

---

# **CITAC / EURACHEM GUIDE**

---

# **Guide to Quality in Analytical Chemistry**

## **An Aid to Accreditation**

---

Prepared jointly by  
**CITAC (The Cooperation on International Traceability in Analytical Chemistry)**  
**and EURACHEM (A Focus for Analytical Chemistry in Europe)**

**Guide  
to Quality in  
Analytical Chemistry**

**An Aid to Accreditation**

---

This document has been produced by a joint Working Group of CITAC and EURACHEM and is based on earlier documents, including CITAC Guide 1, published in 1995 and the EURACHEM WELAC Guide published in 1993. This edition deals with the new requirements of the standard ISO/IEC 17025: 1999 - "General Requirements for the Competence of Testing and Calibration Laboratories".

## **Guide to Quality in Analytical Chemistry**

**An Aid to Accreditation**

**Published 2002**

Copyright of this guide is the property of the  
organisations represented on CITAC and EURACHEM.

This edition has been published by **CITAC and Eurachem**

---

## GUIDE TO QUALITY IN ANALYTICAL CHEMISTRY

### CONTENTS

Section	Title	Page
1.	Aims and objectives	5
2.	Introduction	5
3.	Definitions and Terminology	7
4.	Accreditation	9
5.	Scope	11
6.	The analytical task	12
7.	Specification of the analytical requirement	13
8.	Analytical strategy	13
9.	Non-routine analysis	13
10.	Staff	15
11.	Sampling, sample handling and preparation	16
12.	Environment	20
13.	Equipment	21
14.	Reagents	23
15.	Traceability	24
16.	Measurement uncertainty	25
17.	Methods / procedures for calibrations and tests	28
18.	Method validation	29
19.	Calibration	32
20.	Reference materials	34
21.	Quality control and proficiency testing	36
22.	Computers and computer controlled systems	37
23.	Laboratory audit and review	40

#### References and Bibliography

#### Acronyms

#### Appendices

- A Quality Audit - Areas of Particular Importance in a Chemical Laboratory
- B Calibration Intervals and Performance Checks
- C Comparison Table – ISO/IEC 17025:1999 vs ISO/IEC Guide 25:1990 (ILAC G15:2001)

---

## 1. AIMS AND OBJECTIVES

- 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 (CITAC/EURACHEM Guide reference A1 on page 43).
- 1.2 The guidance is intended to help those implementing quality assurance in laboratories. For those working towards accreditation, certification, or other compliance with particular quality requirements, it will help explain what these requirements mean. The guidance will also be useful to those involved in the quality assessment of analytical laboratories against those quality requirements. Cross-references to ISO/IEC 17025, ISO 9000 and OECD Good Laboratory Practice (GLP) requirements are provided.
- 1.3 This document has been developed from the previous CITAC Guide 1 (which in turn was based on the EURACHEM/WELAC Guide), and updated to take account of new material and developments, particularly the new requirements of the standard, ISO/IEC 17025.
- 1.4 This guide has been produced by a working group comprising David Holcombe, LGC, UK; Bernard King, NARL, Australia; Alan Squirrel, NATA, Australia and Maire Walsh, State Laboratory, Ireland. In addition, over the years leading to the drafting of this and earlier versions of the guide, there has been extensive input from a large number of individuals and organisations, including, CITAC, EURACHEM, EA, ILAC, AOACI, IUPAC, CCQM, and others (Refer Acronyms list on page 48).
- 1.5 This guide concentrates on the technical issues of quality assurance (QA), with emphasis on those areas where there is a particular interpretation required for chemical testing or related measurements. There are a number of additional aspects of QA where no guidance is given as these are fully addressed in other documents, such as ISO/IEC 17025. These include records; reports; quality systems; subcontracting; complaints; supplier's requirements; contract review; confidentiality and data handling.

## 2. INTRODUCTION

- 2.1 The value of chemical measurements depends upon the level of confidence that can be placed in the results. Increasingly, the chemical testing community is adopting QA principles which, whilst not actually guaranteeing the quality of the data produced, increases the likelihood of it being soundly based and fit for its intended purpose.
- 2.2 Appropriate QA can enable a laboratory to show that it has adequate facilities and equipment for carrying out chemical analysis and that the work was carried out by competent staff in a controlled manner, following a documented validated method. QA should focus on the key issues which determine quality results, costs and timeliness and avoid diversion of energies into less important issues.
- 2.3 Good QA practice, including its formal recognition by accreditation, certification etc., help to ensure that results are valid and fit for purpose. However, it is important for both laboratories and their customers to realise that QA cannot guarantee that 100% of the individual results will be reliable. There are two reasons for this:

1. Mistakes/gross errors can occur, where, for example, the results for two samples are mixed-up. In a well-run laboratory, the frequency of mistakes will be small, but not zero.
2. Random and systematic errors also occur, leading to uncertainty in a measured result. The probability of a result lying within the stated uncertainty range depends on the level of confidence employed, but again, even in a well ordered laboratory, deviant results will occasionally occur and very occasionally the deviation will be large.

The business of QA is to manage the frequency of quality failures. The greater the effort taken, the smaller the number of quality failures that can be expected. It is necessary to balance the cost of QA against the benefit in reducing quality failures to an acceptable (non-zero) level.

- 2.4 The principles of QA have been formalised in a number of published protocols or standards. Those most widely recognised and used in chemical testing fall into three groups and are applied according to a laboratory's individual needs. The three groups are:
  - 2.4.1 ISO/IEC 17025:1999: (Ref B1) This standard addresses the technical competence of laboratories to carry out specific tests and calibrations and is used by laboratory accreditation bodies world-wide as the core requirements for the accreditation of laboratories;
  - 2.4.2 ISO 9001:2000: (Ref B2) and its national and international equivalents. This standard relates primarily to quality management, for facilities carrying out production, or providing services, including chemical analysis;
  - 2.4.3 OECD Principles of Good Laboratory Practice (GLP): 1998 (Ref B3) and its national and sectorial equivalents. These guidelines are concerned with the organisational processes and conditions under which laboratory studies related to certain regulatory work are carried out.
- 2.5 In addition, there are Total Quality Management (TQM) approaches to QA which place emphasis on continuous improvement (the new ISO 9001:2000 gives more emphasis here). Central to this guide is the contention that, at the technical level, good practice in analytical QA is independent of the formal QA system adopted.
- 2.6 A laboratory may decide to design its own QA procedures or it may follow one of the established protocols. In the latter case it may claim informal compliance against the protocol or ideally may undergo independent assessment from an official expert body, with the aim of gaining independent endorsement of its quality system. Such independent assessment / endorsement is variously known as accreditation, registration or certification depending on which standard the assessment is made against. In particular areas of analysis, accreditation is sometimes mandatory, however in most cases, the laboratory is free to decide what sort of QA measures it wishes to adopt. The independent assessment route has recognised advantages, particularly where the laboratory's customers require objective evidence of the technical competence of the laboratory. For clarification of the term "accreditation" as used in this guide, see sections 3.2, & 4 below.

### 3. DEFINITIONS AND TERMINOLOGY

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 to understand the distinction between the various terms. A few are presented here. The key reference is ISO Guide 2:1996 - Ref B4. Other terms can be found in ISO 9000:2000 - Ref B5 (Note: ISO 8402:1994 - Quality - Vocabulary - has been withdrawn).

3.1 **QUALITY:** Degree to which a set of inherent characteristics fulfils requirements (ISO 9000:2000)

3.2 **ACCREDITATION:** ‘Procedure by which an authoritative body gives formal recognition that a body or person is competent to carry out specific tasks’ (ISO Guide 2:1996).

3.2.1 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 or specific types of calibrations or tests. The mechanism under which accreditation is granted is described below in section 4 and the core requirements document is ISO/IEC 17025:1999.

3.2.2 Accreditation is also used in the context of ISO 9000 based activities to describe the process whereby a national organisation formally recognises certification bodies as competent to assess and certify organisations as being compliant with the ISO 9000 series of standards (“quality management systems”).

3.3 **CERTIFICATION:** ‘Procedure by which a third party gives written assurance that a product, process or service conforms to specified requirements’ (ISO Guide 2:1996). Certification, (sometimes known as registration) primarily differs from accreditation in that technical competence is not specifically addressed.

3.4 **QUALITY ASSURANCE (QA):** QA describes the overall measures that a laboratory uses to ensure the quality of its operations. Typically this might include:

- A quality system
- Suitable laboratory environment
- Educated, trained and skilled staff
- Training procedures and records
- Equipment suitably maintained and calibrated
- Quality control procedures
- Documented and validated methods
- Traceability and measurement uncertainty
- Checking and reporting procedures
- Preventative and corrective actions
- Proficiency testing
- Internal audit and review procedures
- Complaints procedures
- Requirements for reagents, calibrants, measurement standards & reference materials

- 3.5 **QUALITY CONTROL (QC):** ‘The operational techniques and activities that are used to fulfil requirements for quality’.

Quality control procedures relate to ensuring the quality of specific samples or batches of samples and include:

Analysis of reference materials/measurement standards  
Analysis of blind samples  
Use of quality control samples & control charts  
Analysis of blanks  
Analysis of spiked samples  
Analysis in duplicate

Proficiency Testing

More details on quality control and proficiency testing are given in section 21.

- 3.6 **AUDIT AND REVIEW:** In practice quality audits take two forms. An audit carried out by an independent external body as part of the accreditation process is more usually known as an *assessment*. “Quality audits” carried out within the laboratory, are sometimes subdivided into *audit*, often called ‘internal audit’, (which checks that the quality procedures are in place, and fully implemented) and *review* (which checks to ensure that the quality system is effective and achieves objectives. The review is carried out by senior management with responsibility for the quality policy and work of the laboratory.

In this guide the term *audit* refers to internal audit; *assessment* refers to external audit.

- 3.7 **STANDARD:** This word has a number of different meanings in the English language. In the past it has been used routinely to refer firstly to written standards, i.e. widely adopted procedures, specifications, technical recommendations, etc., and secondly, to chemical or physical standards used for calibration purposes. In this guide, to minimise confusion, *standard* is used only in the sense of *written standards*. 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 corresponding solutions of known concentration; UV filters; weights, etc. Reference materials are one (important) category of measurement standards.

- 3.8 **REFERENCE MATERIAL (RM):** ‘Material or substance one or more of whose property values are sufficiently homogeneous and well established to be used for the calibration of an apparatus, the assessment of a measurement method, or for assigning values to materials.’ (ISO Guide 30 - Ref C1)

- 3.9 **CERTIFIED REFERENCE MATERIAL (CRM):** ‘Reference material, accompanied by a certificate, one or more of whose property values are certified by a procedure, which establishes its traceability to an accurate realisation of the units in which the property values are expressed, and for which each certified value is accompanied by an uncertainty at a stated level of confidence’ (ISO Guide 30: 1992 – Ref C1).

- 3.10 **TRACEABILITY:** ‘Property of the result of a measurement or the value of a standard whereby it can be related to stated references, usually national or international standards,

through an unbroken chain of comparisons all having stated uncertainties.’ (VIM 1993 - Ref B6).

- 3.11 **MEASUREMENT UNCERTAINTY:** a parameter associated with the result of a measurement that characterises the dispersion of the values that could reasonably be attributed to the measurand. (VIM 1993 - Ref B6)

## 4 ACCREDITATION

- 4.1 The references to accreditation in this and successive sections refer to ISO/IEC 17025:1999 (Ref B1). Its requirements will be implemented by laboratories and accredited by accreditation bodies over a 3 year transition period ending December 2002. The standard is substantially longer than its predecessor and contains some new or enhanced requirements, as summarised below, but much of the new material was previously contained in supplementary guidance documents. Thus, the scale of the new requirements is not as great as might first appear. A table comparing the clauses of ISO/IEC 17025:1999 and its predecessor, ISO/IEC Guide 25: 1990 is found in Appendix C.

- 4.2 Briefly, ISO/IEC 17025 includes new or enhanced requirements concerning the following:

- Contract review – pre-contract communications to ensure that the requirements are adequately specified and the services fully meet customer requirements;
- Purchasing services and supplies – a policy and procedures are required to ensure that they are fit for purpose;
- Sampling – a sampling plan and procedures are required where sampling is part of the work of the laboratory;
- Preventative action – proactively seeking to improve the processes thus minimizing the need for corrective action;
- Method validation, traceability and measurement uncertainty – significantly enhanced emphasis on these requirements;
- Opinion and interpretation – this is now allowed in test reports.

