The Background to Equipment and System Qualification and the Practical Implications

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- **Historical background**
- **DQ, IQ, OQ and PQ**
- **Further development until today**
- **What are the implications?**

Historical background

With the development of digital integrated circuits and the consequent development of microprocessors and microcontrollers, laboratory equipment has changed dramatically.

Both the processes and the measurement signals are processed digitally.

This has also changed the way of working in the laboratory. With today's devices, the functionality is far less directly visible than it was the case with old analogue devices.

Often, the algorithms for signal processing are not very well known and are correspondingly non-transparent.

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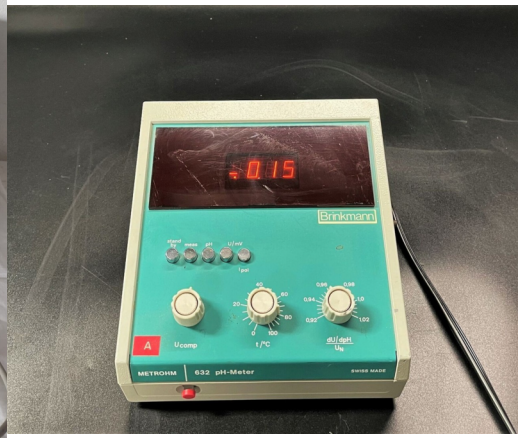
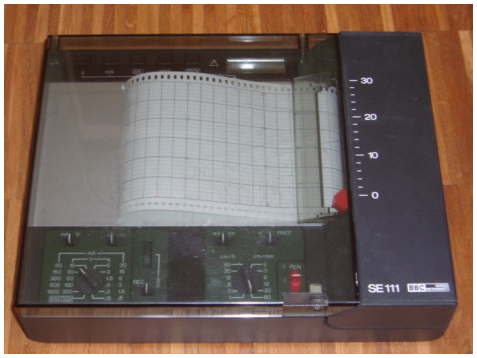
Moving from analog to digital



The fourth dimension

Chart recorder



- Speed
- Attenuation

Integrator

- Speed
- Attenuation
- Integration
- Re-Integration ?!?
  «raw data»

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The period of uncertainty

However, these Standards {Speaker's note: the ISO 9000 series of Standards, Good Laboratory Practice (GLP) and ISO Guide 25} 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 Equipment Qualification is appropriate and of how it should be documented.

Accred. Qual. Assur. (1996) 265 - 274

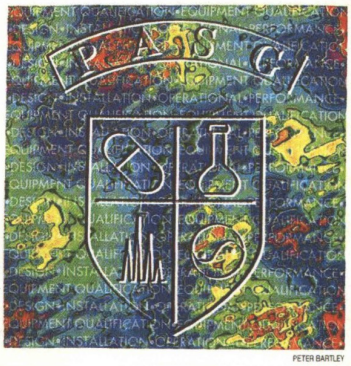
The solution: Publications 1995/96

40 Pharmaceutical Technology Europe NOVEMBER 1995

Position Paper on the Qualification of Analytical Equipment

M. Freeman, M. Leng, D. Morrison, and *R.P. Munden

Equipment qualification (EQ) is important in ensuring the validity of results. This article presents a position paper on EQ as agreed by the Pharmaceutical Analytical Sciences Group (PASG) — an opinion-forming organization in the UK whose membership includes all UK-based pharmaceutical research and development companies. Proposals are made for harmonized definitions of design qualification (DQ), installation qualification (IQ), operational qualification (OQ), and performance qualification (PQ), along with broad guidelines as to what each should include. It is proposed that equipment manufacturers should take a significant part in performing EQ. It is also proposed that for some types of equipment, as a part of PQ, method-specific system suitability criteria (SSCs) are applied in order to provide an ongoing assessment of the equipment. This article was originally presented as a poster at The Second PharmAnalysis Europe Conference, Düsseldorf, Germany, 24–25 April 1995.



PETER BARTLEY

bodies seem to be increasingly turning their attention to this area. However, the response by industry is in danger of being fragmented and on occasion too rigorous. Therefore, there is the usual danger of over reaction and the creation of a new bureaucracy.

