-purpose control chart based on duplicate results obtained from routine test materials. Available from www.rsc.org.

103. ISO/TS 13530:2009, Water quality – Guidance on analytical quality control for chemical and physicochemical water analysis, ISO, Geneva (2009).

104. ISO 13528:2022, Statistical methods for use in proficiency testing by interlaboratory comparison, ISO, Geneva (2022).

105. EA-4/18 G:2021, Guidance on the level and frequency of proficiency testing participation, EA (2021). Available from www.european-accreditation.org.

106. I. Kuselman, A. Fajgelj, IUPAC/CITAC Guide: Selection and use of proficiency testing schemes for a limited number of participants – chemical analytical laboratories (IUPAC Technical Report), Pure Appl. Chem., 82(5),1099-1135 (2010).

107. Eurolab Technical Report No. 2/2006, Guidance for the management of computers and software in laboratories with reference to ISO/IEC 17025/2005, Eurolab (2006). Available from www.eurolab.org.

108. ISO 19011:2018, Guidelines for auditing management systems, ISO, Geneva (2018).

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