

# Choosing the Right Instrument Vendor for Complete, Cost-Effective Spectrometer Compliance

## Key Words

- 21 CFR Part 11
- cGMP
- Compliance
- GLP
- ISO
- Molecular Spectroscopy
- Qualification
- Six Sigma
- Validation
- Verification

## Introduction

Numerous up front considerations can substantially reduce the overall cost of regulatory compliance for molecular spectroscopy (FT-IR, FT-NIR, Raman, UV-Visible) systems and compress the entire process by as much as seventy five percent. However, in order to achieve such efficiency, you must select an experienced instrument vendor with in-depth system knowledge and regulatory expertise. The selection process can be as complex as the compliance process itself, given the lack of comparative criteria for the wide array of available systems, capabilities and services.

This paper discusses the cost considerations, opportunities and risks associated with selecting a spectrometer vendor to partner with based on their compliance capabilities and provides the details required to make an informed decision.

## If You Were Audited Today, Would You Be Ready?

The fact is, compliance has become so complex that it's led to confusion and misconception about what it really takes to comply. As a result, you may have unrecognized gaps in your compliance program or, at the very least, lack 100% confidence in your compliance status should you be audited. An understanding of compliance basics will help you determine the real value of an instrument vendor's compliance capabilities and better evaluate their spectrometer systems.

## Compliance Basics

The term "compliance" generally refers to the overall process of meeting a set of regulations whether government mandated or self-imposed. Figure 1 shows a schematic view of the three levels of the compliance hierarchy. The level that must be achieved is dependent on the regulations or industry requirements that the laboratory falls under. Within compliance lie the qualification and validation processes; terms that are often used interchangeably. However, qualification and validation, in fact, represent two distinct levels within the compliance process. In addition, there is verification, which is an ongoing process that occurs in nearly all spectrometer compliance programs.

## Verification

The verification process, also termed performance verification, demonstrates that at any given time your spectrometer is working properly. It's analogous to checking a clock – over time clocks can lose or gain time and need to be "recalibrated" back to the correct time. Verification, in this case, requires comparing the time on the clock to one that had recently been set to the local time.

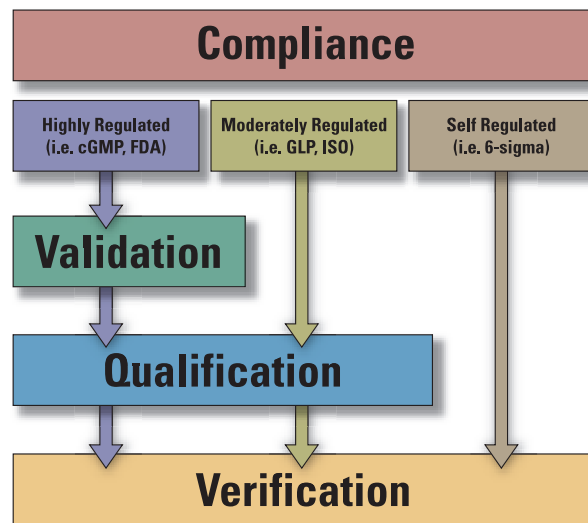


Figure 1: Depending on your industry and the regulations with which you must comply, you may start at a different level within the compliance hierarchy

For a spectrometer, verification basically involves taking a set of specific measurements on a regular basis and monitoring the results for any changes. If the measurements exceed specified acceptance limits, you'll need to make corrections as soon as possible. Verification helps prevent results that are out of specification from entering your process and can minimize instrument downtime by detecting potential problems early.

In moderately to highly regulated environments, spectrometer verification often involves re-running selected qualification tests or measuring specific quality control check samples on a routine basis.

## Qualification

The purpose of qualification is to provide a high degree of confidence that the system will work for its intended purpose and to document this for the regulating agencies. In qualification, a well-documented and rigorous evaluation process is used when both purchasing and commissioning an instrument. As part of this process, a more extensive set of procedures and checks are performed on the spectrometer than in a routine verification program. Where verification only checks the system when it is in the operational phase of its lifecycle, in qualification the system performance is checked and documented at all stages.

