Documenting Distribution Operations: FDA Validation Beyond the Laboratory and Manufacturing Facility

FDA Validation Beyond the Laboratory and Manufacturing Facility

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Introduction

Has your distribution operation been asked to meet Food and Drug Administration (FDA) validation requirements? Even if your answer is no today, eventually you may be asked to provide the documentation necessary to meet FDA requirements. Most FDA regulated industries focus on the laboratory and manufacturing facilities, however there are specific requirements for distribution and fulfillment facilities. Today's economic and governmental regulatory climate forces everyone to take a second look at their operations and ask: "Does this apply to me?"

FDA validation and Current Good Manufacturing Practice (cGMP) regulations are not on the radar screen of many distribution operations in FDA regulated industries. Generally, an independent internal auditor is assigned to monitor compliance, with the focus being upstream in the manufacturing plant or laboratory. Additionally, it has been more concentrated around pharmaceutical and medical device manufacturers than wholesale distributors or cosmetic and food operations. Still, its impact across all regulated industries will only continue to increase with time, and distribution operations need to account for it sooner rather than later.

The following sections of this paper answer basic questions about the FDA validation process within distribution operations, and it provides examples of how systems and processes coincide to real-life scenarios.

Why bother with the distribution aspect?

The FDA has the right to inspect or audit not only the manufacturing facilities but also the distribution facilities for compliance with cGMPs. An FDA auditor may review the physical aspects of the distribution center (DC) as well as the documentation related to the processes

and procedures performed within the facility. This may include the software systems that facilitate or support the physical processes. Non-compliance with cGMP could result in a letter stating the areas of difficulty and a request to become compliant. If these conditions are not met, the FDA may take additional steps to enforce compliance, including stopping shipments.

Is it a burden or a benefit?

Supporting FDA validation really is not that different from distribution and fulfillment operations and warehouse management system (WMS) best practices, although it does require some additional documentation and controls. It is based on a sound process and system design supported by solid written procedures, testing and training – just like any successful WMS implementation project.

Are you not sure where to start with your new or existing WMS or what is required? Sure you can research the different titles related to FDA validation. But to begin, remember the first topic in the *Code of Federal Regulation (CFR) Title 21:* ***Written Procedures***. In other words, you need documentation – functional area specific, detailed process documentation. The FDA wants assurance that an operation is supported by safe, reliable, and repeatable processes and procedures. This is typically provided via a validation plan that is supported by written procedures, control processes and thorough testing. Some operations may see this as a burden rather than an opportunity to enhance and improve current documentation. More importantly, this provides the foundation for next steps in a well-managed process improvement and WMS implementation project.

What information do I need?

Start by identifying what information is currently available. In many instances this includes documents that are readily available but reside in multiple departments. Therefore, the goal is to bring these together in one central repository for identification and accessibility. This includes, but is not limited to, the following documentation:

- Network Architecture
- System Interfaces/Interconnectivity
- Identification of Operating Systems and Software Applications
- Supplemental Equipment, such as barcode scanning devices, printers, and any material handling equipment (sorters, AS/RS, carousels, etc.)

- Test Scripts for the Software and Material Handling Systems
- Training Documentation
- Procedures

Many enterprise resource planning (ERP), manufacturing resource planning (MRP), and supply chain execution software providers can supply reams of documentation to define how the base system operates, but this material alone does not typically meet FDA validation requirements. Although it is a good start, there is much more to be considered. Vendor documentation tends to state how the system works if it is installed with no changes out of the box and as long as it is operating under optimal conditions. Due to the unique operations of each facility and the many different interconnected systems, site- specific configurations, modifications, and problem resolution procedures need to be addressed separately from the vendor documentation.

What are the FDA qualification components?

Once all available data has been collected, it needs to be separated into appropriate categories based on the type of qualification being met. There are three main qualification categories to fulfill for FDA validation. They are:

1. **Installation Qualification (IQ)** – Verifies that the system is installed correctly. This includes hardware, software, equipment, etc. (i.e., system administration guides and databases).
2. **Operational Qualification (OQ)** – Verifies that the components of a system are operating as they are designed (i.e., test scripts, training documentation, and standard operating procedures).
3. **Performance Qualification (PQ)** – Verifies that the full system works as it is designed (i.e., interface design and integration testing).

Once the initial collection of documented data is completed and sorted by qualification type, a thorough examination is performed to determine what additional information is required. From a distribution center perspective, the focus is primarily on the second component, OQ. This includes vendor documentation for any software systems, the testing of those systems, training, and operational procedures for the distribution operations and systems.