- 4.3 The requirements of the leading quality standards/protocols have many common or similar elements. For example, ISO/IEC 17025 incorporates the ISO 9001 (1994) quality system elements which are applicable to laboratories. A comparison of the major standards/protocols is given below:

Title	ISO/IEC 17025:1999	ISO 9001:2000	OECD GLP 1998 Organisation for Economic Cooperation and Development
Scope	1	1	Section I - 1
Normative references	2	2	
Terms and definitions	3	3→ISO 9000:2000	Section I - 2
Management requirements	4	Various	Section II- 1.1
Organisation	4.1		
Study director			Section II- 1.2
Quality Manager	4.1.5	5.5.2	QM ≠ GLP personnel
Quality System	4.2	4	Section II- 2
Quality Policy	4.2.2	5.3	
Quality Manual	4.2.2	4.2.2	
Management commitment to quality	4.2.2	5.1	

Document control	4.3	4.2.3	
Document approval and issue	4.3.2	4.2.3	
Document changes	4.3.3	4.2.3	Section II – 7.1
Review of requests, tenders, and contracts	4.4	7.2	
Subcontraction	4.5		
Purchasing services and supplies	4.6	7.4	
Verification of supplies	4.6.2	7.4.3	Section II – 6.2.3 (test item only)
Customer focus		5.2, 8.2.1	
Service to the client	4.7	7.2.3	
Complaints	4.8	7.2.3	
Control of non-conforming work	4.9	8.3	
Improvement		8.5	
Cause analysis	4.10.2	8.5.2	
Corrective actions	4.10.3, 4.10.4	8.5.2	
Preventive action	4.11	8.5.3	
Control of records	4.12	4.2.4	Section II – 10
Internal audits	4.13, 4.10.5	8.2.2	Section II – 2.2
Management reviews	4.14	5.6	
General technical requirements	5.1		
Personnel	5.2	6.2	Section II – 1.3
Accommodation and environmental conditions	5.3	6.3, 6.4	Section II – 3
Test and calibration methods	5.4	7.5.1	Section II – 7
Method validation	5.4.5	7.5.2	
Measurement uncertainty	5.4.6		
Calculation and transcription checks	5.4.7.1		Section II – 8.3
IT validation	5.4.7.2	6.3	Section II – 1.1.2 (q)
Equipment	5.5	7.5.1	Section II – 4
Equipment qualification	5.5.2	7.5.1, 7.5.2	Section II – 5.1
Measurement traceability	5.6	7.6	
Calibration	5.6	7.6	Section II - 4.2
Reference standards and reference materials	5.6.3	7.6	Section II – 6
Sampling	5.7		
Handling of test or calibration items (transport/storage/identification/disposal)	5.8	7.5.5	
Sample identification	5.8.2	7.5.3	Section II – 8.3.1
Assuring the quality of measurement results	5.9	7.5.1, 7.6, 8.2.3, 8.2.4	Section II - 2
Reporting results	5.10		Section II – 9
Opinions and interpretations	5.10.5		
Electronic transmission	5.10.7		
Amendments to reports	5.10.9	8.3	Section II – 9.1.4

Note: Consideration is being given to the alignment of ISO/IEC 17025:1999 to bring the quality management system requirements in Sec.4 (based on ISO 9001:1994) in line with ISO 9001:2000.

4.4 Accreditation is granted to a laboratory for a specified set of activities (i.e. tests or calibrations) following assessment of that laboratory. Such assessments will typically include an examination of the analytical procedures in use, the quality system and the quality documentation. The analytical procedures will be examined to ensure they are technically appropriate for the intended purpose and that they have been validated. The performance of tests may be witnessed to ensure documented procedures are being followed, and indeed can be followed. The laboratory's performance in external proficiency testing schemes may also be examined. Assessment may additionally include a "performance audit", where the laboratory is required to analyse samples supplied by

- 
- the accrediting body and achieve acceptable levels of accuracy. This performance audit is effectively a form of proficiency testing (see section 21).
- 4.5 It is the responsibility of the laboratory to ensure that all procedures used are appropriate for their intended purpose. The assessment process examines this “fitness-for-purpose” aspect.
- 4.6 Each accreditation body has established procedures against which it operates, assesses laboratories and grants accreditation. For example, the laboratory accreditation bodies themselves work to requirements based on ISO/IEC Guide 58. (Ref C8) Similarly, bodies offering certification schemes work to requirements of ISO/IEC Guide 62 (Ref C9).
- 4.7 Likewise, assessors are chosen against specified criteria. For example, the selection criteria for assessors appointed to assess for laboratory accreditation bodies are specified in ISO/IEC Guide 58. These include the requirement for technical expertise in the specific areas of operation being assessed.
- 4.8 The benefit of accreditation is that it enables potential customers of the laboratory to have confidence in the quality of the work performed by the laboratory. Various international developments mean that the endorsement conferred by accreditation and other assessments have world-wide recognition. Many laboratory accreditation bodies (who have been evaluated and found to satisfy relevant requirements – see 4.6 above) have signed a multilateral agreement (The ILAC Arrangement) to recognise the equivalence of laboratory accreditation schemes. Similar international agreements have been developed for bodies associated with certification schemes.
- 4.9 The guidance given below will be of use to laboratories seeking accreditation against ISO/IEC 17025, certification against ISO 9001, or compliance/registration with GLP principles.

## 5. SCOPE

- 5.1 A laboratory may apply QA to all or part of its operations. Where a laboratory claims compliance against, or certification or accreditation to, a particular standard, it is important to be clear to what this compliance, certification or accreditation applies. The formal statement of the activities which have been certified against ISO 9001, or accredited against ISO 17025 is known as the "scope". ISO 9000 and GLP require only a brief description of the activities covered, but with ISO/IEC 17025, a detailed description of the specific work covered by the accreditation is usually required.
- 5.2 Quality management is aided by a clear statement of activities, which ideally should define the range of work covered, but without restricting the laboratory's operation. Different quality standards have different rules, but for ISO/IEC 17025, the scope may typically be defined in terms of:
- i) the range of products, materials or sample types tested or analysed;
  - ii) the measurements (or types of measurements) carried out;

- 
- iii) the specification or method/equipment/technique used;
- iv) the concentration, range and measurement uncertainty as appropriate.
- 5.3 Definition of scope in specific terms is clearly most easily applied to laboratories carrying out routine testing to established procedures. Where non-routine testing is carried out, a more flexible approach to scope is desirable. The scope must, however, be as specific as is feasible and the QA system maintained by the laboratory must ensure that the quality of the results is under control.
- 5.4 A laboratory wishing to change its scope, either by adding additional tests or changing the methodology of existing tests will require the approval of the accreditation body, who will have 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 assessment may be required.

## 6. THE ANALYTICAL TASK

6.1 Analysis is a complex multistage investigation which may be summarised by the following sub-tasks. Where appropriate the corresponding section in this guide is also listed. Not every step will be required each time a routine measurement is performed. Also, in reality, measurement is often an iterative process rather than the linear series of steps shown below:

- Specification of requirements - c.f. Section 7
- Information review \*
- Creative thought \*
- Study plan \* - c.f. Section 8
- Sampling - c.f. Section 22
- Sample preparation
- Preliminary analysis \*
- Identification/confirmation of composition
- Quantitative analysis
- Data collection and review
- Data interpretation/problem solving
- Reporting/advice

*Those marked \* are of more significance in the context of non-routine analysis*

The process is described in the form of a flow diagram in Figure 1 in Section 19.

6.2 Although different standards emphasise different aspects of QA and some of the above steps are not specifically covered, it is important that the QA of each stage is considered, and where relevant addressed.

## 7. SPECIFICATION OF ANALYTICAL REQUIREMENT

- 7.1 The laboratory has a duty to provide an analytical service for its customers that is appropriate to solving the customers problems.
- 7.2 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 also develop during the course of a commission but should not drift. Any changes are likely to be customer driven but should have the agreement of both customer and laboratory. The specification of the analytical request should address the following issues:
- Analytical context
  - Information required
  - Criticality/acceptable risk
  - Time constraints
  - Cost constraints
  - Sampling
  - Traceability requirements
  - Measurement uncertainty
  - Method requirements, including sample preparation
  - Identification/confirmation/fingerprinting
  - Limit criteria
  - QA/QC requirements
  - Research plan requirements/approval
- 7.3 The level of documentation should be commensurate with the scale and criticality of the task and include the output of any "information review" and "creative thought".

## 8. ANALYTICAL STRATEGY

- 8.1 All analytical work should be adequately planned. Such a plan may, in its most basic form, be simply a notebook entry. More detailed plans will be appropriate for larger, more complicated tasks. For work carried out under GLP, there is a specific requirement that the work be performed to documented *study plans*.
- 8.2 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.

## 9. NON-ROUTINE ANALYSIS

- 9.1 Non-routine analysis can be considered as either tasks, but which are carried out infrequently, where reliable methodology is already established or tasks where every sample requires a different approach and methodology has to be established at the time. Guidance is given in Reference A1.

- 
- 9.2 The costs of chemical measurement reflect the costs associated with the various stages of method development, validation, instrumentation, consumables, ongoing maintenance, staff input, calibration, quality control, 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, unit analytical costs will be comparatively low. Where a method has to be specially developed for just a few samples, the unit analytical costs 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. However, where work is subcontracted, appropriate QA procedures must be in place.
- 9.3 In simple terms, a measurement can conveniently be described in terms of an isolation stage and a measurement stage. Rarely can an analyte be measured without first separating it from the sample matrix. Thus, the purpose of the isolation stage is to simplify the matrix in which 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 to isolate trace metals in foods.
- 9.4 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 a wide variety of analytes. For example, gas chromatography, or UV-visible spectrophotometry.
- 9.5 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. The sort of parameters which might be varied are sample size, amount and type of extraction solvents, extraction conditions, chromatographic columns or separation conditions, or spectrometer wavelength settings.
- 9.6 The value of such methods for non-routine analysis is that where 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 check that the analysis is valid. Sufficient information will need to be recorded in order that the work can be repeated in precisely the same manner at a later date. Where a particular analysis subsequently becomes routine, a specific method may be validated and documented.
- 9.7 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. The onus will be on the laboratory 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 staff involved will be a major factor in determining whether or not such analyses can be accredited.
-

---

## 10. STAFF

- 10.1 The laboratory management should normally define the minimum levels of qualification and experience necessary for the key posts within the laboratory. Chemical analysis must be carried out by, or under the supervision of a qualified, experienced and competent analyst. Other senior laboratory staff will normally possess similar competencies. Lower formal qualifications may be acceptable when staff have extensive relevant experience and/or the scope of activities is limited. Staff qualified to degree level will normally have at least two years relevant work experience before being considered as experienced analysts. Staff undergoing training or with no relevant qualifications may undertake analyses provided that they have demonstrably received an adequate level of training and are adequately supervised.
- 10.2 In certain circumstances, the minimum requirements for qualifications and experience for staff carrying out particular types of analysis may be specified in regulations.
- 10.3 The laboratory must ensure that all staff receive training adequate to the competent performance of the tests and operation of equipment. Where appropriate, this will include training in the principles and theory behind particular techniques. Where possible, objective measures 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 perform tests on samples. Continued competence must be monitored, for example, using quality control techniques. The need to periodically retrain staff must be considered where a method or technique is not in regular use. Although the laboratory management is responsible for ensuring that adequate training is provided, it must be emphasised that a strong element of self-training takes place, particularly amongst more experienced analysts.
- 10.4 The laboratory 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 individual members of staff have been adequately trained and their competence to carry out particular tests has been assessed. In some cases, it may be pertinent to state any particular limitations to evidence about competence. The records should typically include:
- i) academic qualifications;
  - ii) external and internal courses attended;
  - iii) relevant on-the-job training (and retraining as necessary).
- Possibly also:
- iv) participation in QC and/or proficiency testing schemes, with associated data;
  - v) technical papers published and presentations given at conferences.
- 10.5 In some cases it may be more appropriate to record competence in terms of particular techniques rather than methods.

- 10.6 Access to these training records will be necessary in the course of everyday work. Access to other staff records, usually held centrally by the laboratory and listing personal details may be restricted by national legislation on data protection.

