Validation of Spectrometry Software

Part IV — Qualification of the Software and System

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In the previous three parts of this series on the validation of spectrometry software, we have looked at the initial stages of specifying the system, selecting the system, auditing the vendor, and system purchase (1). The next stage after we have purchased our spectrometer and its software is the qualification of the system. Before we get into details of the work we'll have to do, we need to discuss terminology and get our definitions right, because we are dealing with qualification of the instrument (spectrometer) as well as qualification of the application that controls it.

The reason for going back to basics is that the same terminology is used in both equipment qualification and computer system validation, but they mean different things. Unless you understand the difference and get your terminology and meanings correct, problems can occur and you can have gaps in your validation that can give rise to inspectional observations later.

Terminology: Getting It Right

We'll look at the definitions of installation qualification, operational qualification, and performance qualification in the contexts of equipment qualification and computerized system validation. Hopefully the mists will clear and all will be revealed (or not!).

Equipment qualification (EQ). EQ's function is to demonstrate that an item of equipment (such as a spectrometer) is fit for a particular purpose. This implies that all the parameters (for example, wavelength accuracy, linearity of response, and so forth) used by the methods that will run on that instrument are within tested and acceptable limits. Typically these parameters will use recognized or internationally accepted chemical standards. Because many methods can be specific to a single laboratory, the instrument parameters to be qualified can vary from organization to organization. This step is an essential requirement for equipment used in a regulated environment and is the basis for all subsequent analytical method validation work.

The stages of EQ are design qualification (DQ), installation qualification (IQ), operational qualification (OQ), and performance qualification (PQ). These terms are defined in the context of EQ in Table I.

Computerized system validation (CSV). The aim of CSV is to show that the system works as specified; this takes a life cycle approach, as we discussed in the first part of this series (1). So far, so good.

However, when we get to the qualification phase of the life cycle, the terms IQ, OQ, and PQ are used within the context of computerized system validation, as shown in Table 1. However, their context is different, which is the major problem with using the qualification terminology. Even the U.S. FDA has acknowledged the confusion this practice causes in the *Guidance for Industry on the General Principles of Software Validation* (4) and does not mention this approach in the document.

As part of the computerized system that includes the spectrometer, the instrument itself undergoes qualification. Therefore a user will conduct EQ on the instrument (both IQ and OQ), plus CSV on the software (IQ, OQ, and PQ). Confused? Join the club!

Therefore your validation plan should make it clear how this problem will be tackled: will you qualify the instrument separately from the software, or use an integrated approach? Typically, because most spectrometers can't operate without the computer and the software, the integrated approach may be the only option you have open to you.

Qualification Terminology Explained

Table I illustrates the differences between the way these terms are used in EQ and CSV so that the

confusion is minimized. It is important to ensure that the context of the terminology used is established early in a discussion with any other individuals, including regulatory inspectors. This is best described in an overall policy document, or standard operating procedure.

In essence, the DQ and IQ stages outlined earlier are similar between the EQ and CSV terminology, which answers the questions as to whether or not the system is specified and installed correctly. The differences come in the OQ and PQ phases and are due, in part, to the perceived complexity of a computerized system over an analytical instrument. The OQ stage for EQ aims to show that the item is fit for its purpose. This is the laboratory's responsibility, and, after successful completion, the instrument is released for operational use.

CSV has two more stages to go through before the operational release; the OQ shows that the system works as the vendor says it should (anticipated operating ranges); the PQ in the system's normal operating environment is the responsibility of the laboratory. Once the computerized system successfully completes its PQ, it is ready for release into a regulatory environment.

In this series we'll be using the CSV terminology and will concentrate on looking at the IQ and OQ stages. I'll discuss the PQ in the next installment of this series.

Installation qualification. Simply put, IQ is the installation of the components of the order into the system with a check that the system works correctly. The best people to undertake this work will be the vendor's staff, because they know their products best; however, there could be several groups working on the installation qualification, depending on the complexity of the configuration of the instrument.

