amc technical brief

Editor: M Thompson Analytical Methods Committee AMCTB No 28 September 2007

Using analytical instruments and systems in a regulated environment

It is a basic tenet for all analytical scientists that, before the commencement of an analytical procedure, they must ensure the suitability and proper operation of any instrument or system that is part of the measurement process. The increasing prevalence of analyses carried out in regulated industries implies that additional tasks of a procedural and documentary nature are required in order to demonstrate 'fitness for purpose'.

These regulated industries cover several wide and expanding sectors, including the production of pharmaceuticals, medical devices and food, and environmental monitoring. In addition, it is a requirement for ISO certified laboratories that measurement uncertainty information is available. In order for this to be done, analysts need to take into account the uncertainty contributions from all elements of the analytical procedure, including those deriving from the instrument in its calibrated state.

Calibration, Qualification and Validation

As in all areas of analytical science, a defined and consistent terminology is necessary. There is at present, however, a considerable confusion as to the precise meaning of the terms calibration, qualification and validation, in general use, in the literature and in regulation. The guidance provided here (see Box) is designed to contribute towards a framework for an overall approach to the management of analytical data quality rather than to provide a set of rigid provisions.

Calibration

Calibration is the set of operations that establishes, under specified conditions, the relationship between values indicated by a measuring instrument or measuring system, or values represented by a material measure, and the corresponding accepted value of a reference calibrant. There is an expectation that instrumentation should be calibrated or verified at specified intervals, or prior to use, against measurement standards traceable to international or national standards; where no such standards exist, the basis for calibration or verification shall be recorded.[1] The work of the ICSC has been cited as a basis for calibration of analytical instrumentation, HPLC for example[2].

Qualification

Qualification is the collection of documented evidence that an instrument performs suitably for its intended purpose and that it is properly maintained and calibrated. Use of a qualified instrument in analysis contributes to confidence in the veracity of generated data.[3]

Validation

Validation relates to the 'fitness for purpose' of analytical methods and procedures as well as computerised systems. The majority of modern analytical instruments contain hardware, firmware and software in order to function. Many are fully computerised and automated systems. Computerised system validation is defined as 'Establishing documented evidence which provides a high degree of assurance that a specific computer-related system will consistently operate in accordance with pre-determined specifications'[4]. Furthermore, ISO Guide 17025 requires that equipment and its software used for testing, calibrating and sampling shall be capable of achieving the accuracy required and shall comply with specifications relevant to the tests and/or calibrations concerned. [5]

Holistic approaches and 'Fitness for Purpose'

Most modern analytical systems are multi-modular. While individual modules may require individual qualification and/or calibration, such tests alone cannot guarantee the accuracy of analytical results [6]. When the software validation aspects are taken into account, it becomes necessary to adopt a 'holistic' or system suitability approach. These holistic tests are for the purpose of ensuring a satisfactory performance of the overall system. Procedures that fulfil this role include internal quality control, by using one or more control materials as surrogate test materials in every run of analysis. IQC ensures that statistical control is maintained after the initial validation of the system. Proficiency testing and, where appropriate, the analysis of certified reference materials act as a powerful, occasional, but external check on system accuracy.

When this hierarchical approach is linked to analytical data quality management tools, the quality of analytical data and derived information is assured.[7]

A framework for analytical data integrity

The foundations for the confidence in an analytical result, as discussed above, can be summarised in a hierarchical way, requiring the following [8];

- The instrumentation used has been qualified and calibrated.
- The method selected is based upon sound scientific principles and has been shown to be robust and reliable for the type of test material.
- The laboratory sample is representative and sufficiently close to homogeneous.
- A person who is both competent and adequately trained has carried out the analysis.
- The integrity of the calculation used to arrive at the result and its uncertainty is correct and statistically sound.
- Internal quality control is carried out in every run of analysis. (A 'run' is the period in which repeatability conditions prevail.)
- Proficiency testing is undertaken whenever practicable.
- Independent audits and assessments of the whole analytical system are carried out at intervals.

CPD Certification I certify that I have studied this document as a contribution to Continuing Professional Development.

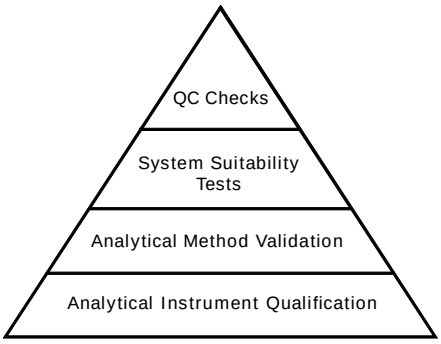
Name…….....

Signature…….…….Date……
…

Name of supervisor……..

Signature…….…….Date……
…

A convenient illustration of this hierarchical approach is shown below .



References

1 ISO 9001:2000, *Quality Management Systems – Requirements*; Section 7.6

2 *Guidance on Equipment Qualification of Analytical Instruments*: HPLC, LGC/VAM/1998/026.2 http://www.vam.org.uk/publications/publications_item.asp?intPublicationID=242

3 *AAPS Pharm Sci Tech* 2004; 5(1) Article 22 (http://www.aapspharmascitech.org)

4 PDA Technical Report 18 1995

5 ISO/IEC 17025 2005, *General requirements for the competence of testing and calibration laboratories*; section 5.5.2

6 *J AOAC International*, **77**(5) 1314-1317.

7 See, for example, Chapter 6; *Analytical Chemistry*, 2nd Edition Wiley-VCH, 2004, ISBN 3-527-30590-4

8 C Burgess, *Valid Analytical Methods & Procedures*, RSC, 2000

This Technical Brief was prepared for the Analytical Methods Committee by the Instrumental Criteria Subcommittee (ICSC) (Chairman Prof S Greenfield) and was drafted by C Burgess.

The **Analytical Methods Committee (AMC)** is the Committee of the Analytical Division Council that handles matters of technical importance to the members of the RSC Analytical Division and the analytical science community in general. The broad aim of the AMC is to participate in national and international efforts to establish a comprehensive framework for appropriate quality in chemical measurement, and to keep the analytical science community informed of developments.

The broad objective of the **Instrumental Criteria Sub-Committee** is to tabulate features of analytical instruments that should be considered when making a comparison between various systems, and thereby to assist purchasers in obtaining the best instrument for their analytical requirements.
See also www.rsc.org/amc for further information.