## **11. SAMPLING, SAMPLE HANDLING AND PREPARATION**

- 11.1 Analytical tests may be required for a variety of reasons, including 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 some sort of sample. Clearly the way samples are taken will depend on the reason for the analysis.
- 11.2 The importance of the sampling stage cannot be overemphasised. If the test portion is not representative of the original material, it will not be possible to relate the analytical result measured to that in the original material, no matter how good the analytical method is nor how carefully the analysis is performed. Sampling plans may be random, systematic or sequential and they may be undertaken to obtain quantitative or qualitative information, or to determine conformance or non conformance with a specification.
- 11.3 Sampling always contributes to the measurement uncertainty. 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 increase the total uncertainty of the measurement process. The measurement uncertainty associated with sub-sampling etc should always be included in the test result measurement uncertainty, but the measurement uncertainty associated with the basic sampling process is commonly treated separately.
- 11.4 In many areas of chemical testing the problems associated with sampling have been addressed and methods have been validated and published. 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.
- 11.5 Selection of an appropriate sample or samples, from a larger amount of material, is a very important stage in chemical analysis. It is rarely straightforward. Ideally, 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 as appropriate as possible. It is a very common pitfall to underestimate the importance of the sampling procedure and delegate it to an unskilled and untrained employee.
- 11.6 The terminology used in sampling is complicated and can be confusing. Also the terms used may not be consistent from one application to another. It is important when documenting a sampling procedure to ensure that all of 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.

11.7 One of the best treatments of sampling terminology is given in recommendations published by IUPAC (Refer E7), which describes the terms used in the sampling of bulk goods or packaged goods. In this example, 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.

11.8 For the purposes of the guidance given below the following definitions as proposed by IUPAC have been used:

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

**Sample handling** : This refers to the manipulation to which samples are exposed during the sampling process, from the selection from the original material through to the disposal of all samples and test portions.

**Subsample** : This refers 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**: Primary material delivered to the laboratory.

**Test Sample**: The sample prepared from the laboratory sample.

**Sample preparation** : This describes the procedures followed to select the test portion from the sample (or subsample) and includes: in-laboratory processing; mixing; reducing; coning & quartering; riffing; and milling & grinding.

**Test portion** : This refers to the actual material weighed or measured for the analysis.

11.9 Once received into the laboratory, the *laboratory sample(s)* may require further treatment such as subdivision and or milling and grinding prior to analysis.

11.10 Unless otherwise specified the test portion taken for analysis must be representative of the laboratory sample. To ensure that the test portion is homogeneous it may be necessary to reduce the particle size by grinding or milling. If the laboratory sample is large it may be necessary to subdivide it prior to grinding or milling. 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 maybe subdivided by a variety of mechanisms, including coning and quartering, riffing, or by means of a rotating sample divider or a centrifugal divider. The particle size reduction step may be performed either manually (mortar & pestle) or mechanically using crushers or mills. Care must be taken 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) during milling or grinding. Many standard methods of analysis contain a section that details the preparation of the laboratory sample prior to the withdrawal of the test portion for analysis. In other instances legislation deals with this aspect as a generic issue.
- 11.11 The analytical operations, begin with the measuring out of a *test portion* from the laboratory sample or the test sample and proceeds through various operations to the final measurement.
- 11.12 There are important rules to be followed when designing, adapting, or following a sampling strategy:
- 11.12.1 The problem necessitating the taking of samples and subsequent analysis should be understood and the sampling procedure designed accordingly. The sampling strategy used will depend on the nature of the problem, *e.g.*:
- the average analyte concentration in the material is required;
  - the analyte profile across the material is required;
  - the material is suspected of contamination by a particular analyte;
  - the contaminant is heterogeneously distributed (occurs in hot spots) in the material;
  - there may be other, non-analytical factors to consider, including the nature of the area under examination.
- 11.12.2 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 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.
- 11.12.3 The properties of the analyte(s) of interest should be taken into account. Volatility, sensitivity to light, thermal lability, and chemical reactivity may be important considerations in designing the sampling strategy and choosing equipment, packaging and storage conditions. 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. The significance of gravimetric or

volumetric errors during sampling should be considered and any critical equipment calibrated. It may be appropriate to add chemicals such as acids, or antioxidants to the sample to stabilise it. This is of particular importance in trace analysis where there is a danger of adsorption of the analyte onto the storage vessel.

- 11.12.4 It may be necessary to consider the use and value of the rest of the original material once a sample has been removed for analysis. Poorly considered sampling, especially if destructive, may render the whole consignment valueless or inoperative.
- 11.12.5 Whatever strategy is used for the sampling, it is of vital importance that the sampler keeps a clear record of the procedures followed in order that the sampling process may be repeated exactly.
- 11.12.6 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.
- 11.12.7 Where the laboratory has not been responsible for the sampling stage, it should state in the report that the samples were analysed as received. If the laboratory has conducted or directed the sampling stage, it should report on the procedures used and comment on any consequent limitations imposed on the results.
- 11.13 Sample packaging, and instruments 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 ensure that the sample can be handled without causing a chemical, microbiological, or other hazard.
- 11.14 The enclosure 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.
- 11.15 The sample label is an important aspect of documentation and should unambiguously identify the sample to related plans or notes. Labelling is particularly important, further into 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.
- 11.16 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”.

- 11.17 Samples must be stored at an appropriate temperature and in such a manner so that there is no hazard to laboratory staff and the integrity of the samples is preserved. Storage areas should be kept clean and organised so that there is no risk of contamination or cross-contamination, or of packaging and any related seals being damaged. Extremes of environmental conditions (e.g. temperature, humidity), which might change the composition of the sample should be avoided, as this can lead to loss of analyte through degradation or adsorption, or an increase in analyte concentration (mycotoxins). If necessary environmental monitoring should be used. An appropriate level of security should be exercised to restrict unauthorised access to the samples.
- 11.18 All staff concerned with administration of the sample handling system should be properly trained. The laboratory should have a documented policy for the retention and disposal of samples. The disposal procedure should take into account the guidelines set out above.
- 11.19 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 assumes that the characteristic being inspected is measurable and follows the normal distribution. Whereas sampling for inspection by attributes is a method whereby either the unit of product is classified as conforming or non conforming, or the number of non-conformities in the unit of product is counted with respect to a given set of requirements. In inspection by attributes the risk associated with acceptance/rejection of non-conformities is predetermined by the *acceptable quality level (AQL)* or the *limiting quality (LQ)*.

## 12. ENVIRONMENT

- 12.1 Samples, reagents, measurement standards and reference materials must be stored so as to ensure their integrity. In particular, samples must be stored in such a way that cross contamination is not possible. The laboratory should guard against their deterioration, contamination and loss of identity.
- 12.2 The laboratory environment should be sufficiently uncrowded, clean and tidy to ensure the quality of the work carried out is not compromised.
- 12.3 It may be necessary to restrict access to particular areas of a laboratory because of the nature of the work carried out there. 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, PCR techniques and trace analysis. Where such restrictions are in force, staff should be made aware of:
- i) the intended use of a particular area;
  - ii) the restrictions imposed on working within such areas;

- 
- iii) the reasons for imposing such restrictions;
  - iv) the procedures to follow when such restrictions are breached.
- 12.4 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.
- 12.5 The laboratory shall provide appropriate environmental conditions and controls necessary for particular tests or operation of particular equipment including temperature, humidity, freedom from vibration, freedom from airborne and dustborne microbiological contamination, special lighting, radiation screening, and particular services. Critical environmental conditions must be monitored and kept within predetermined limits.
- 12.6 A breakdown of critical environmental conditions may be indicated either by monitoring systems or by the analytical quality control within the particular tests. The impact of such failures may be assessed as part of ruggedness testing during method validation and where appropriate, emergency procedures established.
- 12.7 Decontamination procedures may be appropriate where environment or equipment is subject to change of use or where accidental contamination has occurred.

## 13. EQUIPMENT (Also see Appendix B)

### 13.1 *Categories of equipment*

13.1.1 All equipment used in laboratories should be of a specification sufficient for the intended purpose, and kept in a state of maintenance and calibration consistent with its use. Equipment normally found in the chemical laboratory can be categorised as:

- i) general service equipment not used for making measurements or with minimal influence on measurements (e.g. hotplates, stirrers, non-volumetric glassware and glassware used for rough volume measurements such as measuring cylinders) and laboratory heating or ventilation systems;
- ii) volumetric equipment (e.g. flasks, pipettes, pyknometers, burettes etc.) and measuring instruments (e.g. hydrometers, U-tube viscometers, thermometers, timers, spectrometers, chromatographs, electrochemical meters, balances etc.).
- iii) physical measurement standards (weights, reference thermometers);
- iv) computers and data processors.

### 13.2 *General service equipment*

13.2.1 General service equipment will typically only be maintained by cleaning and safety checks as necessary. Calibrations or performance checks 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 documented.

### 13.3 *Volumetric equipment and measuring instruments*

- 13.3.1 The correct use of this equipment is critical to analytical measurements and therefore it must be correctly used, maintained and calibrated in line with environmental considerations (section 12). 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 apparatus may therefore require more regular calibration, depending on use. For example, the performance of pycnometers, 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.
- 13.3.2 Attention should be paid to the possibility of contamination arising either from the fabric of the equipment 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 volumetric equipment may be critical, particularly for trace analyses where leaching and adsorption can be significant.
- 13.3.3 Correct use combined with periodic servicing, cleaning and calibration will not necessarily ensure an 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, the resolution, alignment and wavelength accuracy of spectrometers etc.), see Appendix B.
- 13.3.4 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 equipment. Intervals between checks should be shorter than the time the equipment has been found, in practice, to take to drift outside acceptable limits.
- 13.3.5 It is often possible to build performance checks - system suitability checks - into test methods (e.g. based on the levels of expected detector or sensor response to reference materials, the resolution of component mixtures by separation systems, the spectral characteristics of measurement standards, etc.). These checks must be satisfactorily completed before the equipment is used.

### 13.4 *Physical measurement standards*

- 13.4.1 Wherever physical parameters are critical to the correct performance of a particular test, the laboratory shall have or have access to the relevant measurement standard, as a means of calibration.
- 13.4.2 In some cases, a test and its performance is actually defined in terms of a particular piece of equipment and checks will be necessary to confirm that the equipment conforms to the relevant specification. For example, flashpoint values

for a particular flammable sample are dependent of the dimensions and geometry of the apparatus used in the testing.

13.4.3 Measurement standards materials and any accompanying certificates should be stored and used in a manner consistent with preserving the calibration status. Particular consideration should be given to any storage advice given in the documentation supplied with the measurement standard.

13.5 **Computers and data processors.** Requirements for computers are given in section 20.

## 14. REAGENTS

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

14.2 The grade of any critical reagent used (including water) should be stated in the method, together with guidance on any particular precautions which should be observed in its preparation, storage and use. These precautions include toxicity, flammability, stability to heat, air and light; reactivity to other chemicals; reactivity to particular containers; and other hazards. Reagents and reference materials prepared in the laboratory should be labelled to identify substance, strength, 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.

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

14.4 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.

## 15. Traceability

15.1 The formal definition of traceability is given in 3.10 and a CITAC policy statement has been prepared (Ref A6). A guide on the traceability of chemical measurements is under development (Ref A7). Traceability concerns the requirement to relate the results of measurements to the values of standards or references, the preferred reference points being the internationally recognised system of units, the SI. This is achieved through the use of primary standards (or other high level standards) which are used to establish secondary standards that can be used to calibrate working level standards and related measuring systems. Traceability is established at a stated level of measurement uncertainty, where every step in the traceability chain adds further uncertainty. Traceability is important because it provides the linkage that ensures that measurements made in different laboratories or at different times are comparable. It is a matter of choice, as indicated above, whether to claim traceability to local references, or to international references.