For stand-alone workstations and spectrometers, the following minimum list of activities needs to be completed:

- Installation of the spectrometer and any add-ons — for example, sampling options
- Installation of the workstation
- Installation of any associated equipment, such as a printer or CD burner
- Installation of the software application(s).

These steps are typically performed by the instrument vendor or their approved service agent; with the workstation, there may be a standard-build PC provided via your company's IT department, on which the vendor installs the software.

For networked systems, the following activities would also be required, again depending on the configuration of the system:

- Server (for data storage) installation by the IT department, server supplier, or manufacturer
- Processing or data review workstations, by either the IT department or contractors working on their behalf
- Network connection of the workstations to the corporate LAN
- Installation of the application software for data processing on the workstations.

Many spectroscopists may not be familiar with the detail of the regulations or guidelines under which they are operating; however, you'll need to be proactive to ensure that essential documentation to be collected from these activities is planned and collected proactively. Retrospective documentation of any phase of this work is far more costly and time consuming. Therefore, reiterating the advice given earlier, plan the work in the validation plan, otherwise you'll end up with a large compliance hole and little gain from this phase of work.

Operational qualification. The OQ is carried out after the IQ and is intended to demonstrate that the whole system works the way the vendor says it will. Most vendors will supply OQ scripts. Of necessity, these will only cover a subset of functions and will not be a substitute for the user acceptance tests or PQ tests. Many enterprising vendors will sell part or the whole of their in-house test suites as their OQ packages. What you have to be aware of is that the ven-

Table I. Differences in qualification terminology between equipment qualification and computerized system validation

Term	Equipment qualification	Computerized System Validation
Design qualification (DQ)	DQ or systems requirement specification (SRS) that documents the functional requirements of the instrument and any software features, including *21 CFR 11* and predicate rule compliance	
Installation qualification (IQ)	Assurance that the intended equipment is received as designed and specified (3)	Documented evidence that all key aspects of hardware and software installation adhere to appropriate codes and the computerized system specification (2)
Operational qualification (OQ)	Confirmation that the equipment functions as specified and operates correctly (3) **Operational release of system**	Documented evidence that the system or subsystem operates as intended in the computerized system specifications throughout representative or anticipated operating ranges (2)
Performance qualification (PQ)	Confirmation that the equipment consistently continues to perform as required (3)	Documented evidence that the integrated computerized system performs as intended in its normal operating environment (2) **Operational release of system**
Periodic reviews	Not applicable	Performed to a periodic review SOP to ensure that the system is still validated.

dor OQ material usually only provides sufficient information to demonstrate that the system does what the vendor says it will and no more. It is intended to work on the base software so when you configure the software, you'll have to document and test these changes in the PQ.

Typically the OQ is carried out immediately after the IQ, and the same person will execute both. Ensure before this person starts that he or she is trained to perform this work and that you have documented evidence of this fact, such as a training certificate that is current at the time that the work is carried out.

What should be in an OQ? This depends on the vendor and their marketing approach to this "value added" package. Here is my view on the subject: The purpose of an OQ is to show that the software and system work the way that the vendors state they should.

To more fully understand the purpose of an OQ, you need to understand how software is produced. As the FDA acknowledge in their guidance for industry called *General Principles of Software Validation,* the critical phase of development is the design, writing, and testing of the application. Software production is simply the production of CD media and verification that the disk has been burned correctly. Therefore, the main emphasis in software production is the correct design and release of the system; this is where the vendor's certificate (or equivalent) of conformance/validation/compliance with their internal procedures is important. Most of the work is done at the vendor's site; the IQ (Have the files been installed in their correct locations?) and the OQ (Does the software work correctly?) are confirmation that the software is the same on your system.

The amount of testing can therefore be relatively small because the vendor has carried out the bulk of the work at their development site. The OQ is just a confirmation that the out-of-the-box software works as expected: no configuration will be carried out because this is your responsibility.

In most cases, the OQ does not need to be very extensive to demonstrate that the software works correctly, especially when the software is to be configured before the PQ is carried out for security, macros, custom calculations, and so forth. Extensive testing of the baseline package is of little value because it will bear little relationship to the final operating software application.

