

Computer Systems Validation



COMPUTER SYSTEMS VALIDATION: A PRIMER

Definitions, FDA Guidelines, and Frequent Questions Answered.



Overview	3
What is Validation?	4
What about the FDA?	5
What should be validated?	6
Validation Activities	7
SaaS Considerations	9
Final thoughts	10

Overview

Computer Systems Validation is an activity that presents complex challenges to the life sciences community. Conflicting and, in some cases, minimal details and insight from the FDA have caused confusion within the industry. Industry standards such as GAMP 4 and GAMP 5 have emerged, but questions regarding validation continue. When is validation required? What should be included in the scope of validation? How can risk based validations be performed? What about validation of Software as a Service (SaaS) solutions? Do solutions that are indicated as “pre-validated” by a vendor still need to be validated? These and similar questions occur frequently during compliance conversations within the industry. This white paper will define validation, identify what the FDA says about validation, and answer frequent questions raised around the topic.

What is Validation?

Title 21 CFR Part 11 requires: “Validation of systems to ensure accuracy, reliability, consistent intended performance, and the ability to discern invalid or altered records.”¹

Validation is confirmation by examination and provision of objective (documented) evidence that computer systems conform to user needs and intended uses, requirements are consistently fulfilled, and applicable regulatory requirements (such as 21 CFR Part 203, 21 CFR Part 820, etc.) are satisfied.

Validation, at its most basic level, is the process of ensuring that applications, systems, solutions, and/or environments satisfy intended functionality in a consistent and reliable manner. Primarily, validation is accomplished via software testing – the process of executing a predefined sequence of steps, emulating typical user scenarios and data, to determine if the application, system, solution, and/or environment under evaluation performs as intended. Validation includes verifying:

- Requirements of the system are met (both regulatory and business),
- System performance (speed and accessibility) is acceptable, and
- Data integrity is properly maintained (not lost, improperly modified, etc.).

The primary benefit of validation is a level of assurance that the system will perform as required and intended during operation. A validated system should be more cost effective to maintain, yield greater Return on Investment (ROI), and result in reduced risk of data loss and issues with regulatory requirements.

¹. U.S. Department of Health and Human Services. Food and Drug Administration. Federal Register, Volume 62, Number 54. *21 CFR Part 11 – Electronic Records, Electronic Signatures, Final Rule*. March 20, 1997: 13465.

What about the FDA?

The FDA continues to review and confirm that companies are taking steps to comply with 21 CFR Part 11 requirements, including the requirement for Computer Systems Validation. For example, FDA's Prescription Drug and Marketing (PDMA) inspections have included questions around an organization's approach to the validation requirement, indicating that technically comprehensive validations should continue to be pursued and documented thoroughly. Further, critical to the premise of 21 CFR Part 11 is the requirement that appropriate measures must be taken to ensure the availability and integrity of electronic records and signatures. Validation is a component of Part 11 that helps ensure software systems can manage, maintain, and produce copies of electronic records at all times.

What should be validated?

At a minimum, any electronic system that is used to assist an organization in meeting an FDA requirement should be validated. This includes the requirements defined by:

- 21 CFR Part 203 (PDMA)
- 21 CFR Parts 210/211 (GMP)
- 21 CFR Part 312, etc. (GCP)
- 21 CFR Part 820, etc. (QSR)

For example, 21 CFR Part 203 requires specific entries to be present on a sample request form (name, address, professional title, quantity requested, etc.). If an electronic system is utilized by a pharmaceutical sales representative to meet this Part 203 requirement, then 21 CFR Part 11 (and thus validation) applies. Similarly, alternate sampling channels, including web-based electronic sample requests systems, must also be validated.

Commercial Off-the-Shelf (COTS) software used in electronic record keeping subject to Part 11 (such as Customer Relationship Management [CRM], Sales Force Automation [SFA], and Home Office Sample Management systems) should be validated. The FDA has previously indicated that commercial availability alone typically does not indicate the system is “validated” as commercial vendors may not confirm regulatory specific attributes – particularly attributes that are not also business requirements – and commercial vendors typically do not assert system suitability from a compliance standpoint (although some do).