- 15.2 Chemical measurements are invariably made by calculating the value from a measurement equation that involves the measured values of other quantities, such as mass, volume, concentration of chemical standards etc. For the measurement of interest to be traceable, all the measurements associated with the values used in the measurement equation used to calculate the result must also be traceable. Other quantities not present in the measurement equation, such as pH, temperature etc may also significantly affect the result. Where this is the case, the traceability of measurements used to control these quantities also need to be traceable to appropriate measurement standards.
- 15.3 Establishing the traceability of physical quantities such as mass, volume, etc., is readily achieved using transfer standards, at the level of uncertainty needed for chemical measurements. The problem areas for chemists are usually (chemical) method validation and calibration. Validation establishes that the method actually measures what it is intended to measure. (e.g. methyl mercury in fish). Validation establishes that the measurement equation used to calculate the results is valid. Calibration is usually based on the use of gravimetrically prepared solutions of pure substance reference materials. The important issues here are identity and purity, 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. The uncertainty of a measurement will in part depend on the uncertainty of the purity of the chemical standard used. However, only in the case of some organic materials, where purity and stability problems can be acute, or where high accuracy assay of major components is required, will purity be a major problem.
- 15.4 For many analyses, where extraction, digestion, derivatisation and saponification are commonly required, the main problem can be gaining good knowledge of the amount of analyte in the original sample relative to that in the sample presented to the end measurement process. This bias (sometimes called “recovery”) can be due to processing losses, contamination or interferences. Some of these effects are manifest within reproducibility uncertainties but others are systematic effects that need separate consideration. The strategies available to address method bias include:
- Use of primary or reference methods of known and small bias
  - Comparisons with closely matched matrix CRMs
  - Measurement of gravimetrically spiked samples and blanks
  - Study of losses, contamination, interferences and matrix effects

Establishing the traceability of this part of the measurement process requires relating the measurement bias to appropriate stated references, such as the values carried by matrix matched reference materials. It should be noted that the measurement of the recovery of spiked samples does not necessarily simulate the extraction of the native analyte from the samples. In, practice, this is not normally a problem where the samples are liquid and/or totally digested. However, problems can occur with the extraction of solids. For example, a spiked analyte may be freely available on the surface of the sample particles, whereas the native analyte may be strongly adsorbed within the particles and therefore much less readily extracted.

- 15.5 Most chemical measurement can, in principle, be made traceable to the mole. When, however, the analyte is defined in functional terms, such as fat or protein based on a nitrogen determination, then specification of the measurement in terms of the mole is not feasible. In such cases the quantity being measured is defined by the method. In these

cases traceability is to standards of the component quantities used to calculate the result, for example mass and volume, and the values produced by a standard method and/or the values carried by a reference material. Such methods are called empirical methods. In other case the limitation in achieving traceability to SI derives from difficulty in evaluating bias and its uncertainty, such as the recovery of the analytes in complex matrices. The options here are to define the measurand by the method and establish traceability to stated references, including a reference method/reference material. Such measurements have a 'lower level' of traceability, but also have a smaller Measurement Uncertainty, relative to the stated references. Alternatively, the bias can be estimated and corrected for and the uncertainty due to the bias can also be estimated and included in the overall uncertainty evaluation. This would allow traceability to the SI to be claimed.

## 16. MEASUREMENT UNCERTAINTY

- 16.1 Measurement uncertainty is formally defined in 3.11. Good practice in the evaluation of measurement uncertainty is described in an ISO Guide (Ref B7) and an interpretation for chemical measurement including a number of worked examples is given in a CITAC/EURACHEM Guide (Ref A2). Measurement uncertainty characterises the range of values within which the true value is asserted to lie, with a specified level of confidence. Every measurement has an uncertainty associated with it, resulting from errors arising in the various stages of sampling and analysis and from imperfect knowledge of factors affecting the result. For measurements to be of practical value it is necessary to have some knowledge of their reliability or uncertainty. A statement of the uncertainty associated with a result conveys to the customer the 'quality' of the result.
- 16.2 ISO/IEC 17025:1999 requires laboratories to evaluate their measurement uncertainty. 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). Thus, statement of measurement uncertainty in test reports should become common practice in the future (Ref B18).
- 16.3 A statement of uncertainty is a quantitative estimate of the limits within which the value of a measurand (such as an analyte concentration) is expected to lie. Uncertainty may be expressed as a standard deviation or a calculated multiple of the standard deviation. In obtaining or estimating the uncertainty relating to a particular method and analyte, it is essential to ensure that the estimate explicitly considers all the possible sources of uncertainty and evaluates significant components. Repeatability or reproducibility, for example, are usually not full estimates of the uncertainty, since neither takes full account of any uncertainties associated with systematic effects inherent in a method.
- 16.4 A wide variety of factors make any analytical measurement result liable to deviate from the true value. For example, temperature effects on volumetric equipment, reflection and stray light in spectroscopic instruments, variations in electrical supply voltages, individual analysts' interpretation of specified methods and incomplete extraction recoveries, all potentially influence the result. As far as reasonably possible, such errors must be minimised by external control or explicitly corrected for, for example by applying a suitable correction factor. The exact deviation of a single measurement result from the (unknown) true value is, however, impossible to obtain. This is because the different factors vary from experiment to experiment, and because the effect of each

- 
- factor on the result is never known exactly. The likely range of deviation must therefore be estimated.
- 16.5 The primary task in assigning a value to the uncertainty of a measurement is the identification of the relevant sources of uncertainty and the assignment of a value to each significant contribution. The separate contributions must then be combined (as shown in Sec. 16.13) in order to give an overall value. A record should be kept of the individual sources of uncertainty identified, the value of each contribution, and the source of the value (for example, repeat measurements, literature reference, CRM data etc.).
- 16.6 In identifying relevant sources of uncertainty, consideration must be given to the complete sequence of events necessary to achieve the purpose of the analysis. Typically this sequence includes sampling and sub-sampling, sample preparation, extraction, clean-up, concentration or dilution, instrument calibration (including reference material preparation), instrumental analysis, raw data processing and transcription of the output result.
- 16.7 Each of the stages will have associated sources of uncertainty. The component uncertainties can be evaluated individually or in convenient groups. For example, the repeatability of a measurement may serve as 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 studies of matrix matched certified reference materials and spiking studies.
- 16.8 The size of uncertainty contributions can be estimated in a variety of ways. The value of an uncertainty component associated with random variations in influence factors may be estimated by measuring the dispersion in results over a suitable number of determinations under a representative range of conditions. (In such an investigation, the number of measurements should not normally be less than ten.) Uncertainty components arising from imperfect knowledge, for example of a bias or potential bias, can be estimated on the basis of a mathematical model, informed professional judgement, international laboratory intercomparisons, experiments on model systems etc. These different methods of estimating individual uncertainty components can be valid.
- 16.9 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, and to measure and record individual uncertainty component values where available as a check on the group contribution.
- 16.10 If information from inter-laboratory trials is used, it is essential to consider uncertainties arising outside the scope of such studies. For example, nominal values for reference materials are typically quoted as a range, and where several laboratories use the same reference material in a collaborative trial, the uncertainty in the reference material value is not included in the inter-laboratory variation. Similarly, inter-laboratory trials typically use a restricted range of test materials, usually carefully homogenised, so the possibility of inhomogeneity and differences in matrix between real samples and collaborative trial test materials should also be taken into account.
- 16.11 Typically, uncertainty contributions for analytical results might fall into four main groups:
-

- 
- i) Contributions from short-term random variability, typically estimated from repeatability experiments.
- ii) Contributions such as operator effects, calibration uncertainty, scale graduation errors, equipment and laboratory effects, estimates from inter-laboratory reproducibility trials, in-house intercomparisons, proficiency test results or by professional judgement.
- iii) Contributions outside the scope of inter-laboratory trials, such as reference material uncertainty.
- iv) Other sources of uncertainty, such as sampling variability (inhomogeneity), matrix effects, and uncertainty about underlying assumptions (such as assumptions about completeness of derivatisation).
- 16.12 The uncertainty contributions for each source must all be expressed in the same way, ideally as standard deviations or relative standard deviations. In some cases, this will entail some conversion. For example, reference material limits are often presumed to have absolute limits. A rectangular distribution of width  $W$  has a standard deviation  $W/(2\sqrt{3})$ . Confidence intervals may be converted to standard deviations by dividing by the appropriate value of Student's  $t$  for large (statistical) samples (1.96 for 95% confidence limits).
- 16.13 Once a list of uncertainties is available, the individual components can be combined. Where individual sources of uncertainty are independent, the general expression for the combined standard uncertainty  $u$  is:
- $$u = \sqrt{\sum (\partial R/\partial x_i)^2 \cdot u(x_i)^2}$$
- where  $\partial R/\partial x_i$  is the partial differential of the result  $R$  with respect to each intermediate value (or other 'influence quantity' such as a correction  $x_i$ ) and  $u(x_i)$  is the uncertainty component associated with  $x_i$ .
- 16.14 This expression simplifies considerably for the two most common cases. Where the influence quantities or intermediate results are added or subtracted to give the result, the uncertainty  $u$  is equal to the square root of the sum of the squared contributing uncertainty components, all expressed as standard deviations. Where interim results are combined by multiplication or division, the combined relative standard deviation (RSD) is calculated by taking the square root of the sum of the squared RSDs for each interim result, and the combined standard uncertainty  $u$  calculated from the combined RSD and the result.
- 16.15 The overall uncertainty should be expressed as a multiple of the calculated standard deviation. The recommended multiplier is 2, that is, the uncertainty is equal to  $2u$ . Where the contributions arise from normally distributed errors, this value will correspond approximately to a 95% confidence interval.
- 16.16 It is not normally safe to extend this argument to higher levels of confidence without knowledge of the distributions concerned. In particular, it is commonly found that
-

experimental uncertainty distributions are far wider at the 99% level of confidence than would be predicted by assumptions of normality.

- 16.17 It is often not necessary to evaluate uncertainties for every test and sample type. It will normally be sufficient to investigate the uncertainty once only, for a particular method and to use the information to estimate the measurement uncertainty for all tests carried out within the scope of that method.

## **17. METHODS / PROCEDURES FOR CALIBRATIONS & TESTS**

- 17.1 It is the laboratory's responsibility to use methods which are appropriate for the required application. The laboratory may use its own judgement, it may select a method in consultation with the customer, or the method may be specified in regulation or by the customer.
- 17.2 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 should be suitable for the purpose intended, be adequately validated and documented and provide results that are traceable to stated references at an appropriate level of uncertainty.
- 17.3 The validation of a standard or collaboratively tested methods should not be taken for granted, no matter how impeccable the method's pedigree - the laboratory should satisfy itself that the degree of validation of a particular method is adequate for the required purpose, and that the laboratory is itself able to verify any stated performance criteria.
- 17.4 Methods developed in-house must be adequately validated, documented and authorised before use. Where they are available, matrix matched reference materials should be used to determine any bias, or where this is not possible, results should be compared with other technique(s), preferably based on different principles of measurement. Measurement of the recovery of gravimetrically added spike analyte, measurement of blanks and the study of interferences and matrix effects can also be used to check for bias or imperfect recovery. Estimation of uncertainty must form part of this validation process and in addition to covering the above factors, should address issues such as sample homogeneity and sample stability. Advice on method validation is given in Section 18.
- 17.5 Documentation of methods shall include validation data, limitations of applicability, procedures for quality control, calibration and document control. A laboratory documenting methods may find it convenient to adopt a common format, such as ISO 78-2: (Ref C10), which provides a useful model. In addition, advice on documentation of methods is available from other sources such as national standardisation bodies and accreditation bodies.
- 17.6 Developments in methodology and techniques will require methods to be changed from time to time and therefore method documentation must be subject to adequate document control. Each copy of the method should show issue number/date, issuing authority, and copy number. It must be possible to determine from records which is the most up-to-date version of each method is authorised for use.

- 17.7 Obsolete methods should 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.
- 17.8 When methods are revised then the validation also needs to be updated. The revision may be of a minor nature, involving different sample sizes, different reagents etc. Alternatively, it may involve significant changes, such as the use of radically different technology or methodology. The level of revalidation required increases with the scale of the changes made to the method.

## 18. METHOD VALIDATION

- 18.1 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. These checks are collectively known as validation. 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 analytical problem. The important performance characteristics include:

- Selectivity & specificity (Description of the measurand),
- Measurement range
- Calibration and traceability,
- Bias \*
- Linearity,
- Limit of detection/ Limit of quantitation,
- Ruggedness,
- Precision.

\* In some fields of chemical measurement, the term recovery is used to describe the total bias, in other fields, recovery is used in relation to certain elements of bias.

The above characteristics are interrelated, many of these contribute to the overall measurement uncertainty and the data generated may be used to evaluate the measurement uncertainty (see Section 16 and refer C13) during validation.

Good practice in method validation is described in a EURACHEM Guide (Ref A3). Note that there is no unanimous agreement on the interpretation of some of the above terms nor the conventions used in their determination. Thus, when stating validation data, it is advisable to state any conventions followed.