An over-rigorous approach may be developing because the require-

LEGISLATION AND NORMS

Relevant legislation, legislation plans and related initiatives in different countries and continents

Accred Qual Assur (1996) 1:265–274

P. Bedson
M. Sargent

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

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

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

The birth of DQ, IQ, OQ and PQ

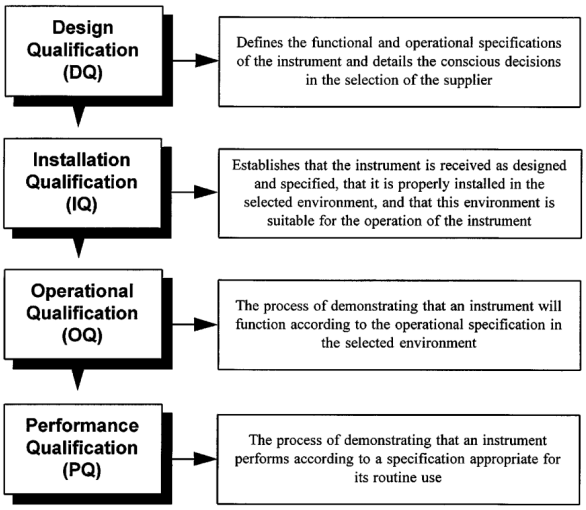


Fig. 1 The equipment qualification process

Publications of VAM

National Measurement System 1997-2000 Valid Analytical Measurement (VAM) Programme

Guidance on Equipment Qualification of Analytical Instruments: High Performance Liquid Chromatography (HPLC)

June 1998

LGC/VAM/1998/026.2

National Measurement System 2000-2003 Valid Analytical Measurement (VAM) Programme

Guidance on Equipment Qualification of Analytical Instruments: UV-Visible Spectro(photo)meters (UV-Vis)

Version 1.0 - September 2000

LGC/VAM/2000/079

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But: What does ISO say?

ISO/IEC 17025:2017; Subclause *6.4 Equipment*

6.4.3 The laboratory shall have a procedure for handling, transport, storage, use and planned maintenance of equipment in order ***to ensure proper functioning*** *and to prevent contamination or deterioration.*

- *6.4.4 The laboratory shall verify that equipment* ***conforms to specified requirements*** *before being placed or returned into services*
- *6.4.5 The equipment used for measurement* ***shall be capable of achieving the measurement accuracy and/or measurement uncertainty required*** *to provide a valid result.*
- 6.4.6 Measuring equipment shall be **calibrated** when: ……..
- *6.4.7 The laboratory shall establish a* ***calibration programme****, which shall be reviewed and adjusted as necessary in order to maintain confidence in the status of calibration.*
- *6.4.8 All equipment requiring* ***calibration*** *or which has a defined period of validity shall be labelled, coded or otherwise identified to allow the user of the equipment to readily identify the status of calibration or period of validity.*

«Calibration»

VIM 2.39 (6.11)

Calibration

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

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

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«Influence quantity»

VIM 2.52 (2.7)

Influence quantity

quantity that, in a direct measurement, does not affect the quantity that is actually measured, but affects the relation between the indication and the measurement result

…..

EXAMPLE 4

Background pressure in the ion source of a mass spectrometer during a measurement of amount-of-substance fraction.

Doubts and uncertainties

Not everything fits into the linear DQ/IQ/OQ/PQ model

- ISO 9001 recognises the "Design and Development" process.
- However, this is a process of the equipment manufacturer. So does DQ belong to the manufacturer of the equipment? Does the future user of the equipment not have a document defining the requirements for the equipment What does it look like?

OQ and PQ cannot always be properly separated

- One manufacturer invents a partial mixture of the two phases: performance verification (PV)

What happens after the equipment is put into operation? Which qualification step is (partially) repeated and when?