## Qualification At-a-Glance

**Design Qualification (DQ)** – Documented verification that a chosen system’s design is appropriate for its intended use. **Purpose:** Ensure that good design process is utilized for both software and hardware and they are fit for the intended purpose. (Pre-purchase activity)

**Installation Qualification (IQ)** – A comprehensive set of procedures documenting installation specific to the laboratory in which the instrument is installed. **Purpose:** Demonstrate that the spectrometer is properly installed in the intended environment.

**Operational Qualification (OQ)** – A comprehensive set of procedures that document the instrument is performing to factory specifications (includes test data and measurement analysis for the instrument and sampling accessories including traceable test standards). **Purpose:** Demonstrate that the spectrometer works the way the instrument manufacturer intended.

**Performance Qualification (PQ)** – Additional procedures that document the instrument can properly perform the measurements specified in the application and SOPs. **Purpose:** Demonstrate that the spectrometer can perform the measurements for your intended application and fit into your specified testing procedures.

In environments where qualification is required, the processes and measurements that make up verification are often based on the Operational Qualification (OQ) and Performance Qualification (PQ) tests. These tests are typically much more controlled than those used in verification-only environments, and often are based on industry “standards” in terms of both methods and reference materials. To use the same analogy of setting the time on a clock, a qualified clock would be set based on the time on a standardized device, such as the NIST atomic clock based in Boulder, Colorado, USA.

For spectrometers, the standards are often methods and materials developed and tested by reputable third-party organizations (i.e. ASTM, NIST, US/European/Japan Pharmacopeia, etc.) or where these are lacking for a specific type of instrument technology or industry, by the instrument vendor themselves.

## Validation

Validation is the process of proving and fully documenting that the spectrometer is appropriate for the intended task or fit for purpose. This process covers the installation and operation of the full system including the software, accessories, the intended application and all the related standard operating procedures (SOPs). Validation also includes documenting the steps and decisions made during the process of evaluating and purchasing the system.

Full system validation is analogous to car maintenance. You can verify that the tires are qualified to do what the tire manufacturer says they will do and that they comply with various safety standards governing tire manufacturing. However, unless you look at the complete system such as alignment, proper balancing, how fast the car can safely go, the weight of vehicle plus passengers plus cargo, etc., qualifying the tires alone is of little value without also considering the impact of other system components and operating conditions. That’s where system validation becomes integral to compliance programs in more highly regulated industries.

It is important to understand that system validation is essential to achieve compliance with FDA 21 CFR Parts 58, 210 & 211, 820 and 11, as well as specific Eudralex regulations.

## Validation At-a-Glance

- Validation Master Plan (VMP)
- User Requirements Specification (URS)
- System Infrastructure & Configuration Requirements
- Functional Requirements Specification (FRS) and gap analysis of vendor’s design
  - Includes design documents from vendor that show the instrument can meet or exceed the requirements stated in the FRS (DQ)
- System Qualification Procedures
  - Typically documentation that involves instructions on how to invoke the IQ, OQ and PQ procedures
- Requirements Traceability Matrix (RTM)
- Validation Summary Report
- Standard Operating Procedures (SOPs)
  - Operation
  - Administration
  - Calibration
  - Preventive Maintenance (PM)

## How to Assess the Value of Compliance Products and Services from Instrument Vendors

To many the term *outsourced compliance* conjures up images of pricey consultants who run up the clock while writing “big documents.” While that may have been the case when the supply of consultants was low and demand high, now there are new alternatives that can not only help you comply, but also help reduce overall cost, complexity and risk of implementing a compliance program for a new spectrometer.

First off, select an instrument vendor with compliance expertise and first-hand experience and you’ll receive great value in terms of efficiency and risk reduction. On the other hand, selecting an instrument vendor that’s lacking in regulatory knowledge or experience in qualifying and validating a system and it could cost you more and take longer to commission your instrument.

One of the biggest mistakes in evaluating the value of these services is to simply consider the cost of the vendor’s recommended compliance program alone. To determine the value of compliance services, you must examine all the related costs. And it’s not simply a question of cost, but a question of overall value. For example, consider whether or not you have the intimate system knowledge and extensive regulatory understanding to qualify the spectrometer and validate the entire system yourself for the same investment as an outside vendor? If not, who does? And if so, what’s the “lost opportunity” cost when you consider your time investment?