- 18.2 The extent of validation must be clearly stated in the documented method so that the user can assess the suitability of the method for their particular needs.
- 18.3 Standard methods will have been developed and validated collaboratively by a group of experts (ref C14-C19). This development should include consideration of all of the necessary aspects of validation and related 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. Even if the validation is complete, the

- user will still need to verify that the documented performance characteristics (eg trueness and precision) can be met in their own laboratory.
- 18.4 As indicated above, there are different opinions concerning the terminology and the process of method validation. The following explanations supplement those in other parts of this guide and are intended as a guide rather than a definitive view.
- 18.5 **Selectivity** of a method refers to the extent to which it can determine particular analyte(s) in a complex mixture without interference from the other components in the mixture. A method which is selective for an analyte or group of analytes is said to be *specific*. 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 in the applicability of the technique should be documented in the method. This work will allow a clear description of the measurand to be made.
- 18.6 **Range**: For quantitative analysis the working range for a method is determined by examining samples with different analyte concentrations and determining the concentration range for which acceptable uncertainty can be achieved. The working range is generally more extensive than the linear range, which is determined by the analysis of a number of samples of varying analyte concentrations and calculating the regression from the results, usually using the method of least squares. The relationship of analyte response to concentration does not have to be perfectly linear for a method to be effective. For methods showing good linearity it is usually sufficient to plot a calibration curve using measurement standards at 5 different concentration levels (+ blank). More measurement standards will be required where linearity is poor. In qualitative analysis, it is common place to examine replicate samples and measurement standards over a range of concentrations to establish at what concentration a reliable cut-off point can be drawn between detection and non-detection (also see section 18.8).
- 18.7 **Linearity** for quantitative methods is determined by the measurement of samples with analyte concentrations spanning the claimed range of the method. The results are used to calculate a regression line against analyte calculation using the least squares method. It is convenient if a method is linear over a particular range but it is not an absolute requirement. Where linearity is unattainable for a particular procedure, a suitable algorithm for calculations should be determined.
- 18.8 For qualitative methods, there is likely to be a concentration threshold below which positive identification becomes unreliable. The response range should be examined by testing a series of samples and measurement standards, consisting of sample blanks, and samples containing a range of analyte levels. At each concentration level, it will be necessary to measure approximately 10 replicates. A response curve of % positive (or negative) results versus concentration should be constructed. From this it will be possible to determine the threshold concentration at which the test becomes unreliable. In the example shown below, positive identification of the analyte ceases to be 100% reliable below  $100 \mu\text{g.g}^{-1}$ .

**Example:**

<i>Concentration (<math>\mu\text{g}\cdot\text{g}^{-1}</math>)</i>	<i>No. Replicates</i>	<i>Positive/Negative</i>
200	10	10/0
100	10	10/0
75	10	5/5
50	10	1/9
25	10	0/10
0	10	0/10

- 18.9 The **limit of detection** of an analyte is often determined by repeat analysis of a blank test portion and is the analyte concentration the response of which is equivalent to the mean blank response plus 3 standard deviations. Its value is likely to be different for different types of sample.
- 18.10 The **limit of quantitation** is the lowest concentration of analyte that can be determined with an acceptable level of uncertainty. It should be established using an appropriate measurement standard or sample, i.e. it is usually the lowest point on the calibration curve (excluding the blank). It should not be determined by extrapolation. Various conventions take the limit to be 5, 6 or 10 standard deviations of the blank measurement.
- 18.11 **Ruggedness:** Sometimes also called **robustness**. Where different laboratories use the same method they inevitably introduce small variations in the procedure, which may or may not have a significant influence on the performance of the method. The ruggedness of a method is tested by 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. Ruggedness is normally evaluated by the originating laboratory, before other laboratories collaborate.
- 18.12 The **bias (sometimes called recovery)** of a measuring system (method) is the systematic error of that measuring system. The issues associated with the estimation of bias and recovery are discussed in Section 15.4.

In addition to evaluating the bias, it is important to estimate the measurement uncertainty associated with the bias and to include this component in the overall estimate of measurement uncertainty.

- 18.13 The **precision** of a method is a statement of the closeness of agreement between mutually independent test results and is usually stated in terms of standard deviation. It is generally dependent on analyte concentration, and this dependence should be determined and documented. It may be stated in different ways depending on the conditions in which it is calculated. Repeatability is a type of precision relating to measurements made under repeatable conditions, i.e.: same method; same material; same operator; same laboratory; narrow time period. Reproducibility is a concept of precision relating to measurements made under reproducible conditions, i.e.: same method; different operator; different laboratories; different equipment; long time period. Precision is a component of Measurement Uncertainty (see Section 16).

- 18.14 Note that these statements of precision relate to quantitative analysis. Qualitative analysis can be treated in a slightly different way. Qualitative analysis effectively is a yes/no measurement at a given threshold analyte value. For qualitative methods the precision cannot be expressed as a standard deviation or relative standard deviation, but may be expressed as true and false positive (and negative) rates. These rates should be determined at a number of concentrations, below, at and above the threshold level. Data from a confirmatory method comparison should be used if such an appropriate method is available. If such a method is not available spiked and unspiked blank samples can be analysed.

$$\% \text{ false positives} = \text{false positives} \times 100 / \text{total known negatives}$$

$$\% \text{ false negatives} = \text{false negatives} \times 100 / \text{total known positives}$$

- 18.15 Confirmation is sometimes confused with repeatability. Whereas repeatability requires the measurement to be performed several times by one technique, confirmation requires the measurement to be performed by more than one technique. Confirmation increases confidence in the technique under examination and is especially useful where the additional techniques operate on significantly different principles. In some applications, for example, the analysis of unknown organics by gas chromatography, the use of confirmatory techniques is essential.

## 19. CALIBRATION

- 19.1 Calibration is a set of operations that establish, under specified conditions, the relationship between values of quantities indicated by a measuring instrument or measuring system, or values represented by a material measure, and the corresponding values realized by standards (refer VIM-B6) The usual way to perform calibration is to subject known amounts of the quantity (e.g. using a measurement standard or reference material) to the measurement process and monitor the measurement response. More detailed information on reference materials is given in the next chapter.
- 19.2 The overall programme for calibration in the chemical laboratory shall be designed to ensure that all measurements that have a significant effect on test or calibration results are traceable to a measurement standard, preferably a national or international measurement standard such as a reference material. Where appropriate and where feasible, certified reference materials should be used. Where formally designated measurement standards are not available, a material with suitable properties and stability should be selected or prepared by the laboratory and used as a laboratory measurement standard. The required properties of this material should be characterised by repeat testing, preferably by more than one laboratory and using a variety of validated methods (see ISO Guide 35: Ref C6).
- 19.3 Analytical tests may be sub-divided into general classes depending on the type of calibration required:
- 19.3.1 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. In

addition, the calibration of measuring devices used to establish the purity or amount concentration of the chemical standards, need to be considered.

- 19.3.2 Where a test is used to measure an empirical property of a sample, such as flashpoint, equipment is often defined in a national or international standard method and traceable reference materials should be used for calibration purposes where available. New or newly acquired equipment must be checked by the laboratory before use to ensure conformity with specified design, performance and dimension requirements.
- 19.3.3 Instruments such as chromatographs and spectrometers, which require calibration as part of their normal operation, should be calibrated using reference materials of known composition (probably solutions of pure chemicals).
- 19.3.4 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 reference material that has been subjected to the same full analytical process as the sample. The reference material may be either a synthetic mixture prepared in the laboratory from materials of known (and preferably certified) purity, or a purchased certified matrix reference material. However, in such cases, a close match between the test sample and the matrix reference material, in terms of the nature of the matrix, and the concentration of the analyte has to be assured.
- 19.4 However, in many cases, calibration is only performed on the final measurement stage. For example calibration of a gas chromatography method may be carried out using a series of measurement standards which are synthetic solutions of the analyte of interest at various concentrations. Such calibration does not take into account factors such as contamination or losses that occur during the sample preparation and extraction or derivatisation stages. It is therefore essential during the method validation process to explore the potential problems of contamination and losses by taking matrix reference materials or spiked samples through the whole measurement process, and design the day-to-day calibration procedure and quality control checks accordingly (Also see Section 15.4).
- 19.5 Individual calibration programmes shall be established depending on the specific requirements of the analysis. Also, it may be necessary to check instrument calibration after any shutdown, whether deliberate or otherwise, and following service or other substantial maintenance. The level and frequency of calibration should be based on previous experience and should be at least that recommended by the manufacturer. Guidance on calibration is given in Appendix B and includes typical calibration intervals for various types of simple instruments and indicates the parameters which may require calibration in more complex analytical instruments. The frequency of calibration required will depend on the stability of the measurement system, the level of uncertainty required and the criticality of the work.
- 19.6 Procedures for performing calibrations shall be adequately documented, either as part of specific analytical methods or as a general calibration document. The documentation should indicate how to perform the calibration, how often calibration is necessary, action to be taken in the event of calibration failure. Frequency intervals for recalibration of physical measurement standards should also be indicated.

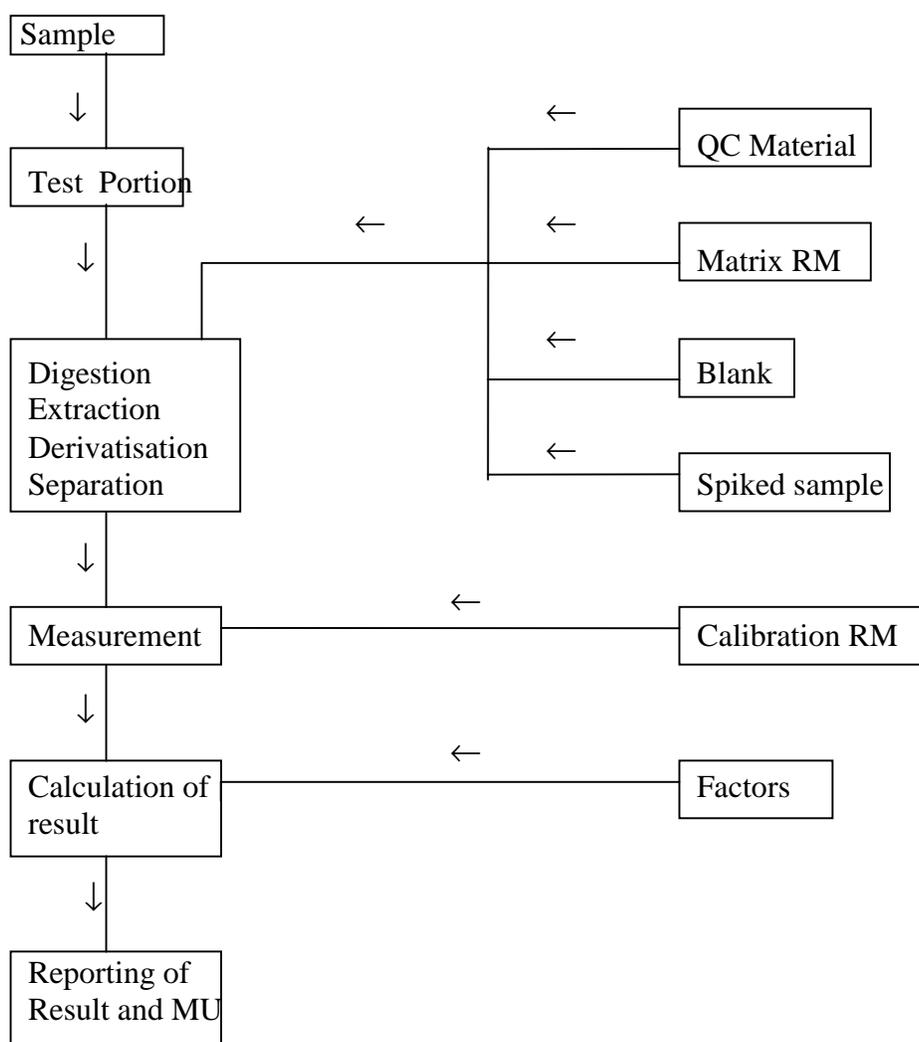


FIGURE 1

- 19.7 The calibration of volumetric glassware normally relates to a particular solvent at a particular temperature. The calibration is rarely valid when the glassware is used with other solvents because of different densities, wetting characteristics, surface tension etc. This is particularly pertinent for volumetric glassware calibrated to deliver a certain volume. Other volumetric equipment may be affected when using solvents with high rates of thermal expansion. In such situations the glassware should be recalibrated using the relevant solvent, at the correct temperature. Alternatively, for the highest accuracy, measurements can often be made by mass rather than by volume.
- 19.8 Figure 1 is a typical analytical process and illustrates the role of calibration in relation to method validation and quality control.

