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Accred Qual Assur (1996) 1:265–274

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The development and application of guidance on equipment qualification of analytical instruments

Abstract This paper describes the development of guidance for the equipment qualification (EQ) of analytical instruments. EQ is a formal process that provides documented evidence that an instrument is fit for its intended purpose and kept in a state of maintenance and calibration consistent with its use.

Key words
Equipment qualification (EQ) · Design qualification (DQ) · Installation qualification (IQ) · Operational qualification (OQ) · Performance qualification (PQ)

Introduction

EQ is becoming increasingly important to analytical laboratories. For many laboratories it is no longer sufficient to just do things right; they must also provide documented evidence to demonstrate the integrity of their data and validity of their results. Many laboratories achieve this through formal quality systems which are generally implemented in accordance with one or more of the three main internationally recognised quality Standards: the ISO 9000 series of Standards [1], Good Laboratory Practice (GLP) [2,3] and ISO Guide 25 [4].

However, these Standards are deliberately written in broad terms, so as to be as widely applicable as possible, and they do not go into detail on many issues. All stipulate general requirements such as instruments must be fit for purpose, properly maintained and calibrated to national or international standards, but are not specific as to what is actually required or how it should be achieved. It is also unclear as to where and when formal EQ is appropriate and of how it should be documented. A key objective in developing the guidance was, therefore, to provide users and suppliers of analytical instruments, as well as those responsible for the assessment, certification and monitoring of analytical laboratories, with a clear and consistent approach for the qualification of analytical instruments. The guidance has been prepared with the primary aim of assisting the interpretation of formal quality Standards in order to satisfy regulatory and accreditation requirements.

An important consideration in preparing the guidance was that it should be widely accepted and take account of current practice. In order to achieve this, the Laboratory of the Government Chemist (LGC) established an Instrumentation Working Group under the auspices of Eurachem-UK with support from the DTI VAM Initiative [5]. The working group has brought together a wide cross-section of instrument manufacturers, representatives of accreditation bodies and regulatory authorities, and users of analytical instruments. A full list of those individuals and organisations represented on the working group is given in Annex 2.

In preparing the guidance document, the Working Group reviewed a variety of different manufacturers' own procedures and protocols, papers and articles published in the open literature, and the requirements of the ISO 9000 series of Standards, Good Laboratory Practice and ISO Guide 25. The guidance sets out an approach to EQ based on four stages of qualification; design qualification (DQ), installation qualification (IQ), operational qualification (OQ) and performance qualification (PQ). Additional sections cover the requirements for and provide advice on documentation, calibration and traceability, and requalification. There are also sections on NAMAS accreditation, GLP compliance, and ISO 9000 certification, which highlight the specific requirements and emphasis of each Standard.

The Working Group identified several aspects of EQ which caused particular problems. DQ is seen as primarily for manufacturers of instruments. Clearly this is true in relation to the design of the instrument itself, but an important aspect of the guidance has been to emphasise the role that users of instruments have in considering the intended use of the instrument and agreeing appropriate specifications with manufacturers and suppliers prior to its purchase. There is also confusion regarding the distinction between OQ and PQ. The Working Group attempted to resolve this issue by focusing on what each stage is trying to achieve, rather than the activities carried out in order to achieve it. The aim of OQ is to provide evidence that an instrument performs according to the key performance characteristics agreed between the user and supplier at the time of purchase, whereas PQ is concerned with providing evidence that the instrument performs according to a specification appropriate for its routine use. If the key performance characteris-

tics agreed at the time of purchase are the same as those appropriate for routine use, then the checks and tests carried out may be the same for both OQ and PQ.

In view of the wide variety of analytical instrumentation, the Working Group decided to adopt a modular approach to the preparation of the guidance document. The first module offers general guidance applicable to a wide range of analytical instruments. A draft of this module is attached at Annex 1 and it will be supplemented by modules offering more detailed guidance for specific types of instruments. Modules for gas chromatography, high performance liquid chromatography and capillary electrophoresis are in preparation and these will be published in due course. The Working Group would welcome comments on these modules. Following any revision, it is intended to combine the general and supplementary guidance and publish them as a consolidated guide. It is also envisaged that instrument manufacturers will adopt aspects of the guidance as part of their own EQ documentation.

Comments on the guidance, or views on the equipment qualification of analytical instruments, should be sent to the authors of this paper at LGC.

Acknowledgements The development of the guidance was supported under contract with the United Kingdom Department of Trade and Industry as part of the National Measurement System Valid Analytical Measurement Programme. The guidance has been drafted by the Laboratory of the Government Chemist with assistance from the Eurachem-UK Instrumentation Working Group. The members of this working group have played a major role in developing the guidance and their help is gratefully acknowledged together with those who commented informally on the guidance during the drafting process.