As an example, full system validation covering the spectrometer, software, accessories and standard operating procedures may take from 6 to 12 man-months to complete, depending on the complexity of the hardware and

application. An additional 4 man-months is needed to verify and maintain compliance over the life of a typical spectrometer system. When evaluating the amount of effort being done by internal resources it is important to recognize that the time spent on compliance related activities is time taken away from completing core business tasks. To fully harness the value of your compliance investment means ramping up quickly and maintaining compliance efficiently throughout the product’s life cycle.

### How Much Does Compliance Really Cost?

Qualification and validation costs vary depending on the approach taken to complete the implementation and execution. What a given laboratory does is determined by:

1. The degree of regulation (high, moderate, or self-imposed) within their industry or company; or the criticality of the instrumental measurements being made.
2. The availability and cost-effectiveness of using their company’s human resources to perform the necessary compliance-related tasks.
3. The degree of compliance expertise of those human resources in developing, documenting and/or performing the necessary tasks.

Regardless of who does the implementation, certain tasks are required to achieve a given level of compliance. These can be broken into commissioning costs and compliance maintenance costs. The table below provides an overview of the estimated costs broken out by who develops and executes the implementation – Internal resources, a third-party validation consultant, or an instrument vendor with a full range of compliance offerings and regulatory expertise.

## Estimated Costs of Compliance Tasks for a Typical Spectrometer: Commissioning and Compliance Maintenance

### Commissioning Cost

System Compliance Tasks	Internal Effort	Cost	Consultant Effort	Cost	Vendor Effort	Cost
Performance Verification <sup>1</sup>	8 – 12 man-days at \$500/day	\$4,000 to \$6,000	8 -12 man-days at \$2,500/day	\$20,000 to \$30,000	0.5 man-days at \$2,000/day	\$1,000
System Qualification <sup>2</sup>	28 – 42 man-days at \$500/day	\$14,000 to \$21,000	18 – 32 man-days at \$2,500/day	\$45,000 to \$80,000	1-2 man-days at \$2,000/day	\$2,000 to \$4,000
System Validation	160 – 240 man-days at \$500/day	\$80,000 to \$120,000	120 – 160 man-days at \$2,500/day	\$300,000 to \$400,000	30-60 man-days at \$2,000/day	\$60,000 to \$120,000
Total Commissioning Time & Cost	188 to 282 man-days	\$94,000 to \$141,000	138 to 192 man-days	\$365,000 to \$510,000	31 to 62 man-days	\$62,000 to \$124,000

### Compliance Maintenance Cost (10 year lifetime)

System Compliance Tasks	Internal Effort	Cost	Consultant Effort	Cost	Vendor Effort	Cost
Daily Performance Verification <sup>3</sup>	50 man-days at \$500/day	\$25,000	N/A		N/A	
Annual or Event-based Requalification	20 man-days at \$500/day	\$10,000	10 man-days at \$2,500/day	\$25,000	10 man-days at \$2,000/day	\$20,000
Event-based Revalidation	15 man-days at \$500/day	\$7,500	15 man-days at \$2,500/day	\$37,500	15 man-days at \$2,000/day	\$30,000
Total Maintenance Time & Cost <sup>4</sup>	35 man-days	\$17,500	25 man-days	\$62,500	25 man-days	\$50,000

<sup>1</sup> Performance verification testing typically included as part of System Qualification

<sup>2</sup> Assumes vendor has a well developed, comprehensive system qualification offering available that meets system owner’s needs

<sup>3</sup> Effort for analyst to perform daily tests to verify system performance

<sup>4</sup> Does not include daily tests to verify system performance

The instrument qualification portion of compliance takes fewer man-days and costs much less compared to full system validation. Therefore, it's no surprise that full system validation comprises the greater portion of upfront compliance costs. The complexity of full system validation requires greater resource allocation and extensive knowledge of the instrument and software, analytical techniques and regulatory requirements including overall validation master plans, IQ, OQ, PQ, and secure documentation. Selecting a vendor who understands the impact of compliance on your overall system can help minimize the total cost while helping you manage complexity. The advantage such a vendor brings is their familiarity with their own system and software and the fact that they have:

1. Established performance verification tests for the instrument
2. Developed a system qualification package for the instrument and with the development costs amortized over the many systems they sell
3. Created templates and protocols that allow them to validate the instrument and software quickly and efficiently within the system owner's environment

A third party consultant will have experience with the validation requirements and have templates to create the validation documents. However, they will require extensive effort to develop specific tests and protocols to qualify and validate a system that they may not be familiar with.