## 20. REFERENCE MATERIALS

- 20.1 A series of ISO Guides relating to reference materials are available (Ref C1 – C6).

- 
- 20.2 *Reference materials and certified reference materials* are defined in section 3. They are used for calibration, method validation, measurement verification, evaluating Measurement Uncertainty and for training purposes.
- 20.3 Reference materials may take a variety of forms, including pure substance RMs, matrix RMs and solutions or mixtures. The following are all examples of reference materials:
- 95% pure sodium chloride;
  - an aqueous solution containing 1% (w/v) copper (II) sulphate and 2% (w/v) magnesium chloride;
  - a powdered polymer with a particular weight distribution range;
  - a crystalline solid melting in the range 150-151°C;
  - a dried milk powder containing a known amount of vitamin C
- 20.4 For many types of analysis, calibration may be carried out using reference materials prepared within the laboratory from chemicals of known purity and composition. Some chemicals may be purchased with a manufacturers certificate stating purity. Alternatively, chemicals of a stated but uncertified purity may be purchased from reputable suppliers. Whatever the source, it is the users' responsibility to establish that the quality of such materials is satisfactory. 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 for reference material purposes should be purchased from producers with demonstrated QA systems. However a QA system 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 analysis, where they may cause interferences. Due regard should be paid to the manufacturers recommendations on storage and shelf life. In addition, caution is needed, as suppliers do not always provide information about all impurities.
- 20.5 The use of appropriate reference materials can provide essential traceability and enable analysts to demonstrate the accuracy of results, calibrate equipment and methods, monitor laboratory performance and validate methods, and enable comparison of methods by use as transfer (measurement) standards. Their use is strongly encouraged wherever appropriate.
- 20.6 The uncertainty of purity of a pure substance reference material, needs to be considered in relation to the uncertainty associated with other aspects of the method. Ideally, the uncertainty associated with a reference material, used for calibration purposes, should not contribute more than one third of the overall measurement uncertainty
- 20.7 The composition of the certified reference material should be as close as possible to that of the samples. Where matrix interferences exist, ideally a method should be validated using a matched matrix reference material certified in a reliable manner. If such a material is not available it may be acceptable to use a sample spiked with a reference material.
- 20.8 It is important that any certified reference material used has been produced and characterised in a technically valid manner. Users of CRMs should be aware that not all

materials are validated with the same degree of rigour. Details of homogeneity trials, stability trials, 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 the pedigree. The material must be accompanied by a certificate, which includes an estimate of uncertainty of the certified value (see Section 16). ISO Guide 34 (Ref C5) and an ILAC Guide (Ref B15) deal with criteria for the competence of reference material producers. These guides may provide the basis for future assessment of reference material producers.

- 20.9 Reference materials and certified reference materials should be clearly labelled so that they are unambiguously identified and referenced against accompanying certificates or other documentation. Information should be available indicating shelf life, storage conditions, applicability, and restrictions of use. Reference materials made up within the laboratory, e.g. as solutions should be treated as reagents for the purposes of labelling, see Section 14.2.
- 20.10 Reference materials and measurement standards should be handled in order to safeguard against contamination or degradation. Staff training procedures should reflect these requirements.

## 21. QUALITY CONTROL AND PROFICIENCY TESTING

- 21.1 The meaning of the terms 'quality control' and 'Quality Assurance (QA)' often vary according to the context. In practical terms, QA relates to the overall measures taken by the laboratory to regulate quality, whereas quality control describes the individual measures which relate to the quality of individual samples or batches of samples.
- 21.2 As part of their quality systems, and to monitor day-to-day and batch-to-batch analytical performance, laboratories must operate an appropriate level of internal quality control (QC) checks and participate wherever possible in appropriate proficiency testing schemes (external QC). The level and type of QC will depend on criticality, nature of the analysis, frequency of analysis, batch size, degree of automation, and test difficulty and reliability.
- 21.3 **Internal QC:** This may take a variety of forms including the use of: blanks; measurement standards; spiked samples; blind samples; replicate analysis and QC samples. The use of control charts is recommended, particularly for monitoring QC control samples (Ref C20-22).
- 21.3.1 The level of QC adopted must be demonstrably sufficient to ensure the validity of the results. Different types of quality control may be used to monitor different types of variation within the process. QC samples, analysed at intervals in the sample batch will indicate drift in the system; use of various types of blank will indicate what are the contributions to the instrument besides those from the analyte; duplicate analyses give a check of repeatability, as do blind samples.
- 21.3.2 QC samples are typical samples which are sufficiently stable and available in sufficient quantities as to be available for analysis over an extended period of time. Over this period the random variation in performance of the analytical process can be monitored by monitoring the analysed value of the QC sample, usually by plotting it on a control chart. As long as the QC sample value is

acceptable, it is likely that results from samples in the same batch as the QC sample can be taken as reliable. The acceptability of the value obtained with the QC sample should be verified as early as practicable in the analytical process so that in the event of system failure as little effort as possible has been wasted on unreliable sample analysis.

- 21.3.3 It is the responsibility of the analyst to set and justify an appropriate level of quality control, based on a risk assessment taking into account the reliability of the method, and the criticality of the work. It is widely accepted that for routine analysis, a level of internal QC of 5% has been identified as reasonable, i.e., 1 in every 20 samples analysed should be a QC sample. However, for robust routine methods with high sample throughput, a lower level of QC may be reasonable. For more complex procedures, a level of 20% is not unusual and on occasions even 50% may be required. For analyses performed infrequently, a full system validation should be performed on each occasion. This may typically involve the use of a reference material containing a certified or known concentration of analyte, followed by replicate analyses of the sample and spiked sample (a sample to which a known amount of the analyte has been deliberately added). Those analyses undertaken more frequently should be subject to systematic QC procedures incorporating the use of control charts and check samples.
- 21.4 **Proficiency testing (External QC):** One of the best ways for an analytical laboratory to monitor its performance against both its own requirements and the norm of other laboratories, is to participate regularly in proficiency testing schemes (Refer C7). Proficiency testing helps to highlight not only repeatability and reproducibility performance between laboratories, but also systematic errors, i.e. bias. Proficiency testing and other types of intercomparisons are accepted as being an important means of monitoring quality at national and international levels.
- 21.5 Accreditation bodies also recognize the benefit of these schemes as objective evidence of competence of the laboratory and of the effectiveness of the assessment process itself. Where possible, laboratories should select Proficiency Testing schemes which operate according to good international practice (Refer C7) and have transparent evidence of quality, eg. by accreditation or other peer review (Refer B16). Accredited laboratories are normally required to participate in proficiency testing, (where suitable schemes exist), as an integral part of their QA protocols. It is important to monitor proficiency testing results as a means of checking performance and to take corrective action as necessary.

## 22. COMPUTERS AND COMPUTER CONTROLLED SYSTEMS

22.1 In chemical testing laboratories, computers 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;
- design and performance of statistical experiments;
- 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;
  - matching of sample and library data;
  - generation of test reports;
  - word processing;
  - communication.
- 22.2 Interfaces and cables provide physical connections between different parts of the computer or between different computers. It is important that interfaces and cables are chosen to suit the particular application since they can seriously affect speed and quality of data transfer.
- 22.3 The chemical testing environment creates particular hazards for the operation of computers and storage of computer 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.
- 22.4 Initial validation should verify as many aspects of a computer's operation as possible. Similar checks should 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, for validation of that function, it is usually sufficient to assume correct operation if the computer produces expected answers when input with known parameters. Computer programs 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. In chemical testing, suitable checks on the data gathering and handling functions could be made using a Certified Reference Material for the initial validation, with a secondary measurement standard such as a quality control material used for regular repeat checks. Any recommendations made by the manufacturer should be taken into consideration. The validation procedure used for a particular system and any data recorded during validation should be documented. It may be difficult to validate these systems in isolation from the analytical instrument producing the original signal. Usually the whole system is validated in one go, by using chemical measurement standards or reference materials. Such validation is normally acceptable. It is convenient to illustrate validation using examples of typical applications:
- 22.4.1 **Word-processing packages** are widely used in laboratories to generate a wide 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 hard copies. More sophisticated systems read and process data to automatically produce reports in predetermined formats. Such systems will require additional checks.
- 22.4.2 **Microprocessor controlled instruments** will normally have a self-checking routine which is activated when the 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 reference materials, physical or chemical measurement standards or quality control samples.

- 22.4.3 ***Data handling or processing systems, integration systems.*** Before it can be processed, the output from the analytical instrument will usually need to be converted to a digital signal using an analogue/digital converter. The digitised data is then translated into a recognisable signal (numbers, peaks, spectra according to the system) by the software algorithm. The algorithm makes various decisions (such as deciding where peaks start and finish, or whether a number should be rounded up or down) according to programmed instructions. The algorithm is a common source of unexpected performance and validation should test the logic behind the decisions made by the algorithm.
- 22.4.4 ***Computer controlled automated system.*** This may embrace one or more of the foregoing examples, operated either simultaneously or in controlled time sequence. Such systems will normally be validated 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 validation should consist of a validation 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. One important consideration is that the computer, interfaces and connecting cabling have sufficient capacity for the required tasks. If any part of the system is overloaded, its operation will slow down and possibly data may be lost. This could have serious consequences where the operations include time sequenced routines. Where possible the controlling software should be tailored to identify and highlight any such malfunctions and tag associated data. The use of quality control samples and standards run at intervals in the sample batches should then 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 should be checked to ensure that no corruption has occurred during transmission. This can be achieved on the computer by the use of 'verification files' but, wherever practical, the transmission should be backed-up by a hard copy of the data.
- 22.4.5 ***Laboratory Information Management Systems.*** LIMS systems are increasingly popular as a way of managing 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 analytical 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; quality control; financial control; and report generation. 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 analytical instrumentation 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 remote, perhaps transmitted via

a modem or electronic mail. Similarly the information could be downloaded to a disk. Where data crosses 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 entry 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 is transmitted electronically it will be necessary to build in safety checks to guard against data corruption and unauthorised access.

## 23. LABORATORY AUDIT AND REVIEW

- 23.1 See Section 3.6 for terminology.
- 23.2 An important aspect of quality management is the periodic re-examination of the quality system by the laboratory's own management. In general, all aspects of the quality system should be examined at least once a year. The system should be examined in two ways. Firstly, it should be examined to ensure that it is sufficiently well documented to enable adequate and consistent implementation, and that staff are actually following the system described. This examination is commonly known as auditing (as opposed to the external auditing or assessment carried out by accreditation or certification bodies). Secondly, the system should be examined to see 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 quality system should evolve to continue to fulfil its purpose. This second type of examination is commonly known as review and should be carried out at least annually. It is carried out by the laboratory management and draws on information from a number of sources, including results from internal audits, external assessments, proficiency testing scheme participation, internal quality control studies, market trends, customer complaints and compliments, etc.
- 23.3 The programme of audits and review is normally co-ordinated by the laboratory quality manager, who is responsible for ensuring that auditors have the correct training, guidance and authority necessary for their work. Audits are normally carried out by laboratory staff who work outside of the area they are examining. This is of course not always possible where staff numbers are small.
- 23.4 Audits may be carried out in two basic ways. In the horizontal audit, the auditor will examine in detail single aspects of the quality system, for example calibration or reports. In the vertical audit the auditor will select a sample and follow its progress from receipt to disposal, examining all aspects of the quality system relating to its testing.
- 23.5 A check list, detailing the aspects of a chemical laboratory which should be examined during a quality audit is listed in Appendix A of this Guide.
- 23.6 The management review should be carried out at regular intervals. Once a year is normally sufficient, although, for laboratories with extensive scopes of accreditation it may be necessary to split the review into discrete modules, that can be examined during the course of the year. Issues which should be covered at the annual review include the

quality system and issues which affect analytical quality, internal audits, corrective and preventative action, client feedback and complaints.

---

## REFERENCES AND BIBLIOGRAPHY

The following section provides useful References (Subsections A, B, C - these are referred to in the text - Website addresses (D), a Bibliography (E)).