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3. "Good Laboratory Practice for Non-clinical Laboratory Studies"; Food and Drug Administration (FDA); 21 CFR Ch.1 Part 58
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5. Further information on the DTI Valid Analytical Measurement (VAM) Initiative can be obtained from the VAM Helpdesk at the Laboratory of the Government Chemist, Queens Road, Teddington, Middlesex, TW11 0LY, UK (tel. 0181 943 7393)

Annex 1: Guidance on equipment qualification of analytical instruments

Contents

1. Glossary of terms

Many of the terms in this document are currently used in different ways to convey a variety of meanings. The following descriptions explain how these terms should be interpreted in this document:

1.1 **Instrument** all types of measuring equipment ranging from simple stand-alone instruments through to complex multi-component instrument systems.

1.2 **User** the organisation purchasing the instrument including its management and staff.

1.3 **Supplier** the instrument manufacturer, vendor, lessor or approved agent.

1.4 **Operational specification** the key performance characteristics of the instrument and ranges over which the instrument is required to operate and consistently perform, as agreed between the user and supplier.

1.5 **Functional specification** The functional specification defines the overall requirements of the instrument including the operational specification (see above) and other critical factors relating to its use (e.g. level of training/expertise required by operators).

1.6 **Equipment Qualification** (**EQ**) the overall process of ensuring that an instrument is appropriate for its intended use and that it performs according to specifications agreed by the user and supplier. EQ is often broken down into Design, Installation, Operation and Performance qualification:-

1.7 **Design Qualification** (**DQ**) covers all procedures prior to the installation of the system in the selected environment. DQ defines the functional and operational specifications of the instrument and details the conscious decisions in the selection of the supplier.

1.8 **Installation Qualification** (**IQ**) covers all procedures relating to the installation of the instrument in the selected environment. IQ establishes that the instrument is received as designed and specified, that it is properly installed in the selected environment, and that this environment is suitable for the operation and use of the instrument.

1.9 **Operational Qualification** (**OQ**) is the process of demonstrating that an instrument will function according to its operational specification in the selected environment.

1.10 **Performance Qualification** (**PQ**) is defined as the process of demonstrating that an instrument consistently performs according to a specification appropriate for its routine use.

1.11 **Validation** is the process of evaluating the performance of a specific measuring procedure and checking that the performance meets certain pre-set criteria. Validation establishes and provides documented evidence that the measuring procedure is fit for a particular purpose.

1.12 **System Suitability Checking** (**SSC**) A series of tests to check the performance of a measurement process. SSC may form part of the process of validation when applied to a particular measuring procedure. SSC establishes that the operational conditions required for a specific measurement process are being achieved.

1.13 **Calibration** The set of operations which establish, under specified conditions, the relationship between values indicated by a measuring instrument or process and the corresponding known values of the measurand.

1.14 **Traceability** The property of a result of a measurement whereby it can be related to appropriate standards, generally national or international standards, through an unbroken chain of comparisons.

2 Introduction

2.1 Formal quality systems and/or regulatory requirements require various levels and combinations of equipment qualification, calibration, verification of performance, and system suitability checking. The standards and other documents which specify these requirements are mostly general purpose and do not go into detail on many issues. They are, therefore, open to varying interpretation. Good Laboratory Practice (GLP)[1,2] deliberately puts an onus on the laboratory to set and justify its own level of compliance. However, in some cases, guidance is provided to indicate specific requirements in certain areas (e.g. the NIS documents provided by UKAS for use with the NAMAS M10 Standard[3]). This general lack of detail leads to differences in interpretation between different regulatory bodies, different countries, different assessors and different professional advisors. The result is frequently confusion and misunderstanding amongst those who have to meet the requirements and decide what is necessary in order "to comply".

2.2 This document provides guidance to users and suppliers of analytical instruments on best practice for undertaking the "qualification" of instruments. It aims to explain the qualification process and to provide advice on what needs to be done at each stage of an instrument's qualification.

2.3 The document sets out a general approach to the qualification of instruments. As far as possible, the advice provided is compatible with the requirements of ISO Guide 25[4], the ISO 9000 series of Standards[5] and Good Laboratory Practice (GLP). The guidance will, therefore, also be useful to those involved in the assessment, certification and monitoring of analytical laboratories.

2.4 The document provides generic guidance which is applicable to a wide range of analytical instrumentation. It is intended that the document will be supplemented by more detailed guidance on the qualification of specific types of instruments.

2.5 The requirements set out in this document are not intended to be a compulsory series of tests that must be carried out. Users of this guide should exercise their professional judgement as to the extent to which individual requirements are applicable and the level of detail required for proper qualification of instruments.

2.6 Although the approach, and many of the requirements, may be applicable to other equipment, e.g. that used for sample preparation or that which forms part of a manufacturing process, this equipment is outside the scope of this guide.

2.7 Most instruments have varying combinations of computer or microprocessor hardware and software. The formal validation of these components is outside the scope of this document. Where necessary, users must ascertain and seek documented evidence from suppliers that such components have been developed and manufactured to appropriate Standards and formally validated during production. Guidance on the validation of computerised systems is available elsewhere [6,7,8,9,10,11].

2.8 The terms "validation" and "qualification" are used widely and often to convey the same meaning. The approach taken in this guidance document is that validation is application orientated and relates to a specific measurement method or process, whereas qualification is instrument orientated and relates primarily to the operational specification of the instrument.