### **The Hidden Cost of Compliance**

When evaluating compliance products and services from different vendors, what's often overlooked is the *total* cost of compliance and its impact on your resources over the life of your system. These are effectively "hidden costs" because they don't reflect the opportunity cost of reallocating a full-time resource to the instrument commissioning, qualification and, depending on your regulatory environment, validation. That alone could take upwards of six to nine months. Few laboratories lacking dedicated compliance experts can sustain the resulting lost productivity and throughput.

For a start-up or small to mid-size company, these lost opportunity costs can have a significant impact on profitability. For large companies with many instruments, the complexity of organizational dynamics can lead to costs that are multiplied if instrument procurement and commissioning is not managed effectively.

### **Selecting an Instrument Vendor with Compliance Expertise Can Minimize Cost and Manage Complexity**

As the complexity of the compliance effort increases, so does the cost and burden on a company's internal resources. However, compliance expertise and service are no longer the exclusive domain of expensive independent consultants. Instead, instrument manufacturers, are now packaging specific compliance-related products and services with their spectrometers. The goal is to help companies in regulated environments streamline the installation process while minimizing the cost and burden of achieving full compliance.

The key benefits of selecting experienced instrument vendors with extensive system knowledge and regulatory expertise include:

- Shorter implementation time due to vendors intimate knowledge of system
- Reduced overhead because of compliance expertise provided
- Ramp up to production faster
- Lower overall cost of compliance
- Minimize risk of audits uncovering areas of non-compliance
- Improve laboratory human resource allocation

### **Streamline Commissioning by Up to 75% While Minimizing Risk**

Provided by the right instrument vendor, instrument validation can cut commissioning time on new instruments by seventy five percent. However, to truly deliver an "out-of-the-box-into-the-lab" installation, the instrument vendor's qualification offering should include:

1. Complete documentation for instrument design qualification (DQ).
2. Fully documented procedures with signoffs for installation and operational qualification (IQ/OQ) for the entire system.
3. Software and traceable reference materials to complete the qualification and for ongoing performance qualification (PQ).
4. Certified service engineers specifically trained on the technical service and qualification procedures for the specific spectrometer and software purchased.
5. Factory certification of instrument performance results when system is installed and qualified by company service representatives.

All five elements are necessary to ensure that the qualification will withstand any regulatory or audit challenges. They also ensure that the vendor can complete the qualification process in the minimum amount of time to get the instrument ready for routine operation. With all five elements in place, a typical spectrometer system can be fully qualified and ready for first measurements on the same day it's installed. Without it, at best, you could be left with significant additional work to do on your own; at worst, the qualification may not stand up to an audit.

When the validation process is required, such as in highly regulated environments like pharmaceutical and food products, a truly compliance-ready instrument vendor is of great value. Since no two companies' regulations, functional requirements, PQ methods and limits or SOPs are alike, a consultative relationship with the vendor is required to create a customized validation solution and documentation package. However, unlike third part consultants who need to start from scratch with each new instrument, the spectrometer vendor can combine its regulatory expertise, extensive technical knowledge and existing documentation for the instrument systems they provide to deliver a fully tailored solution. The result is a much faster implementation at a significantly reduced cost and with minimal audit risk. This is an ideal solution for time-constrained laboratories or those with limited person-power or regulatory knowledge.