### A. CITAC and EURACHEM GUIDES

(available on CITAC [www.citac.ws](http://www.citac.ws) and EURACHEM [www.eurachem.org](http://www.eurachem.org))

1. Quality Assurance for Research and Development and Non-Routine Analysis: 1998 (CITAC/EURACHEM)
2. Quantifying Uncertainty in Analytical Measurement: 2000 (CITAC/EURACHEM) (see also website – ref D12)
3. The Fitness for Purpose of Analytical Methods: A Laboratory Guide to Method Validation and Related Topics: 1998 (EURACHEM)
4. Harmonised Guidelines for the Use of Recovery Information in Analytical Measurement: 1998 (EURACHEM/IUPAC/ISO/AOACI)
5. Selection, Use & Interpretation of Proficiency Testing (PT) Schemes by Laboratories: 2000 (EURACHEM)
6. CITAC Policy Statement on Traceability in Chemical Measurement: 2000
7. CITAC/EURACHEM Guide on Traceability in Chemical Measurements: 2002 (under preparation)

### B. KEY REFERENCES

1. ISO/IEC 17025:1999 General requirements for the competence of testing and calibration laboratories
2. ISO 9000:2000 Quality Management Systems - Fundamentals & Vocabulary
3. OECD Principles of Good Laboratory Practice: 1998 (Code: ENV/MC/CHEM(98)17 download: <http://www1.oecd.org/ehs/ehsmono/01E88455.pdf>)
4. ISO/IEC Guide 2:1996 Standardization and related activities - General vocabulary (currently under revision as ISO 17000)
5. ISO 9001:2000 Quality Management Systems - Requirements
6. International vocabulary of basic and general terms in metrology (VIM) - 2<sup>nd</sup> edition 1993 (ISO/BIPM/IEC/IFCC/IUPAC/IUPAP/OIML)
7. Guide to the Expression of Uncertainty in Measurement (GUM), ISO Geneva Switzerland, 1995.
8. Meeting the Measurement Uncertainty and Traceability Requirements of ISO/IEC 17025 in Chemical Analysis" - B King, Fresenius Journal, 2001
9. The selection and use of reference materials - A basic guide for laboratories and accreditation bodies - draft EEEE/RM 2002 - prepared by B King 2000

- 
10. [Position of third party quality assessment of reference materials and their production EEEE/RM/069 rev 1: Draft 2001](#)
  11. [APLAC Policy and Guidance on the Estimation of Uncertainty of Measurement in Testing - Draft April 2002](#)
  12. [ILAC P10: 2002 ILAC Policy on Traceability of Measurements Results](#)
  13. [ILAC G8: 1996 Guidelines on Assessment and Reporting of Compliance with Specification](#)
  14. [ILAC G9: 1996 Guidelines for the Selection and Use of Certified Reference Materials](#)
  15. [ILAC G12: 2000 Guidelines for the Requirements for the Competence of Reference Material Producers](#)
  16. [ILAC G13: 2000 Guidelines for the Requirements for the Competence of Providers of Proficiency Testing Schemes](#)
  17. [ILAC G15: 2001 Guidance for Accreditation to ISO/IEC 17025](#)
  18. [ILAC G17: 2002 Guidance for Introducing the Concept of Uncertainty of Measurement in Testing in Association with the Application of the Standard ISO/IEC 17025](#)

*Note: Other Guidelines produced by Regional Accreditation Bodies are also relevant here (see website addresses in Sec. D, nos. 7, 8 & 9 below). In addition most national accreditation bodies issue guidance in support of their requirements (usually based on ISO standards).*

#### **C. OTHER REFERENCES (ISO Guides and Standards)**

1. ISO Guide 30:1992 Terms and definitions used in connection with reference materials
2. ISO Guide 31:2000 Reference materials -- Contents of certificates and labels
3. ISO Guide 32:1997 Calibration in analytical chemistry and use of certified reference materials
4. ISO Guide 33:2000 Uses of certified reference materials
5. ISO Guide 34:2000 General requirements for the competence of reference material producers
6. ISO Guide 35:1989 (under revision) Certification of reference materials -- General and statistical principles
7. ISO/IEC Guide 43:1997 Proficiency testing by interlaboratory comparisons - Part 1: Development and operation of proficiency testing schemes and Part 2: Selection and use of proficiency testing schemes by laboratory accreditation bodies
8. ISO/IEC Guide 58: 1993 Calibration and testing laboratory accreditation systems - general requirements for operation and recognition. (To be replaced by ISO/IEC 17011 General requirements for bodies providing assessment and accreditation)
9. ISO/IEC Guide 62:1996 General requirements for bodies operating assessment and

- 
- certification/registration of quality systems
10. ISO 78-2:1999 Chemistry -- Layouts for standards -- Part 2: Methods of chemical analysis
  11. [ISO/DIS 10576-1:2001 Statistical Methods - Guidelines for the evaluation with specified requirements Pt 1. General principles](#)
  12. ISO 3534 Statistics -- Vocabulary and symbols -- Parts 1, 2 and 3 (1999)
  13. ISO/DTS 21748-2002 (under preparation) Guide to the use of repeatability and reproducibility and trueness estimates in measurement uncertainty estimation
  14. ISO 5725-1:1994 Accuracy (trueness and precision) of measurement methods and results -- Part 1: General principles and definitions  
ISO 5725-1:1994/Cor 1:1998
  15. ISO 5725-2:1994 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
  16. ISO 5725-3:1994 Accuracy (trueness and precision) of measurement methods and results -- Part 3: Intermediate measures of the precision of a standard measurement method
  17. ISO 5725-4:1994 Accuracy (trueness and precision) of measurement methods and results -- Part 4: Basic methods for the determination of the trueness of a standard measurement method
  18. ISO 5725-5:1998 Accuracy (trueness and precision) of measurement methods and results -- Part 5: Alternative methods for the determination of the precision of a standard measurement method
  19. ISO 5725-6:1994 Accuracy (trueness and precision) of measurement methods and results -- Part 6: Use in practice of accuracy values
  20. ISO 7870:1993 Control charts - General guide and introduction
  21. ISO 7966:1993 Acceptance control charts
  22. ISO 8258:1991 Shewhart control charts.
- D. [USEFUL WEBSITE ADDRESSES](#)**
1. [CITAC - www.citac.ws](#)
  2. [EURACHEM - www.eurachem.org](#)
  3. [ISO - www.iso.ch](#)
  4. [\(ISO\)REMCO - www.iso.org/remco](#)
-

- 
5. [COMAR \(Reference Material Data Base\) - www.comar.bam.de](http://www.comar.bam.de)
  6. [AOAC - www.aoac.org](http://www.aoac.org)
  7. [ILAC - www.ilac.org](http://www.ilac.org)
  8. [APLAC - www.ianz.govt.nz/aplac](http://www.ianz.govt.nz/aplac)
  9. [EA - www.european-accreditation.org](http://www.european-accreditation.org)
  10. [BIPM - www.bipm.fr](http://www.bipm.fr)
  11. [OECD – www.oecd.org](http://www.oecd.org)
  12. [www.muttraining.com](http://www.muttraining.com) (web based training on measurement uncertainty and accreditation)
  13. [www.measurementuncertainty.org](http://www.measurementuncertainty.org) (MU forum/search engine – linked to Ref A2)

#### **E. BIBLIOGRAPHY**

1. AOAC International - ISO 17025 and the Laboratory - An Introduction to Laboratory Accreditation: 2000
2. AOAC International - Quality Assurance Principles for Analytical Laboratories - 3<sup>rd</sup> Edition 2000 - F M Garfield, E Klesten, J Husch ISBN-0-935584-70-6
3. Crosby, Neil T; Patel, Indu, General principles of good sampling practice, Cambridge: Royal Society of Chemistry, 1995
4. Enell, J. W., "Which Sampling Plan Should I Choose?", Journal of Quality Technology 1984, 16(3), 168-171
5. Garfield, F. M., "Sampling in the Analytical Scheme.", J. - Assoc. Off. Anal. Chem. 1989, 72(3), 405-411
6. Gy, Pierre, Sampling for analytical purposes, Chichester: Wiley, 1998
7. Horwitz, W., "Nomenclature for sampling in Analytical Chemistry", IUPAC, Pure Appl. Chem. 1990, 62(6), 1193-1208
8. Horwitz, W., "Problems of Samplings and Analytical Methods", J. - Assoc. Off. Anal. Chem. 1976, 59(6), 1197-1203
9. Horwitz, W., "Design, conduct and interpretation of method performance studies", IUPAC Protocol, 1994
10. Kateman, G., Buydens, L., Quality Control in Analytical Chemistry, 2nd ed. New York: Wiley, 1993
11. Keith, L. H., Environmental Sampling and Analysis., A Practical Guide, Lewis Publishers, Chelsea, MI, 1991

12. Keith, L. H., Principles of Environmental Sampling, ACS, Washington DC, 1988
13. Keith, Lawrence H (Ed), Principles of environmental sampling. 2nd ed, Washington, D.C. American Chemical Society c1996
14. Kratochvil, B., Wallace, D., and Taylor, J. K., "Sampling for Chemical Analysis", Anal. Chem. 1984, 56(5), 113R-129R
15. Miller, J.C.; Miller, J.N. Statistics for Analytical Chemistry, 4th ed Ellis Horwood 1998
16. Prichard, E, Analytical Measurement Terminology - (UK's Valid Analytical Measurement Program, LGC Ltd) ISBN 0-85404-443-4, 2000
17. Prichard, E., Quality in the Analytical Chemistry Laboratory, ACOL, Wiley 1997
18. Stoeppler, Marcus (Ed), Sampling and sample preparation: practical guide for analytical chemists Berlin: Springer Verlag, 1997
19. Taylor, B. N., Kuyatt, C. E., Guidelines for evaluating and expressing uncertainty in NIST measurement results, NIST technical note 1297, 1994, National Institute of Standards and Technology
20. Taylor, J. K., "Quality Assurance of Chemical Measurements", Lewis Publishers, Michigan, 1987
21. UK DTI VAM Programme - General Guidelines for use with a Protocol for QA of Trace Analysis 1998
22. Youden, W. J., and Steiner, E. H., Statistical manual of the Association of Official Analytical Chemists. Statistical techniques for collaborative tests. Planning and analysis of results of collaborative tests. Washington DC: AOAC, 1975

## ACRONYMS

Some common acronyms follow:

AOAC - Association of Official Analytical Chemists (USA)

APLAC - Asia-Pacific Laboratory Accreditation Cooperation

BIPM - International Bureau of Weights and Measures

CCQM - Consultative Committee for Amount of Substance

CITAC - Cooperation on International Traceability in Analytical Chemistry

EA -European Cooperation for Accreditation

IEC - International Electrotechnical Commission

ILAC - International Laboratory Accreditation Cooperation

ISO - International Organisation for Standardisation

ISO/REMCO - International Organisation for Standardisation, Committee on Reference Materials

IUPAC - International Union of Pure and Applied Chemistry

JCTLM - Joint Committee on Traceability in Laboratory Medicine

OECD - Organisation for Economic Cooperation and Development

OIML - International Organisation on Legal Metrology

---

## APPENDIX A.

### *Quality Audit - Areas of particular importance to a chemistry laboratory.*

#### 1. Staff

- i) Staff have the appropriate blend of background, academic or vocational qualifications, experience and on-the-job training for the work they do.
- ii) On-the-job training is carried out against established criteria, which wherever possible are objective. Up-to-date records of the training are maintained.
- iii) Tests are only carried out by authorised analysts.
- iv) The performance of staff carrying out analyses is observed by the auditor.

#### 2. Environment

- 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.
- vi) Adherence to safety regulations is consistent with the requirements of the quality management standard.

#### 3. Equipment

- i) The equipment in use is suited to its purpose.
- ii) Major instruments are correctly maintained and records of this maintenance are kept.
- iii) Appropriate instructions for use of equipment are available.
- iv) Critical equipment, e.g. balances, thermometers, glassware, timepieces, pipettes etc. are uniquely identified, appropriately calibrated (with suitable traceability), and the corresponding certificates or other records demonstrating traceability to national measurement standards are available.
- v) Calibrated equipment is appropriately labelled or otherwise identified to ensure that it is not confused with uncalibrated equipment and to ensure that its calibration status is clear to the user.
- vi) Instrument calibration procedures and performance checks are documented and available to users.
- vii) 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.
- viii) Records of calibration, performance checks and corrective action are maintained.

#### 4. Methods and Procedures

- i) In-house methods are fully documented, appropriately validated and authorised for use.
- ii) Alterations to methods are appropriately authorised.
- iii) Copies of published and official methods are available.
- iv) The most up-to-date version of the method is available to the analyst.
- v) Analyses are (observed to be) following the methods specified.
- vi) Methods have an appropriate level of advice on calibration and quality control.