3 The equipment qualification (EQ) process

3.1 The primary requirement for all equipment used in analytical laboratories is that it must be fit for its intended purpose. The equipment qualification (EQ) process must therefore establish that an instrument's operational specification is appropriate for its intended use and that the instrument performs according to that specification. EQ must also establish that an instrument is, and will be, kept in a state of maintenance and calibration consistent with its use.

3.2 There is often confusion with regard to what is included in the EQ process and, in particular, what is covered by the individual stages (DQ-IQ-OQ-PQ) of qualification. This can arise because different suppliers offer varying levels of support for EQ and, at present, there is no uniform acceptance of what is covered by each stage nor what each stage will be called.

3.3 The EQ process described in this document is summarised in Figure 1 and is based on four stages of "qualification": design qualification (DQ); installation qualification (IQ); operational qualification (OQ); and performance qualification (PQ). Subsequent sections of this guidance document describe, individually, these four stages of qualification in more detail and provide broad guidance as to what each stage should include.

3.4 The applicability of each stage of EQ will vary during the lifetime of an instrument. All four stages will be applicable to the purchase of a new instrument. Aspects of DQ and IQ may need to be repeated following major changes (see Section 10). PQ, and many aspects of OQ, should be carried out throughout the entire life of the instrument and provide a reference against which the instrument's continued performance can be judged.

3.5 The EQ process and the requirements of each qualification stage are generic and therefore applicable to both complex and simple instruments. However, specific operational tests carried out during qualification will, of course, vary according to the type of instrument (e.g. the tests to demonstrate that a HPLC autosampler is performing to specification are quite different from those employed in testing a UV/VIS spectrometer).

3.6 Each stage of the qualification process involves the same general approach: the preparation of a qualification plan defining the scope of qualification (e.g. the tests to be performed and the acceptance criteria to be used); the execution of the plan (during which the results of the tests are recorded as the tests are performed); and the production of a report (and, if required, a certificate) in which the results of EQ are documented.

3.7 The user is responsible for the validation of the measurement process and for the quality and reliability of the data produced. The user is therefore responsible for ensuring that an instrument is suitable for its intended use and that it is operating satisfactorily. Thus, the user is responsible for EQ.

3.8 The user must establish the level of EQ required and what aspects of

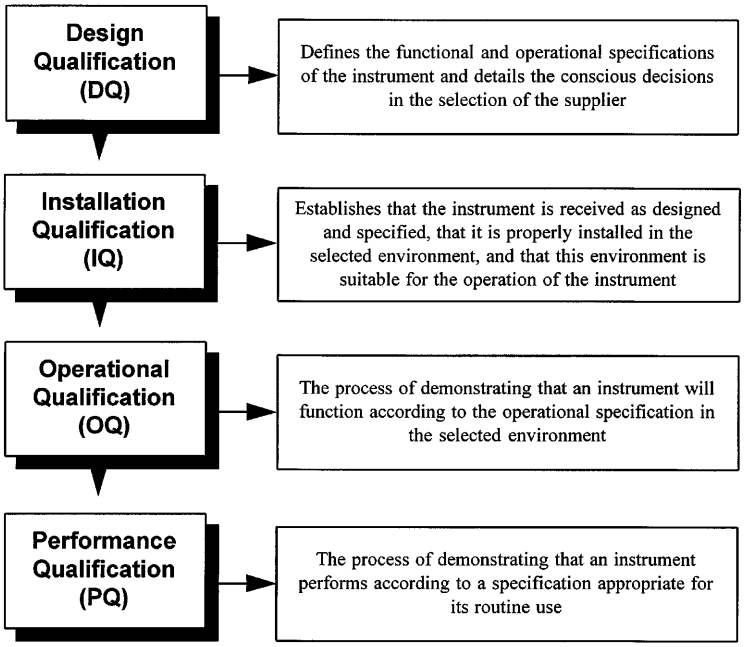

Fig. 1 The equipment qualification process

EQ will be done in-house and what will be carried out by a third party, which may be the original supplier. The extent to which this is carried out by the user will depend on the experience and competence of the user.

3.9 The supplier should provide clear guidance on what can be carried out by the user, what can be carried out by either the user or the supplier, and what can only be undertaken by the supplier. The supplier should make available documents, tools and services to assist EQ and, in particular, to provide clear instructions and details of tests required to demonstrate satisfactory performance. Such testing (an integral part of OQ/PQ) can be carried out by the supplier or the user, but must remain under the control of the user (see section 8.5).

3.10 Where any aspect of EQ, and/or a performance check or test, is undertaken by the supplier or a third party, users must satisfy themselves that it has been carried out competently and correctly (the installer's training record may provide basic evidence of competence).

3.11 The success or failure of all EQ checks and tests performed should be formally recorded and, where these have been carried out by the supplier or a third party, the results of these checks and tests must be communicated to the user;

3.12 Users may expect suppliers to undertake aspects of EQ, but accept that such services will often incur a charge.

3.13 Wherever maintenance and calibration operations are necessary, they must be carried out before EQ.

4 Documentation

4.1 This section provides guidance on requirements relating to documentation covering the EQ process. It is not intended to cover other documentation relating to operation or servicing (e.g. manuals) of the instrument.