A comprehensive validation program from your instrument vendor should include the following:

- Validation Master Plan (VMP)
- User Requirements Specification (URS)
- System Infrastructure & Configuration Requirements
- Functional Requirements Specification (FRS) and DQ gap analysis
- Documentation on using the vendor-supplied IQ/OQ procedures
- PQ Test Scripts
- Requirements Traceability Matrix (RTM)
- Validation Summary Report
- Standard Operating Procedures (SOPs)
  - Operation
  - Administration
  - Calibration
  - Preventive Maintenance (PM)

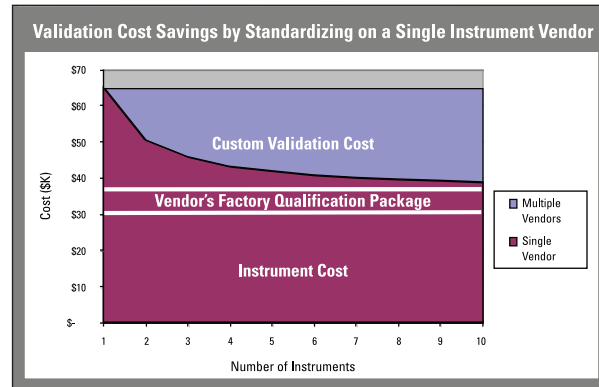
### How to Reduce Total Cost of Ownership and the "Multiple" Effect

From a business perspective, having your instrument vendor provide compliance services enables you to amortize the costs of instrument qualification or full scale system validation over the life of the instrument by including these costs in the initial capital requisition. This lowers your overall cost of compliance compared to the ongoing cost of hiring and training dedicated resources.

Additionally, only by partnering with a single instrument vendor can you avoid the "multiple effect" – paying again for similar compliance services and conducting the same compliance work on subsequent instruments used for the same measurement application.

For example, a manufacturer with multiple facilities, each using the same brand spectrometer and testing methods, would only need to develop a validation program and documentation on one instrument. The program can be applied to all instruments of the same model in the same measurement application. The only additional cost and effort would be to execute the qualification and validation procedures and sign off on the validation documentation.

By selecting a different instrument vendor for another site, the per instrument compliance costs and workload would be effectively doubled. The "multiple effect" is demonstrated in the chart below titled Validation Cost Savings by Standardizing on a Single Instrument Vendor. The chart shows that the cost of commissioning subsequent instruments of the same type from the same vendor decreases substantially.



### How to Avoid the "Compliance Compromise"

When you're commissioning a new spectrometer system, there is a compromise between focusing on your laboratories core expertise and placing the system into service. Compliance services from your instrument vendor enable your in-house resources to focus more effectively on core compliance-related activities, from developing and validating analytical methods to training laboratory personnel on the use of the methods. These activities fall squarely within the expertise of the in-house resources and are typically things you would not want done by people outside of your organization.

By choosing the right instrument vendor and tasking them with the qualification and validation tasks they can do most effectively, essential in-house functions can be done without compromising new system commissioning and you'll get it done faster. In many cases, vendor compliance experts can develop and deploy a full scale compliance program similar to the one previously described in just one month.

However, an important advantage of investing in your instrument vendor's compliance services is flexibility. A compliance savvy instrument vendor will offer a modular approach so that you can optimize your time and resources by investing in the components that will reduce the compromise. Avoid a "one-size-fits-all" approach that requires you to buy something you don't need or won't ever use.



## How to Increase the Probability of a Successful Audit

It's important to note that two of the main purposes of choosing an instrument vendor with compliance expertise and modular services is to bring in the person power you may not have available or supplement your in-house regulatory competency. Your instrument vendor should have in-depth knowledge of the system and the regulations that will stand up to the rigors of an audit.

An added benefit of choosing an instrument vendor with in-depth system knowledge and regulatory expertise is the value of having a "third-party" provider for the system's qualification (i.e. using the instrument vendor's qualification package and certified service engineers to complete the system IQ/OQ). Third party qualification is often looked upon more favorably by auditors because it provides additional assurance that the company using the instrument is not "grading their own homework."

In addition, documentation packages and certification processes provided by a spectrometer vendor appropriately represent the flow and format that most auditors use to evaluate your process and can increase the likelihood of a favorable audit outcome.

## Conclusion

For achieving spectrometer compliance in any regulated organization, working with the instrument vendor is a good starting point because they have first-hand technical knowledge of the equipment they sell. In many cases, the instrument vendor can be a viable compliance supplier, provided they have the right products, services, extensive regulatory knowledge and the experience required to accomplish the job in an effective and timely manner.