- **Vendor Documentation:** This is any documentation provided by the software vendor that is related to the use of the application, but it only goes so far to meet validation requirements. There are also procedural processes separate from the systematic processes that need to be defined.
- **Systems Testing:** Each operation is unique in its functionality and requirements. Therefore, both the positive test scenarios and any possible negative test scenarios

must be considered and documented. Companies must also be able to prove that failed test scenarios have been tested again and resolved.
- **Training:** All associates working in the DC or associated with the distribution operations need to be trained. Do not limit training to system operations, but include the overall process. Also collect signed attendance records to provide proof that training has been performed.
- **Operational Procedures:** Sometimes referred to as standard operating procedures (SOPs). This is the written definition of what is to happen under normal and exception (negative test conditions) operations. It includes not only the system application but also the manual processes that are to be followed.

Do e-records and e-signatures apply to me?

If your company/operation is subject to Part 11 of Title 21, then, yes, e-records and e-signatures apply to you. As part of regulatory requirements, the document *Guidance for Industry 21 CFR Title 11; Electronic Records; Electronic Signatures Validation* references that "[persons] employ procedures and control designed to ensure the authenticity, integrity, and, when appropriate, the confidentiality of electronic records, and to ensure that the signer cannot readily repudiate the signed record as not genuine."

This applies to manual and electronic signatures. Therefore, similar testing, training and documentation are necessary. However, system application testing is only one part of the electronic record keeping. There is the maintenance, archival, and security of the signatures. This includes the ability to ensure a signature is authentic, which may mean additional processes to ensure users are not sharing their usernames and passwords. It could also mean that operators re-enter their usernames and passwords each time certain functions are performed rather than just when the user initially logs into the system.

When do I validate my system and update my documentation?

There is no cut and dry answer to this question. First, the FDA publication *General Principles of Software Validation; Final Guidance for Industry and Staff* references "medical equipment." However, in practice, this is extended much further than just medical equipment and devices. In essence, this FDA publication states that when new software is introduced or existing software is updated, it is time to create or update the documentation. But, there is no reference to any kind of time limit for creating the validation documentation.

Second, *CFR Title 21 parts 211.142 and 211.150* reference providing written documentation as related to warehousing and distribution operations respectively. Again, no timeline is identified. However, additional information is provided as to what specifically needs to be documented. Therefore, documentation can be created at any time, but most organizations find that it is easier and more beneficial to other aspects of the business if the

documentation is written and/or updated as changes are implemented rather than after.

Furthermore, anyone who has written test scripts or SOPs knows that although it may sound easy, the execution is actually difficult and time consuming. In an existing application, operational procedures may have changed since the implementation. Additional modifications may have been made but not documented. However, with a new implementation, all of the documentation must be created from scratch (or near scratch) and maintained. Even then, the normal life-cycle of an implementation can make unexpected twists and turns. Teams can become so overwhelmed with the day-to-day tasks that documentation becomes secondary to accomplishing the actual testing.

The complexity of your application also has a bearing on the FDA validation process. Each and every process or procedure within the facility is to be documented under normal circumstances and worst case scenarios (positive and negative test conditions). In this way, any unexpected elements can be addressed prior to the actual occurrence and procedures put in place to handle the situation.

Summary

The FDA is not asking that every process and every piece of WMS functionality be covered by a validation plan, only the components that impact the safety and reliability of the overall operation. Organizations are encouraged to perform a risk assessment so that they can concentrate on efforts where they are really needed.

Many organizations look at regulatory compliance merely as a cost of doing business. This is not restricted to the life sciences. Consider Sarbanes-Oxley, IATA/DOT hazardous shipping requirements, country of origin / denied trade screening – sometimes distribution seems more about producing paper and electronic records than shipping product. Add the inevitability of electronic pedigrees and product serialization to the mix and it is easy to throw our hands into the air. But the answer is not about getting around all these requirements with the least amount of trouble or creating a regime dedicated to compliance for the sake of compliance. It is about building safe, reliable and efficient supply chain operations.

About Tompkins Associates

Tompkins Associates designs and integrates global end-to-end solutions for companies that embrace supply chain excellence. For more than 30 years, Tompkins has evolved with the marketplace to become the leading provider of global supply chain services, distribution operations consulting, technology implementation, material handling integration, and benchmarking and best practices. The company is headquartered in Raleigh, NC. For more information, visit www.tompkinsinc.com.

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