4.2 EQ must be documented. EQ documentation can be prepared and provided by the user, the supplier, or both. Where it is provided by the supplier (e.g. in a qualification protocol), it remains the responsibility of the user and should be written in such a way that it can be readily followed and understood by the user. Documentation covering EQ should satisfy the following requirements:

a) The instrument and all modules and accessories must be uniquely identified, particularly Reports and Certificates, including:
   - The supplier's name, instrument name, model and serial number;
   - Any identifying number allocated by the user;
   - The version and date of issue of any computer hardware, firmware and software;

   It may also be useful to include a brief description of instrument and its role in the measurement process.

b) State clearly the intervals at which aspects of EQ and/or specific checks and tests should be performed, and the responsibility level of the operator required to perform the tests;

c) Provide details of each check and test to be performed, the specification and acceptance criteria to be used. This information should be concise enough to allow the operator to make an unambiguous judgement on the result of the test;

d) Provide sufficient information on the procedures and materials required to perform each check and test. This should also advise on where there is a need to achieve traceability to national or international standards and how this can be achieved;

e) Where qualification of one part of the instrument is dependant on the correct functioning of another part, any assumptions made must be recorded;

f) State the date on which qualification was performed and the result of qualification and each check or test;

g) State the reason for performing qualification (e.g. following installation of a new instrument, following routine service, or following instrument malfunction);

h) Provide clear information on the action to be taken in the event of test or qualification failure;

i) State the circumstances which may or will necessitate re-qualification of the instrument (e.g. following service or re-calibration);

j) Contain the name(s) and signature(s) of the person(s) who actually performed qualification and/or each individual check and test. Contain the name and signature of the user authorising completion of qualification.

4.3 It is strongly recommended that log-books are kept for all instruments. Quality Standards, particularly NAMAS M10 and GLP, place a heavy emphasis on keeping records of instrument history. Maintaining an up-to-date log-book of the overall history of an instrument provides a convenient mechanism for recording information and can provide the basis for satisfying the requirements of NAMAS M10, GLP and ISO 9001.

4.4 Instrument log-books should identify the individual modules and accessories that constitute the instrument

and be used to record the overall history of the instrument (e.g. the date of purchase, the initial qualification and entry into service; the dates of when subsequent maintenance, calibration and qualification have been performed and when these are next due). In some circumstances it may be appropriate for all relevant information to be recorded in, or appended to, the instrument log-book (e.g. operating instructions and SOPs, maintenance and calibration records, and qualification and qualification protocols and reports). In others, it may be more appropriate to use the log-book as a summary record of key information which references where more detailed procedures, reports and certificates can be accessed.

4.5 Following qualification, the instrument log-book must be updated with the results of qualification. The instrument itself should also be 'labelled' to provide a clear indication of when the next qualification, calibration or performance test is due.

5 Design Qualification (DQ)

5.1 Design Qualification is concerned with what the instrument is required to do and links directly to fitness for purpose. DQ provides an opportunity for the user to demonstrate that the instrument's fitness for purpose has been considered at an early stage and built into the procurement process.

5.2 DQ should, where possible, establish the intended or likely use of the instrument and should define appropriate operational and functional specifications. This may be a compromise between the ideal and the practicalities of what is actually available. Whilst it is the responsibility of the user to ensure that specifications exist, and that they are appropriate, they may be prepared by the user, the supplier(s), or by discussion between the two.

5.3 The operational specification should define the key performance characteristics of the instrument and ranges over which the instrument is required to operate and consistently perform.

5.4 The functional specification should consider the overall requirements of the instrument including the operational specification (see above) and other critical factors relating to its use, for example:

a) the overall business requirement;
b) documentation relating to the use of the instrument (e.g. clear, easy to use operating manuals, identified by version and date; protocols for IQ, OQ and PQ; model SOPs etc.);
c) the level of skill required to operate the instrument and details of any training necessary and courses provided by the supplier;
d) sample throughput, presentation and introduction needs;
e) data acquisition, processing and presentation needs;
f) requirements for, and expected consumption of, services, utilities, and consumables (e.g. electricity, special gases);
g) environmental conditions within which, or range over which, the instrument must work;
h) suggested contents of, intervals between and procedures for maintenance and calibration of the instrument, including the cost and availability of any service contracts;
i) the period for which support (qualification, maintenance, parts etc.) for the instrument can be guaranteed;
j) information on health and safety and environmental issues and/or requirements.

5.5 In undertaking DQ, information and knowledge of existing equipment should be taken into account. If an instrument is mature in design and has a proven track record, this may provide a basic confidence and evidence about its suitability for use. For new techniques or instruments DQ may require more effort.