However, there is one caveat: experience and expertise can vary greatly among instrument vendors. Research their offerings carefully and remember to look at the broader perspective – the total long-term cost of compliance. Your instrument vendor should be able to look at your entire process and establish a program that streamlines the process and saves you time and money in the long run on a single instrument purchase as well as subsequent instrument acquisitions. With the right instrument provider, you can achieve hassle-free compliance for your new spectrometers quickly and cost effectively.

## Case Study:

### *Large Biopharmaceutical Company Streamlines Validation by Over 75%*

The company had an aggressive time-to-market goal on a newly approved drug of 180 days following approval. In order to accomplish their goal, they needed to compress the qualification and validation processes.

Although the company had the in-house resources, they chose to invest in compliance services for both instrument qualification and full system validation to avoid over allocating their resources and compromising their time-to-market goal. They used their in-house resources to oversee and approve the process and selected their instrument supplier, Thermo Fisher Scientific, to take full responsibility for the implementation. The company also streamlined their internal paperwork and approval process by including the equipment, factory qualification and validation services on a single purchase order.

### Cost Analysis

In this case, the company was able to save approximately \$90,000, and save 6 months of valuable time. As the company expands and adds new instruments of the same brand, the cost will continue to decrease because new instruments fall within the same validation master plan. This does not take into account the savings that were realized by having internal resources working on other tasks or the financial gains of getting their drug to market early. The value of these savings could far outweigh the Thermo Fisher Scientific commissioning cost, but this information was not available for our analysis.

### Case Study Snapshot

**Company:** Large biopharma

**Situation:** Rapid ramp-up for newly approved drug

**Requirements:** System validation within cGMP environment; full 21 CFR Part 11 compliance

**Solution:** Vendor-provided system qualification and custom end to end validation

**Result:** cut commissioning time by 75% and saved \$90,000

Thermo Fisher Compliance Solution	Estimated In-house Effort	Savings
2 months	8 months	6 months
\$30,000	\$120,000	\$90,000

## The Thermo Fisher Scientific Solution for Spectrometer Compliance

Thermo Fisher Scientific has a well-established history as a comprehensive supplier of products and services to customers in regulated industries and quality-conscious organizations. Within the field of molecular spectroscopy applications, Thermo Fisher is an innovator in compliance products and services. Our market-leading compliance solutions have helped numerous pharmaceutical and other externally or self-regulated companies simplify the compliance process and reduce the time and cost of achieving compliance. A strategy of growth and innovation in compliance services has enabled us to:

- Become one of the first to integrate ASTM E1421 FT-IR test methodology into our system performance verification procedures (1996).
- Respond quickly to growing market need for vendor-supplied qualification documentation and services for FT-IR instruments (1999).
- Release the first factory-certified FT-NIR instrument with comprehensive system qualification (2001).
- Develop and deploy network-enabled software for remote management of instrument system security, data integrity and electronic signatures policies required to facilitate 21 CFR Part 11 compliance (2003).
- Acquire a compliance services company and integrate their processes and templates for delivering fully validated systems (2003).

- Deploy the first factory-certified dispersive and FT-Raman instruments with comprehensive system qualification (2005).

Many instrument vendors take a one-size-fits-all approach to compliance – “what’s good for one industry must be good for all.” However, based on our extensive experience with customers in a variety of industries and applications, Thermo Fisher Scientific has taken a unique approach. We offer a portfolio of products and services for all of our molecular spectroscopy instruments (FT-IR, NIR, Raman and UV-Vis systems). This concept allows you to purchase and maintain your spectrometers with the right mix of tools and services for verification, qualification and validation based on:

1. The degree of regulation (high, moderate, or self) over your industry and instrumental measurements.
2. The availability and cost-effectiveness of using your company human resources to perform the necessary compliance-related tasks.
3. The degree of compliance expertise of those human resources in developing, documenting and/or performing these necessary tasks.

The table below will help you assess how Thermo Fisher Scientific’s solutions address your specific compliance needs. The table provides a list of commonly asked questions that everyone in a regulated environment should ask a potential spectrometer vendor.

