QUALITY MATTERS

How much does quality really matter?

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This column is titled quality matters and in most analytical laboratories this topic matters very greatly. The steady growth of laboratory quality systems and the associated accreditation to ISO 17025 shows just how much time, effort and money can be invested in a quality system. In this short article I will argue that whilst the BS EN ISO/IEC 17025 2005 (better known as just ISO 17025) standard is good, it has one clear flaw which, if cured, would make it a quality system that should stand above all others.

So how is quality in an analytical laboratory achieved? For the moment, the answer is by using an audited quality system; for analytical chemists, this is usually the aforementioned ISO 17025. Whilst the drive to use ISO 17025 really started to gather momentum in about 2005 with the publication of the latest version of ISO 17025, which included all the main points of ISO 9000, quality systems are nothing new. As is explained later, there have been "internal" systems of considerable rigour in place in many areas of analytical chemistry for almost as long as the profession has existed.

Setting up and maintaining a commercial analytical laboratory is far from cheap and it is a fact of life that in most such laboratories the laboratory and quality managers are squeezed between the sometimes conflicting demands of meeting the customer's expectation for service and performance and the owner's demands to make a good return on their not inconsiderable investment. But for an accredited laboratory it is not the owners who judge the quality of the output of the laboratory, it is the external, independent auditors representing the "standard"; in the UK that means the UKAS Auditors.

To believe that ISO 17025 was the first such system is a mistake that can be forgiven: long before ISO 17025 first started to be adopted by analytical laboratories, the "old pretender" had been setting the standard for laboratory quality management! Known now as cGMP, it was developed in the pharmaceutical industries from the better-known GMP or Good Manufacturing Practice quality system that had been around for many years, and has resulted in a robust and reliable quality system that helps make sure that drugs are what they were supposed to be and more importantly are the same, lot after lot.

Since the arrival of ISO 17025 in 1995 and its major revisions in 1999 and 2005, these two systems have rubbed along, generally ignoring each other as the priests and disciples of each system worked away in their own worlds. But in recent years the rampant outsourcing of non-core services introduced by the global pharmaceutical industry into independent testing laboratories has brought the two quality systems into direct contact. Over the last couple of years, I have been much involved with these labs, working with a foot in both the ISO 17025 and cGMP camps and have come to believe that whilst both are good quality systems they each have a single and different deficiency that if corrected would make them better… and virtually the same!

As many readers will know, ISO 17025 accreditation of an analytical method is based on a rigorous method validation, using CRMs where available and then controlled by using analytical quality control samples (AQC) on a daily basis for within- and between-batch control. This is supported by participation in an externally organised proficiency testing (PT) programme, where available. The method validation has to be repeated whenever there is a significant change to the analytical system, and providers of CRMs and PT should be accredited to ISO 17025 together with ISO Guide 34 and ISO 17043, respectively.

When running a cGMP-based quality system, the process has some differences: cGMP demands an IQ/OQ/PQ approach demonstrating that analytical systems are qualified using written procedures, with traceable materials, to pre-defined set-points and acceptance criteria.

The first stage in the chain is DQ, or design qualification (DQ), where the design of the analytical system is validated. DQ is usually an instrument supplier's job, but DQ can also be performed by the user, by confirming through review and testing that the equipment meets the written acquisition specification. Once the instrument appears to be working, installation qualification (IQ), operational qualification (OQ) and performance qualification (PQ) all follow. Done properly the IQ/OQ/PQ approach gives a solid foundation upon which method validation can rest.

In essence, the three protocols (IQ/OQ/PQ) check whether a product or service fulfils all specified, in some cases legally binding, requirements and conforms to the specification and requirements.

IQ involves checking that installation of equipment follow the blueprints given at the beginning of the project. This step also requires that the supplier delivers sufficient documentation to the client to enable future maintenance.

Once the equipment has been installed, OQ confirms the equipment's

operating processes. This check includes running through a standard operating procedure (SOP) for each state of the equipment.

Finally, the PQ checks make sure the equipment is able to perform the task for which it was purchased at the required throughput.

The procedures used for validation must be method independent and in most cases the PQ/OQ part of the validation process has to be re-done whenever there is a significant change, such as a replacement detector and may be done even if the change is as apparently minor as the installation of a new column. The laboratory or quality manager can control this process and is free to create his/her own documentation and test parameters. However, within the pharmaceutical industry it is frequently outsourced, to the OEM—original equipment manufacturer (who offer widely varying levels of quality and sophistication to these qualification processes) or to an independent company who will provide a more harmonised approach covering all the instruments in a particular organisation.

One would assume that with instrument qualification and method validation in place then obtaining reliable quality data would be a formality. Although analysts will be expected to have the necessary educational qualifications and training records are maintained, the cGMP environment seems often to have less rigorous ongoing AQC requirements than under an ISO 17025 quality system and, from this author's perspective, strangely it seems that there is no stated requirement for any proficiency testing.

The 2005 edition of ISO 17025 does not include a formal requirement for anything that would be recognised by a cGMP quality manager as part of a formal DQ/IQ process. In Section 5.5, Equipment, the standard states that "… *Equipment and its software used for testing, calibration and sampling shall be capable of achieving the accuracy required and shall comply with specifications relevant to the tests and or calibrations concerned*". Further on there is a requirement that "*Before being placed in service the equipment shall be calibrated or checked to establish it meets the laboratories requirements*"… and later there is also a comment that it shall be checked or calibrated before use. But compared with the requirements for validation understood in a cGMP environment this is almost superficial.

I believe that failure to properly validate the correct functioning of the analytical system often means that labs waste much time and effort trying to validate a method using an analytical system that is not functioning properly. Indeed over the last 12 years most of the "CRM Problems" reported to me have been traced back to an analytical system that is not working as it should. The rigorous use of AQC and PT does mean that any systemic failures are picked up quickly, but then the Quality Manager can spend far too long searching for the cause than is really needed. PT participation also means that the quality and competence of operators can be monitored and compared and the performance of different labs running the same tests can be easily compared.

In the cGMP world it is clear that, if method validation is started using a known and proven analytical system, it should proceed relatively easily. But once set up, there is much less chance that systemic failures will be picked up and there is no opportunity to compare operators, or labs, instruments or departments.

In summary, the ISO 17025 world sees analysis with proven performance on their analytical methods via Proficiency Testing resting on analytical systems with no proven operational performance! A hybrid ISO/cGMP with PT and AIQ (Analytical Instrument Qualification) would vastly improve the confidence in the final analytical data.

Yes, there may be a cost, as both analytical system validation and proficiency testing are normally paid for services, but this would be offset by time and material saved and would together raise the bar on analytical laboratory performance.

If you think that quality matters enough to take the best of both quality systems and cross fertilise the other let me know. I would be very interested in your opinions.