5.6 The selection of the supplier and instrument is entirely at the discretion of the user. However, in selecting the supplier and instrument, the user should bear in mind that regulators are likely to require evidence of: the use of rigorous design and specification methods; fully documented quality control and quality assurance procedures; the use, at all times of suitably qualified and experienced personnel; comprehensive, planned testing of the system at all levels of the system; and the application of stringent change control, error reporting and corrective procedures. A suitable questionnaire, third party audit, or independent certification of the supplier to an approved quality scheme may provide the user with evidence that regulatory requirements have been met. Where such evidence is not available, it is the responsibility of the user to carry out more extensive qualification in order to provide the necessary assurance of the instrument's fitness for use.

5.7 Where instruments are made to make measurements supporting regulatory studies, the user may also need to seek confirmation that the manufacturer is prepared, if required, to allow regulatory authorities access to detailed information and records relating to the instrument's manufacture and development, for example: source codes; instrument development records and procedures; calibration and qualification documentation; batch test records and reports; hardware and software qualification documentation; and credentials of staff involved with the development of the instrument.

6 Installation Qualification (IQ)

6.1 There is a fine line between what is included in Installation Qualification and what is included in Operational Qualification. Indeed, the line may be drawn differently for different manufacturers and/or different instruments. In this document IQ covers the installation of the instrument up to and including its response to the initial application of power.

6.2 IQ involves formal checks to confirm that the instrument, its modules and accessories have been supplied as ordered (according to specifications agreed between the user and supplier), and that the instrument is properly installed in the selected environment. IQ must be formally documented (see Section 4) and should confirm the following:

a) that the instrument (including all modules and accessories) has been delivered as ordered (delivery note, purchase order, agreed specifications), and that the instrument has been checked and verified as undamaged;
b) that all required documentation has been supplied and is of correct issue (e.g. operating manuals - which should also include their issue number and date of issue; the supplier's specification; and details of all services and utilities required to operate the instrument);
c) that recommended service, maintenance, calibration and qualification intervals and schedules have been provided. Where maintenance can be carried out by the user, appropriate methods and instructions should be referenced along with contact points for service and spare parts;
d) that any required computer hardware, firmware and software has

been supplied and is of correct issue;

e) that information on consumables required during the normal operation of the instrument system, and during start-up or shut-down procedures, has been provided;

f) that the selected environment for the instrument system is suitable, with adequate room for installation, operation and servicing, and appropriate services and utilities (electricity, special gases etc.) have been provided. (Note: significant time and effort can be saved if these basic requirements are checked prior to formal IQ of the instrument);

g) that health and safety and environmental information relating to the operation of the instrument has been provided. It is the responsibility of the supplier to provide appropriate safety information, on which the user must act, and document the acceptance of this guidance;

h) that the response of the instrument to the initial application of power is as expected or that any deviations are recorded (if the system is designed to perform any automatic diagnostic or start-up procedures the response to these should also be observed and documented).

6.3 IQ may be carried out either by the supplier and/or the user. However, it should be noted that, in some cases, the complexity of the instrument alone may preclude the user performing IQ and, in others, the unpacking of the equipment by the user may invalidate the warranty.

6.4 IQ must be undertaken by a competent individual and in accordance with the supplier's instructions and procedures. The success or failure of each of the IQ checks performed should be formally recorded and, where these have been carried out by the supplier, the results of these tests must be communicated to the user.

7 Operational Qualification (OQ)

7.1 The purpose of Operational Qualification (OQ) is to demonstrate and provide documented evidence that the instrument will perform according to the operational specification in the selected environment.

7.2 OQ normally takes place after the IQ of a new instrument or after a significant change to the instrument or a component such as repair or service.

7.3 OQ may be carried out either by the supplier or the user, but must remain under the control of the user. However, for complex instruments, it may only be possible for the supplier to undertake OQ.

7.4 OQ should be carried out in accordance with the supplier's instructions and procedures, using suitable materials and protocols, and should satisfy the general requirements set out in Section 3 - Equipment Qualification. It is not possible to give further general guidance on OQ requirements, because, at this stage, the checks and tests necessary to demonstrate an instrument's compliance with its operational specification are specific and vary depending on the type of instrument undergoing qualification. However, OQ must be formally documented in accordance with the general requirements set out in Section 4 - Documentation.

8 Performance Qualification (PQ)

8.1 The purpose of PQ is to ensure that the instrument functions correctly and to a specification appropriate for its routine use. This specification may be the original operational specification or one more appropriate for its current use. PQ provides the continuing evidence of control and acceptable performance of the instrument during its routine use.

8.2 The frequency of, and need for, PQ should be specified in in-house operating manuals or an SOP and should be based on need, type and previous performance of the instrument, including the time that the instrument calibration has been found, in practice, to remain within acceptable limits.

8.3 Where possible, all operational checks and tests should be performed using parameters as close as possible to those used during normal routine operation of the instrument. For most analytical instruments there will be a "grey" area between the optimum and unacceptable levels of performance. Wherever this is the case, the user must identify a threshold below which the instrument's performance is deemed to be unacceptable and it should not be used until its performance is improved.