### Compliance Selection Criteria

### Thermo Fisher Scientific Capability

*Does the vendor have quality controlled and fully documented product development and manufacturing processes?*

All molecular spectroscopy products are developed, manufactured and tested according to specific ISO 9001:2000 certified procedures. The procedures and organizational compliance is reviewed bi-annually by independent auditors such as the British Standards Institution (BSI) and KEMA-Registered Quality, Inc. In addition, self audits are performed regularly to check for continuous adherence to published procedures.

Copies of the ISO-9001:2000 certificates are included in all system qualification documents, and are available upon request or via download from the Thermo Scientific Web site ([www.thermo.com/comply](http://www.thermo.com/comply)).

*Can the vendor adequately demonstrate adherence to its quality procedures, such as maintenance of the design documentation, change control procedures and ongoing support, throughout a product’s lifecycle?*

The Design Qualification documentation provided as part of system qualification packages includes detailed information on how the system’s design and manufacture meets Thermo Fisher Scientific’s standards and procedures for molecular spectroscopy instruments. Some examples include:

- Detailed information on the company’s Product Development Process (PDP) and associated quality procedures.
- Pertinent development project records are maintained as prescribed by the US FDA’s Quality System Regulations documented in 21 CFR Part 820 and are made accessible for inspection by regulatory agencies or customers as needed.
- All reported quality issues, their current status, and date of resolution are formally recorded and tracked.
- All changes to a product’s manufacture or design throughout its lifecycle are managed and documented by a Change Control Notice (CCN) procedure.
- All systems are provided with a declaration of conformity documenting adherence to the pertinent regulations.

*Does the vendor readily respond to compliance questionnaires as well as permit on-site auditing of their quality program and design and manufacturing processes?*

Thermo Fisher Scientific employs individuals specifically tasked with responding to customer quality and compliance questionnaires as well as hosting on-site audits for inspection of documentation, and assessment of practices and procedures for its molecular spectroscopy products.

Completed questionnaires, audit reports and findings are kept on file to aid in ongoing process improvement and to reduce customer time investment for audits from the same company in the future.

*Does the vendor-supplied Installation Qualification (IQ) cover all components of the system (instrument, accessories and software)?*

The system qualification binder includes procedures, checklists and approval documentation that cover the entire system as installed; including every step from unpacking and inspecting the instrument to installing and checking the software and accessories.

For specific system models being installed in highly regulated applications, the system may be supplied with the Thermo Scientific Software IQ tool which automatically compares software files on the installation CD to the files installed on the system computer and generates a report showing pass/fail status.

*How difficult is it to perform the Operational Qualification (OQ) according to the vendor-supplied procedures?*

Detailed, step-by-step instructions for executing the OQ procedures (using the provided traceable reference materials) and checklists for recording and approving the results are included in the system qualification binder.

To streamline the OQ process, the majority of systems are supplied with software which is configured to run the specified test methods for the purchased spectrometer configuration and accessories. This software also provides printable reports for approval signature and insertion into the qualification binder and electronically records the OQ results each time it is executed to provide a complete audit trail.

## Compliance Selection Criteria

## Thermo Fisher Scientific Capability

*How reliable are the test methods and pass/fail criteria in the vendor-supplied Operational Qualification (OQ) procedures in determining actual performance of the system as delivered?*

All OQ test methods are specifically selected to assess the operational characteristics of the system that affect the accuracy and repeatability of a sample measurement (i.e. noise, stability, resolution, wavelength accuracy and photometric linearity). The methods and reference materials are selected from industry accepted standards (i.e. ASTM, European/Japanese/US Pharmacopeias) as well as internally developed methods.

To reliably determine the pass/fail limits, instruments and related accessories are taken directly from the manufacturing line and tested in their delivered configurations using the selected test methods.

During the testing process, system components are reconfigured in a round-robin fashion to randomize any systematic variation and yield data on typical system performance against each test. For those test methods that do not have published or industry-specified pass/fail limits, the test data collected from all systems is statistically analyzed and the limits are set accordingly.

For the majority of systems, the limits are hard-coded into the OQ software provided to enable quick execution of the test methods as well as eliminate the possibility for tampering with the factory-determined values.