However, before dismissing any vendor's OQ as a total waste of time and effort, you should, as part of a critical review of the approach, map your requirements to the vendor's package and find out what is being done, and to see if it can form a substitute for work you would need to do in the PQ. Some examples include detailed instrument control functions and where your requirements match what is undertaken in the OQ (typically for simpler software applications). Where a lot of laboratory customization of the application exists — for example, a spectral library involving your specific compounds — the vendor's OQ package is of less or little help.

Assess Vendor Qualification Documentation

Any documentation provided by a vendor must be critically reviewed. Never, never, never accept documentation from a vendor without evaluating it and approving it. Why? Let's go back to the regulations. Look at the *21 CFR 11* current Good Manufacturing Practice requirements under Laboratory Controls and read section 211.160, subtitled "General Requirements" (5):

> (a) The establishment of any specifications, standards, sampling plans, test procedures, or other laboratory control mechanisms required by this subpart, including any change in such specification, standards, sampling plans, test procedures, or other laboratory control mechanisms, shall be drafted by the appropriate organizational unit and reviewed and approved by the quality control unit. The requirements in this subpart shall be followed and shall be documented at the time of performance. Any deviation from the written specifications, standards, sampling plans, test procedures, or other laboratory control mechanisms shall be recorded and justified.

In essence, you need to have a written plan that is approved by the quality control or quality assurance group within your organization. How many of you don't do this for vendor-supplied documentation? In fact, how many vendor documents give space for the QC or QA group to sign off that they have reviewed the documentation? (A clue: the answer is between −1 and +1.) However, the regulations go further — much further, as we'll see from the next section.

> (b) Laboratory controls shall include the establishment of scientifically sound and appropriate specifications, standards, sampling plans, and test procedures designed to assure that components, drug product containers, closures, in-process materials, labeling, and drug products conform to appropriate standards of identity, strength, quality and purity.

What? A regulation is asking us to be scientifically sound? Yes. Now you see the reason for assessing the vendor IQ and OQ documentation. The regulations require that, before execution, the protocols have to be approved by the QC/QA unit and also that whatever is written in them needs to be scientifically sound. That is why you must review this documentation and see what you are getting for your money.

Also, look at the requirements of the draft guidance for industry on *21 CFR 11* validation (6); in section 5.4.3, entitled "How Test Results Should Be Expressed," the following comment is found:

> Quantifiable test results should be recorded in quantified rather than qualified (for example, pass/fail) terms. Quantified results allow for subsequent review and independent evaluation of the test results.

Therefore, this gives you an additional factor for critical review of what you are purchasing. Explicitly stated ac-

ceptance criteria must also be available, rather than implying that if all expected and observed results match, then the system passes.

If in doubt, here's an example of someone who did not do what I suggested. In the warning letter the U.S. FDA sent to Spolana (7), a Czech company, in October 2000, there appears the following citation:

> Written procedures had not been established for the calibration of analytical instruments and equipment in the Quality Control laboratories used for raw material, finished API and stability testing. Furthermore, calibration data and results provided by an outside contractor were not checked, reviewed and approved by a responsible Q.C. or Q.A. official.
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> Enough said?

Moving Forward to PQ

In the next installment or two, we'll look at the PQ of your spectrometer software that covers the use of the system as you intend to use it.

References

1. R.D. McDowall, *Spectroscopy* **16**(2), 32–43 (2001).
2. R.D. McDowall, *Spectroscopy* **16**(7), 30–34 (2001).
3. R.D. McDowall, *Spectroscopy* **17**(2), 64–77 (2002).
4. "Guidance for Industry, General Principles of Software Validation," Food and Drug Administration Center for Devices and Radiological Health, Rockville, MD, 2002.
5. Current Good Manufacturing Practice regulations, *21 CFR 11.*
6. "FDA Draft Guidance for Industry, *21 CFR 11* Electronic Records and Electronic Signature Validation," Food and Drug Administration, Washington, DC, 2001.
7. Spolana warning letter, October 2000, posted on the FDA web site, www.fda.gov. ■