8.4 Aspects of performance qualification are often built into analytical methods or procedures. This approach is often called System Suitability Checking (SSC) which demonstrates that the performance of the measuring procedure (including instrumental operating conditions) is appropriate for a particular application. SSC should be used before and during analysis to provide evidence of satisfactory operation or to flag up when performance is no longer acceptable.

8.5 Where a complete measuring system is provided by the supplier, PQ can be performed by the supplier, but must remain under the control of the user. In some circumstances, PQ may also involve repeating many of the checks and tests carried out during OQ and, as such, these can also be performed by the supplier. However, wherever PQ is performed by the supplier, it is likely that the user will also have to undertake more frequent checks and tests to confirm the continued satisfactory performance of the instrument during routine use.

8.6 PQ should be carried out in accordance with the general requirements set out in Section 3 - Equipment Qualification. It is not possible to give further general guidance on PQ requirements, because, at this stage, the checks and tests necessary to demonstrate an instrument's satisfactory performance are specific and dependant on both the instrument type and the analytical application. However, PQ must be formally documented in accordance with the general requirements set out in Section 4 - Documentation.

9 Calibration and Traceability

9.1 ISO Guide 25, the ISO 9000 series of Standards and Good Laboratory Practice all require that, where relevant and possible, calibrations should be traceable to national or international standards. The importance of traceability to national and international standards is in establishing the accuracy of the data produced during the measurement process. Where this is not relevant or possible, the basis for calibration or establishing the accuracy of results must be documented.

9.2 Where instruments are used to determine absolute values of a parameter (e.g. temperature, wavelength) the instrument should be calibrated using reference materials or standards traceable to national or international standards. Most analytical instruments are not used in this way. Instead, the parameter measured (e.g. mV) is compared with the value for a known quantity of the determinand of interest, in a calibrant, in a way which obeys definable laws. Thus, the traceability of the actual parameter measured (mV) is uni-

mportant so long as the standard used to calibrate the measurement is traceable and the instrument response in relation to the concentration of the determinand is predictable.

9.3 For many applications, the accuracy of the instrument's operating parameters (e.g. mobile phase flow rates in HPLC systems) is not critical and hence the need for traceable calibration to national or international standards is less important. In such circumstances, the accuracy of the operating parameter is secondary provided it remains consistently reproducible during the analysis of both the sample and the standard, and the satisfactory performance of the measuring system can be demonstrated (e.g. by System Suitability Checking).

9.4 However, in other circumstances, the accuracy of an instruments operating parameters and hence calibration traceable to national or international standards will be more important, for example, where an analytical procedure developed in one laboratory is to be transferred for routine use in another laboratory or where the accuracy of the parameter may have a critical impact on the performance of the measurement process.

9.5 Traceability to national and international standards is usually, and often most efficiently, established through the use of certified reference materials or standards which are themselves traceable in this way.

9.6 Users should avoid over-specifying calibration and/or traceability requirements (e.g. for parameters that are not critical to the method) because assessors will be justified in expecting users to demonstrate that any tolerances specified in procedures can reasonably be met.

10 Requalification

10.1 In general, an instrument will undergo a variety of change during its life. This can vary from the routine replacement of a single consumable part, through to very significant changes affecting the entire instrument system. Examples of such circumstances include:-

- Movement or relocation of the instrument
- Interruption to services or utilities
- Routine maintenance and replacement of parts
- Modification (e.g. instrument upgrades or enhancements)
- A change of use

10.2 Whenever such changes take place it is essential to repeat relevant aspects of the original qualification process. This procedure is widely referred to as requalification.

10.3 The level of requalification required will depend on the extent to which change has occurred and its impact on the instrument system. In many cases, requalification can be performed using the same EQ protocols and checks and tests which were undertaken prior to the routine use of the instrument.

10.4 The nature of, and reason for, any change to the instrument system, along with the results of all requalification checks and tests performed, should be formally documented according to the requirements set out in Section 4 - Documentation.

10.5 Requalification may not necessarily mean repeating the entire EQ process. However, it must cover the change and requalify those parts of the instrument system that are affected by the change.

10.6 For example, the replacement of a detector source (e.g. deuterium lamp) would require the detector to be requalified using appropriate OQ/PQ procedures and protocols, but would be unlikely to require the individual requalification of other components of the instrument (e.g. injector or pump). However, because the change affected the instrument as a whole, it would also be necessary to carry out PQ checks on the entire system to demonstrate its satisfactory performance following the change.

10.7 Similarly, for some 'modular' systems it is often possible to interchange components depending on the application and intended use of the instrument. Changes to the instrument system configuration (e.g. replacing one detector with another) may not necessarily require requalification of the individual modules, but would require requalification of the instrument system as a whole.

10.8 Significant changes to the instrument system, for example, major component or software upgrades, or enhancements which increase the instrument's capabilities, will normally require more extensive requalification. Indeed for such substantial changes, there is often a fine line between what is considered to be requalification and what constitutes qualification of a new component.