- Various manufacturers suggested steps after commissioning of the equipment:
  - MQ Maintenance Qualification
  - RQ Re-Qualification

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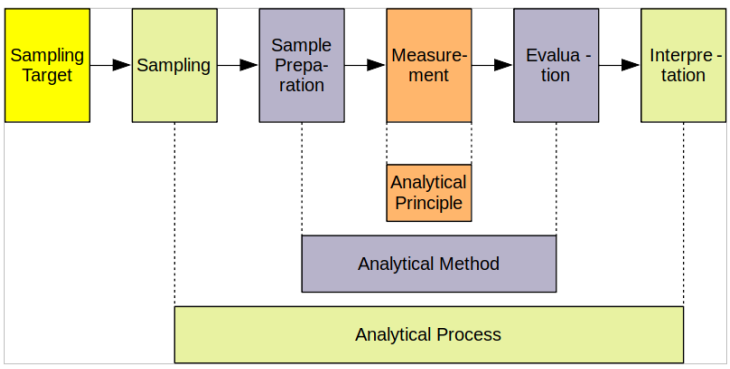
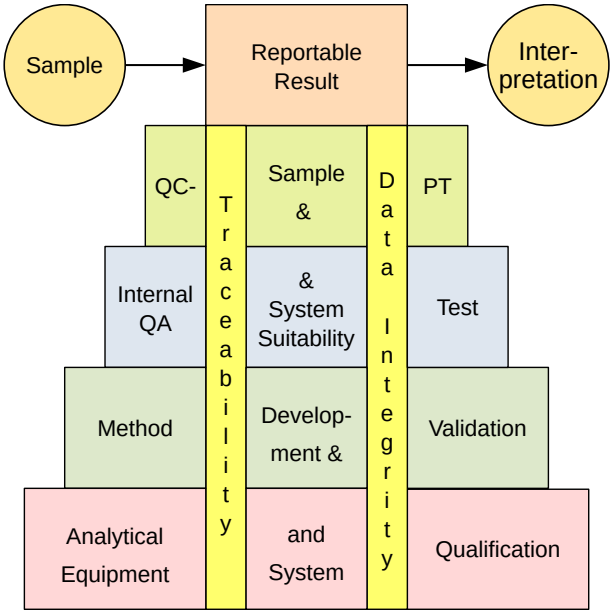
How is EQ integrated into the analytical process?

What process are we talking about here?



The Pyramid of Quality



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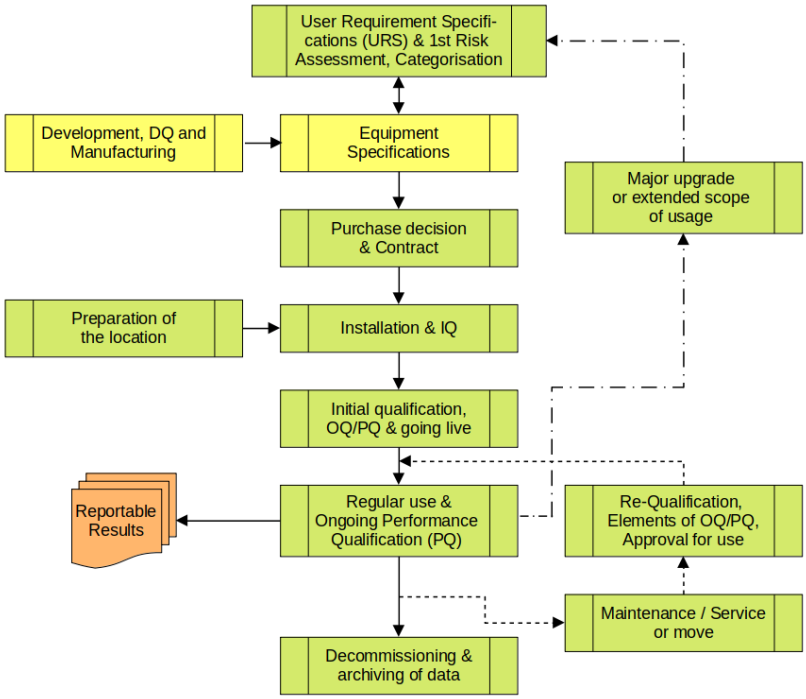
Fitness for intended use



Impact of EQ on...

- Method development and validation
  - Selection of parameters for robustness
  - Are the intended parameters of the method reproducible in practice at all?
- Investigation with uncertain results
- Method transfer
  - e.g. can a particular instrument be used or must another be adopted?
- Complex evaluations require reproducible measurement conditions
- Influence quantities with different devices must have comparable influences on the result

The list can be continued here....