*Do the Operational Qualification (OQ) tests and pass/fail limits reflect the performance of the system under measurement conditions that will be used for actual samples?*

Systems configured for transmission measurements are qualified using tests designed for that configuration with pass/fail limits set according to the factory tests. This is accomplished using manual standards, or using an automated testing wheel.

Systems fitted with a qualified sampling accessory, are additionally tested using standard materials designed to work with the accessory. This ensures the qualification reflects the measurement conditions at the sampling-interface. This yields separate factory-set qualification test values and pass fail/limits used specifically when the instrument is configured with the accessory.

*Are the vendor's service engineers trained and certified to perform the system qualification procedures?*

Prior to installing any qualified system, a Thermo Fisher Scientific service engineer must complete multiple levels of training and pass a certification exam.

For each system model they work with, the service engineer must undergo training on standard installation, Installation Qualification and Operational Qualification procedures before they are certified to perform qualified installations. Service engineers are also required to update their training bi-annually to maintain their certification.

*Does the vendor provide factory-certification for the qualification results of their installed systems?*

When you order a molecular spectroscopy instrument from Thermo Fisher Scientific with full qualification as part of the installation, the qualification tests are performed at the factory. Results and data are permanently archived and included with the shipped system.

When the system is installed at your site, a fully trained and certified Thermo Fisher Scientific field service engineer will perform the qualification. Using the factory data as the baseline, the engineer will establish traceability to the factory and record the results in the qualification binder.

A signed Certificate of Qualification is placed in the qualification binder and a System Qualification Badge is affixed to the instrument to indicate the factory-certified status and the date of certification.

Any factory-certified system can be re-certified when it is serviced, moved or the certification expires.

*Is the vendor-supplied system software capable of being fully compliant with the FDA 21 CFR Part 11 rule for Electronic Records and Electronic Signatures?*

No software product can be "21 CFR Part 11 compliant." Compliance is only assured by an organization's practices and procedures with respect to how they allow operators to access their instruments, how they secure their electronic data and their internal policies for acceptance of electronically signed and stored information in lieu of paper records. However, vendor-supplied software must provide features that enable it to be configured to meet this regulation's strict requirements.

All Thermo Scientific molecular spectroscopy instruments are available with software that can be configured according to any organization's electronic records and signatures policies in order to fully comply with 21 CFR Part 11.

*How much effort is involved in configuring the vendor's systems to be complaint with 21 CFR Part 11?*

Instrument application access control and program and signature policies are easily configured within the Thermo Security Administration (TSA) software. Operator policies are controlled according to their company-wide network login ID and password.

TSA software automatically maintains and enforces the operator's access to the instrument, data files and software functions based on their Windows login ID and the assigned permissions. In addition, any actions configured to require operator approval will automatically prompt for an electronic signature.

In organizations with multiple Thermo Scientific molecular spectroscopy instruments, the TSA software can be configured to automatically deploy the policies and procedures to each system over the company's computer network. There is no need to perform additional configurations at the individual instrument workstations. Enforcement of the operator's policies is immediate and automatic, regardless of which instrument on the network the operator accesses.

*Can the vendor supply a complete, customized validation package for their systems?*

The Thermo Fisher Scientific compliance services group is specifically set up to work with customers to achieve full validation for their instruments.

During the quoting process, this group works directly with you and your sales representative to understand your specific regulatory requirements, your internal compliance expertise and capabilities and your planned standard operating procedures for the system and define the scope of the validation solution needed.

To minimize the system commissioning time, the validation services group works directly with you during the purchase and installation phases to extract and compile the necessary information into the templates for the required validation documentation.

When the system is installed, a representative from the validation services group delivers the completed validation package and assists you in completing the documentation and executing the procedures to achieve full validation.

*Does the vendor provide and document the user's training on system and software operation?*

Training is provided during installation of the system and is documented as part of the operational qualification procedures. Supplemental training courses are available at Thermo Fisher Scientific Training Institutes around the world or on site at your facility. Many of these courses are CEU accredited and certificates are provided to document the training.

*In addition to these offices, Thermo Fisher Scientific maintains a network of representative organizations throughout the world.*

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