10.9 Upgrades to the instrument and/or its software should be fully documented and describe the reasons for, and differences, new features and benefits of, the change. Users should ascertain and seek documented evidence from suppliers that upgrades have been developed and manufactured to appropriate Standards and formally validated during production. Software upgrades should, as far as possible, be compatible with previous versions and, where this is not possible, the supplier should offer a 'validated' transfer of existing data to the upgraded system.

10.10 Following installation of the upgrade, the instrument should be requalified using appropriate checks and tests. Where possible, the checks and tests used for requalification should be designed so that the results can be compared with those obtained using earlier versions, Any differences in the test results obtained from old and new versions should be identified, documented and resolved.

11 NAMAS Accreditation

This section has been prepared in consultation with the United Kingdom Accreditation Service (UKAS).

11.1 NAMAS requirements are set out in the NAMAS M10 Standard and its Supplement[12]. Both the NAMAS Standard, its Supplement and other documentation produced by UKAS (e.g. NIS documents) list detailed requirements which are relevant to the qualification of instruments and it is not the intention to repeat these here.

11.2 The basis of NAMAS accreditation is to provide users and their customers with confidence in the quality of the users testing activities, and in the technical and commercial integrity of the user's operations. The philosophy of NAMAS is based around the "test". Users are normally assessed and accredited to perform specific tests in specific fields of measurement.

11.3 As with other Standards, the basic requirement under NAMAS is that instruments must be fit for purpose and suitable for their intended use. A primary consideration of NAMAS assessors will be to assess the instrument's fitness for purpose in the context of the test concerned and the accuracy required of results. In this respect, consideration must be given to the overall measurement uncertainty, which will include a contribution from the instrument.

11.4 A difference between NAMAS and other Standards is that NAMAS explicitly states that instruments shall normally be owned by, or on long-term lease to, the user and where, exceptionally, other instruments are used, the user must have evidence to show that the requirements of the NAMAS M10 Standard are satisfied.

11.5 Instruments must be protected, as far as possible, from deterioration and abuse, and must be kept in a state of maintenance and calibration consistent with their use. They must be capable of achieving the accuracy required, and to comply with any standard specifications relevant to the tests concerned. Records of maintenance and calibration must be kept.

11.6 Although the NAMAS M10 Standard does not explicitly specify Equipment Qualification requirements, it does necessitate that instruments used are of established design. Where other instruments are used, the user must demonstrate that they are suitable for their intended purpose. New equipment must be checked for compliance with appropriate specifications, commissioned and calibrated before use.

11.7 Instruments must only be operated by authorised and competent staff, and these must be named in the appropriate procedures. Adequate, up-to-date, written instrument operating instructions must be readily available for use by staff.

12 GLP Compliance

This sections has been prepared in consultation with the United Kingdom Department of Health Good Laboratory Practice Monitoring Authority.

12.1 Good Laboratory Practice (GLP) is concerned with the organisational processes and the conditions under which laboratory studies are planned, performed, monitored, recorded and reported. GLP compliance is based upon the application and interpretation of a set of principles rather than by means of adherence to prescriptive regulations, and that compliance with these principles assures the quality and integrity of analytical data generated for regulatory purposes.

12.2 This approach is necessary because of the very wide variety of study types which are undertaken in accordance with GLP. It should be noted that GLP refers to studies where a single study can consist of very many different tests which might be considered separately under other accreditation schemes, for example, NAMAS.

12.3 The exact way in which the GLP principles are applied in any particular situation can vary. It is the role of inspectors to assess whether, in their opinion (based on knowledge of the types of processes in use and the current industry norms), the basic GLP principles are being complied with.

12.4 The principles of Good Laboratory Practice and the operation of the United Kingdom Compliance Monitoring Programme are set out in "Good Laboratory Practice - The United Kingdom Compliance programme"(1) which is available from the UK Department of Health. The principles of GLP embodied in the Compliance programme were first developed by the OECD and have international acceptance.

12.5 Some test facilities operate quality management systems such as NAMAS or ISO 9000 in addition to GLP compliance. It is usually possible to establish systems and procedures which satisfy the requirements of the different assessors and inspectors. However, it must be remembered that for certain activities, usually referred to as non-clinical safety evaluation studies, GLP compliance is a mandatory regulatory requirement.

12.6 The principles of GLP require that all equipment and apparatus are suitable for their intended purposes and have adequate capacity to meet the requirements of the studies and tests which will be carried out. A complex validation exercise would not necessarily be required, but Inspectors would expect to see evidence that new instruments were subject to some form of evaluation before being approved for use on regulatory studies. It is important to remember that, however, most, if not all, items of automated equipment will have microprocessor/computer control. The principles of GLP require that all computer systems are themselves subject to a formal evaluation before being used.

12.7 There should be documented procedures for the use, maintenance and calibration of instruments. This information might be in SOPs or in user manuals etc. In the latter case, the user manuals must be referenced in an appropriate SOP or Policy Document and handled in a controlled manner. It is for test facility management to determine what maintenance and/or calibration procedures are appropriate for each item of equipment. However, if during an inspection there was evidence of equipment malfunction, poor performance etc., then this would be taken as an indication that existing procedures are inadequate.