- 
- vii) Uncertainty has been estimated.

### **5. Chemical and Physical Measurement Standards, Certified Reference Materials and Reagents.**

- i) The measurement standards required for the tests are readily available.
- ii) The measurement standards are certified or are the "best" available.
- iii) The preparation of working measurement standards and reagents is documented.
- iv) Measurement standards, reference materials and reagents are properly labelled and correctly stored. Where appropriate "opening" and "use-by" dates are used.
- v) New batches of measurement standards, and reagents critical to the performance of the method are compared against old batches before use.
- vi) The correct grade of materials is being used in the tests.
- vii) Where measurement standards, or reference materials are certified, copies of the certificate are available for inspection.

### **6. Quality Control**

- i) There is an appropriate level of quality control for each test.
- ii) Where control charts are used, performance has been maintained within acceptable criteria.
- iii) QC checksamples 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.
- iv) Results from the random re-analysis of samples show an acceptable measure of agreement with the original analyses.
- v) Where appropriate, performance in proficiency testing schemes and/or inter-laboratory comparisons is satisfactory and has not highlighted any problems or potential problems.
- vi) There is an effective system for linking proficiency testing performance into day-to-day quality control.

### **7. Sample Management**

- i) There is an effective documented system for receiving samples, identifying samples against requests for analysis, showing progress of analysis, issue of report, and fate of sample.
- ii) Samples are properly labelled and stored.

### **8. Records**

- i) Notebooks/worksheets or other records show the date of test, analyst, analyte(s), sample details, test observations, quality control, all rough calculations, any relevant instrument traces, rough data, and relevant calibration data.
- ii) Notebooks/worksheets are indellible, mistakes are crossed out rather than erased or obliterated, and the records are signed by the analysts.
- iii) Where a mistake is corrected the alteration is traceable to the person making the correction.
- iv) The laboratory has procedures for checking data transfers and calculations and is using them.

### **9. Test Reports**

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

### **10. Miscellaneous**

- i) Documented procedures are in operation to handle queries and complaints and system failures.
-

- ii) There is adequate evidence of corrective action (in the case of system failures) and preventive action. Effectiveness is evaluated in both cases.
- iii) The Laboratory Quality Manual is up-to-date and is accessible to all relevant staff.
- iv) There are documented procedures for sub-contracting work, including verification of suitability.
- v) 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) have not highlighted any problems.

## APPENDIX B

### *Calibration intervals and Performance Checks.*

- B1. Guidance is given in Table App B-1 on the calibration of equipment in common use in analytical laboratories and on which the calibration of other instruments may be dependent. More comprehensive advice is available in the literature (see bibliography #32) and also in equipment manuals.

**Table App B-1**

	<i>Type of Instrument</i>	<i>Frequency of Check</i>	<i>Parameters to be Checked</i>
(a)	Balances	Depends on use	Linearity, Zero point, Accuracy (using calibrated weights)
(b)	Volumetric Glassware	Depends on Use	Accuracy, Precision (pipettes/burettes)
(c)	Hydrometers (working)	Annually	One point calibration versus reference hydrometer
(d)	Hydrometers (reference)	5 years	One point calibration using measurement standard of known specific gravity
(e)	Barometers *	5 years	One point
(f)	Timers (see note)	2 years or less depending on use	Accuracy
(g)	Thermometers (reference)	5 years Annually	Critical points on scale, fixed points e.g ice point
(h)	Thermometers	Annually depending on use	Check specific points against reference thermometer

Note: Those instruments marked \* will normally be calibrated in an accredited calibration laboratory, but should at least show traceability to national measurement standards.

National radio-time signals, or telephone time signals, provide a suitable source of traceable calibration of both absolute time and time difference. Timers with quartz/electronic movements are generally more accurate and stable than conventional mechanical timers and will need to be calibrated less often.

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

B2.1 *Chromatographs (general):*

- 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/thermostating (accuracy, precision, stability, ramping characteristics).
- v) Autosampler (accuracy and precision of time routines).

B2.2 *Liquid and ion Chromatography:*

- i) Composition of mobile phase.
- ii) Mobile phase delivery system (precision, accuracy, 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, reproducibility.
  - iii) Heating/cooling rates and cycles.
  - iv) 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, ultra-violet/visible and X-ray fluorescence:*
- i) Selected wavelength accuracy, precision, stability.
  - ii) Source stability.
  - iii) Detector performance (resolution, selectivity, stability, linearity, accuracy, precision).
  - iv) Signal to noise ratio.
  - v) Detector calibration (mass, ppm, 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) Accuracy and precision of timing systems.
  - ii) Reliability of sequencing programmes.
  - iii) Accuracy and precision of sample delivery systems.

## APPENDIX C

Comparison between ISO/IEC 17025:1999 and ISO/IEC Guide: 1990 (This table is reproduced from ILAC G15:2001, Guidelines for Accreditation to ISO/IEC 17025)

Item from contents list of ISO/IEC 17025	ISO/IEC 17025 Clause	ISO/IEC Guide25
<b>Scope</b>	1.1	1.1
	1.2	-
	1.3	-
	1.4	1.3
	1.5	7.6 Note
	1.6	Intro
<b>Normative references</b>	2	2
<b>Terms and definitions</b>	3	3
<b>Management requirements</b>		
<b>Organisation</b>		
	4.1.1	4.1
	4.1.2	1.2
	4.1.3	4.1
	4.1.4	-
	4.1.5 (a)	4.2 a)
	4.1.5 (b)	4.2. b)
	4.1.5 (c)	4.2. i)
	4.1.5 (d)	4.2.c)
	4.1.5 (e)	5.2 b), 5.2 c)
	4.1.5 (f)	4.2.d)
	4.1.5 (g)	4.2.e)
	4.1.5 (h)	4.2 f)
	4.1.5 (i)	4.2.g)
	4.1.5 (j)	4.2 h)
<b>Quality system</b>	4.2.1	5.1
	4.2.2	5.1, 5.2 a)
	4.2.2 (a)	5.1
	4.2.2 (b)	5.2a)
	4.2.2 (c)	5.2 a)
	4.2.2 (d)	5.1
	4.2.2 (e)	5.2
	4.2.3	5.2 m)
	4.2.4	5.2 e)
<b>Document control</b>	4.3.1	5.2 d)
	4.3.2.1	5.2 d)
	4.3.2.2 (a)	5.1, 5.2 d)

	4.3.2.2 (b)	5.2 d)
	4.3.2.2 (c)	5.2 d)
	4.3.2.2 (d)	5.2 d)
	4.3.2.3	5.2 d)
	4.3.3.1	5.2 d)
	4.3.3.2	5.2 d)
	4.3.3.3	5.2 d)
	4.3.3.4	5.2 d)
<b>Review of requests, tenders and contracts</b>	4.4.1	5.2 i)
	4.4.1 (a)	5.2 i)
	4.4.1 (b)	5.2 i)
	4.4.1 (c)	5.2 i)
	4.4.2	5.2 i)
	4.4.3	5.2 i)
	4.4.4	5.2 i)
	4.4.5	5.2 i)
<b>Subcontracting of tests and calibrations</b>	4.5.1	14.1
	4.5.2	14.1
	4.5.3	-
	4.5.4	14.2
<b>Purchasing services and supplies</b>	4.6.1	10.8, 15.2
	4.6.2	15.1
	4.6.3	-
	4.6.4	15.3
<b>Service to the client</b>	4.7	-
<b>Complaints</b>	4.8	16.1
<b>Control of nonconforming work</b>	4.9.1	5.2 o)
	4.9.1 (a)	5.2 o)
	4.9.1 (b)	5.2 o)
	4.9.1 (c)	5.2 o)
	4.9.1 (d)	5.2 o), 13.6
	4.9.1 (e)	5.2 o)
	4.9.2	16.2
<b>Corrective action</b>	4.10.1	5.2 o)
	4.10.2	5.2 o)
	4.10.3	5.2 o)
	4.10.4	5.2 o)
	4.10.5	16.2
<b>Preventive action</b>	4.11.1	-
	4.11.2	-
<b>Control of records</b>	4.12.1.1	12.1
	4.12.1.2	12.2

	4.12.1.3	12.2
	4.12.1.4	10.7 e)
	4.12.2.1	12.1
	4.12.2.2	-
	4.12.2.3	-
<b>Internal audits</b>	4.13.1	5.3
	4.13.2	5.3
	4.13.3	5.5
	4.13.4	-
<b>Management reviews</b>	4.14.1	5.4
	4.14.2	5.5
<b>Technical requirements</b>		
<b>General</b>	5.1.1	-
	5.1.2	-
<b>Personnel</b>	5.2.1	6.1
	5.2.2	6.2
	5.2.3	-
	5.2.4	5.2 e)
	5.2.5	6.3
<b>Accommodation and environmental conditions</b>	5.3.1	7.1, 7.2
	5.3.2	7.3
	5.3.3	7.4
	5.3.4	7.5
	5.3.5	7.6
<b>Test and calibration methods and method validation</b>	5.4.1	10.2, 10.1, 10.5
	5.4.2	10.3
	5.4.3	-
	5.4.4	10.4
	5.4.5.1	-
	5.4.5.2	10.4
	5.4.5.3	-
	5.4.6.1	10.2
	5.4.6.2	10.2
	5.4.6.3	-
	5.4.7.1	10.6
	5.4.7.2	10.7
	5.4.7.2 (a)	10.7 b)
	5.4.7.2 (b)	10.7 c)
	5.4.7.2 (c)	10.7 d)
<b>Equipment</b>	5.5.1	8.1
	5.5.2	9.1
	5.5.3	10.1

	5.5.4	-
	5.5.5 (a)	8.4 a)
	5.5.5 (b)	8.4 b)
	5.5.5 (c)	-
	5.5.5 (d)	8.4 d)
	5.5.5 (e)	8.4 f)
	5.5.5 (f)	8.4 g)
	5.5.5 (g)	8.4 h)
	5.5.5 (h)	8.4 i)
	5.5.6	8.2
	5.5.7	8.2
	5.5.8	8.3
	5.5.9	-
	5.5.10	-
	5.5.11	-
	5.5.12	-
<b>Measurement traceability</b>	5.6.1	9.1
	5.6.2.1.1	9.2
	5.6.2.1.2	9.3
	5.6.2.2.1	9.2
	5.6.2.2.2	9.3
<b>Measurement traceability (cont.)</b>	5.6.3.1	9.4, 9.5
	5.6.3.2	9.7
	5.6.3.3	9.6
	5.6.3.4	-
<b>Sampling</b>	5.7.1	10.5
	5.7.2	-
	5.7.3	-
<b>Handling of test and calibration items</b>	5.8.1	11.4
	5.8.2	11.1
	5.8.3	11.2
	5.8.4	11.3
<b>Assuring the quality of test and calibration results</b>	5.9	5.6, 5.6 a)
	5.9 (a)	5.6 c)
	5.9 (b)	5.6 b)
	5.9 (c)	5.6 d)
	5.9 (d)	5.6 e)
	5.9 (e)	5.6 f)
<b>Reporting the results</b>	5.10.1	13.1
	5.10.2.(a)	13.2 a)
	5.10.2. (b)	13.2 b)
	5.10.2. (c)	13.2 c)

---

	5.10.2. (d)	13.2 d)
	5.10.2 (e)	13.2 h)
	5.10.2. (f)	13.2 e), 13.2 f)
	5.10.2. (g)	13.2 g)
	5.10.2. (h)	13.2 i)
	5.10.2. (i)	13.2 k)
	5.10.2. (j)	13.2 m)
	5.10.2 (k)	13.2 n)
	5.10.3.1 (a)	13.2 j)
	5.10.3.1 (b)	-
	5.10.3.1 (c)	13.2 l)
	5.10.3.1 (d)	-
	5.10.3.1 (e)	-
	5.10.3.2 (a)	-
	5.10.3.2 (b)	-
	5.10.3.2 (c)	-
	5.10.3.2 (d)	-
	5.10.3.2 (e)	-
	5.10.3.2 (f)	-
	5.10.4.1 (a)	13.2 j)
	5.10.4.1 (b)	13.2 l)
	5.10.4.1 (c)	-
	5.10.4.2	-
	5.10.4.3	-
	5.10.4.4.	-
	5.10.5	-
	5.10.6	13.3
	5.10.7	13.7
	5.10.8	13.4
	5.10.9	13.5