12.8 Calibration should, where appropriate, be traceable to national or international standards. When this is not possible or applicable, inspectors would expect that adequate procedures exist for establishing the accuracy and/or integrity of results. The level and frequency of calibration will depend on the application. It is generally expected that instruments actually generating study raw data are subject to higher levels of care than equipment used in a supporting role.

12.9 There should be records of all instrument operation, including routine and non-routine use, maintenance and calibration. Any damage, malfunction, modification and repair should be recorded. These records should be to GLP standards; although not raw data, these data would be necessary to support or allow reconstruction of completed studies.

12.10 There should be records demonstrating that personnel have been suitably trained (or have experience) to allow them to use the equipment correctly.

12.11 Under GLP, it is laboratory management who is responsible for demonstrating that an instrument is suitable for its intended purpose within the laboratory. Manufacturers or suppliers can assist, but cannot assume this responsibility. Computer software is a good example: The supplier can carry out testing to show that the software functions as expected, but the laboratory must still show that the complete instrument system and associated software functions correctly in the user environment.

12.12 The principles and requirements of FDA GLP are set out in the Food and Drug Administration 21 CFR(2). Although the requirements and principles of FDA GLP are inherently the same as those set down in the UK Compliance programme, the FDA principles do expand and provide more detail on requirements relating to SOPs and records for instruments.

12.13 FDA GLP expands on the requirements of SOPs necessitating that

they set forth in sufficient detail the methods, materials and schedules used in routine inspection, cleaning, maintenance, calibration and standardisation of instruments, and, where appropriate, specify the remedial action to be taken in the event of instrument failure or malfunction. SOPs also need to designate the person responsible for each operation.

12.14 Written records must include the date of inspection, maintenance, calibration and standardisation operations and describe whether maintenance was routine and followed the SOP. Written records must be kept of non-routine repairs, performed as a result of failure or malfunction, and these records need to document the nature of the defect, how and when it was discovered, and any remedial action taken in response to the defect.

13 ISO 9000 Certification

This section has been prepared in consultation with the United Kingdom Accreditation Service (UKAS).

13.1 The requirements of the ISO 9000 series of Standards relating to instrumental qualification are covered by BS EN ISO 9001: 1994(2). The philosophy behind ISO 9000 requirements is based on the establishment of documented procedures and processes to ensure that instruments are adequately controlled. ISO 9001 lists a number of requirements relating to the control of inspection, measuring and test equipment and it is not intended to repeat these here.

13.2 ISO 9001 requirements are very similar to, but not generally as specific or detailed as those of NAMAS. However, as with NAMAS and GLP, there remains the same basic requirement that instruments should be fit for purpose and kept in a state of maintenance and calibration consistent with their intended use. Perhaps the only difference, and only in application rather than in principle, is the emphasis that ISO 9000 places on design, and with this in mind, the broad guidance provided under Section 5 - Design Qualification should help users to demonstrate that adequate design has been built into ensuring that instruments are fit for purpose.

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BOOK REVIEWS

Accred Qual Assur (1996) 1:274

Accreditation and quality assurance in analytical chemistry

Helmut Günzler (ed.)
Springer, 1996

This book, published in German in 1994, is now available to a wider public in English translation. Thanks to the editor, the text has been brushed up and updated in accordance with the events and changes that have taken place since 1994. The authors of the different chapters are indeed the gurus of their specialities, and the reader gets first-hand information on the broadest aspects of the subject in 266 pages. It is certainly interesting to read through the whole book from start to finish (the chapters are in a logical sequence); however, it can also be used as a lexicon or reference book.

There is no doubt that analytical laboratories should devote ever more attention to assuring the quality of their results. It is also true that in certain countries it is still possible to get laboratory accreditation for very vaguely defined fields of work without specifying matrices, concentration limits or quality parameters of results. The situation will change, and laboratories should prepare themselves for this. The book gives them all the basic information and references needed for this preparation. The reviewer visited a considerable number of laboratories in developing countries that are rightly concerned with their future and are eager to learn what they should do. Well, this is the book that they, too, need to study very carefuly. If UNIDO still has some funds to devote for real help, this monograph is the right choice. Send copies of it to analytical laboratories in developing countries and you will disseminate very useful information at modest cost.

The reader will be surprised to see in Prof. de Bièvre's chapter on Traceability of Measurements of SI (p. 185 Fig. 12 and p. 186 Fig. 13) the considerable number of unacceptable results presented by laboratories – among which there could be quite a few that have been in fact accredited! It follows from this that users of services of analytical laboratories cannot be sure that the results of accredited laboratories are necessarily in all cases free of errors. Probably the confidentiality of interlaboratory studies should be lifted – with the consensus of the laboratories – and made public. Until that time, in the case of sensitive fields, e.g. clinical laboratories, analysis of toxic elements in food, the environment etc., clients of analytical laboratories should rather insist on their own assessment of their partners' performance.

The reliable factual information in this book is its main asset. It can be recommended to chemists of analytical laboratories that want to exist and prosper in years to come.

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