Complicating matters for vendor acquired solutions is that the true validation status of a system or application acquired from an outside vendor can at times be difficult to ascertain, as terms such as “pre-validated,” “validated out-of-the-box,” “validation ready,” etc. are becoming more prevalent. In general, these claims from vendors should be scrutinized to ensure whatever level of validation or pre-validation has occurred is consistent with the FDA’s requirements for Computer Systems Validation. The FDA expects the final, deployed version of the solution to be validated (meaning any custom changes in regulated areas likely will require further validation), and the FDA will not take stock in a vendor’s claim of validation alone – the FDA expects the acquirer to confirm that the solution is in fact validated. While there are vendors that have a sound approach to “pre-validating” their solutions (and for these vendors the pre-validation represents true cost savings and benefits to their customers), a confirmation of suitability of the “pre-validation” process should be formally accomplished and documented by the organization acquiring the system or solution.

Regardless, it is incumbent on those with systems subject to FDA’s Part 11 requirements to ensure validation of their systems – commercial Off-the-Shelf solutions, internally developed systems, and others – to avoid potential FDA action.

Validation Activities

Validation can be segmented into a series of distinct activities, all of which require thorough documentation capturing the plan, execution, and results of the validation effort.

A typical validation effort should include:

- Risk Assessment / Risk Management: FDA and others are actively embracing the advantages of a “risk based” approach to validation. A formalized risk assessment can guide the scope of the entire validation effort, strategically targeting more intensive testing in highly regulated or high risk areas while minimizing testing in lower risk areas. A risk based approach also affords the opportunity for potentially significant cost savings since comprehensive validation test coverage may be minimized or eliminated in low risk areas of the application.
- Validation Planning: A Validation Plan is developed to establish the “game plan” for the validation effort. Testing methodology and processes are highlighted, individual phases of testing are described, results reporting is discussed, and critical milestones and dependencies are identified. The Validation Plan guides the entire validation effort and should be completed prior to the start of the actual testing activities.
- Installation Qualifications (IQ): Execution of a predefined series of steps that demonstrate the system is properly installed and ready for production usage.
- Operational Qualifications (OQ): Execution of a predefined series of steps, emulating typical user scenarios, that demonstrate the system meets all applicable functional and regulatory requirements (appropriate screens are displayed, data can be entered and manipulated, data integrity is maintained, etc.).
- Performance Qualifications (PQ): Execution of a predefined series of steps that demonstrate the system performs consistently within required benchmarks for availability and throughput. The PQ frequently follows a “system test” approach where a “day in the life” of the user is emulated to ensure all functionality is suitable.
- Validation Reporting: One or more Validation Reports are developed summarizing the results of the validation effort. All testing results are reported, including system deficiencies (issues with the system), regulatory implications, and recommended actions. An overall statement indicating whether the system under evaluation can be considered validated for usage or not is also included.

The time and resource commitment to accomplish a typical Computer System Validation can be a major challenge to an organization attempting to perform validation work in house as validations can vary widely, depending on the size and scope of the system, the degree to which the system is used to satisfy regulatory requirements, etc. It is not uncommon for a full Computer System Validation to require at least 6-8 weeks of effort – and sometimes longer – with a minimum of 3-4 resources. The necessary high regulatory and testing skill set needed for validation resources,

coupled with the infrequent manner in which validations occur, can make validation an ideal candidate for outsourcing to a third party vendor that specializes in efficient validation executions. Outsourcing validation can be more cost effective for an organization and it can yield a higher confidence that the validation executions are efficient and in compliance with FDA expectations. A key to any potential decision to outsource validation includes properly screening potential validation vendor(s) and asking questions, such as do they have regulatory compliant approaches to validation, have they “passed” FDA PDMA inspections, etc.

SaaS Considerations

SaaS solutions are becoming more prevalent in industry today. These solutions – which may support multiple customers/tenants, may be subject to more frequent functionality changes, may include robust tool sets that allow customer’s to configure aspects of their applications “on the fly,” etc. – present additional challenges to ensuring that the system at all times stays fully validated. SaaS solutions should still be validated by the vendor, the customer, or an outside firm. Evidence of validation testing coverage to confirm appropriate segmentation of multiple customers’ data sets (if applicable) should be included. In addition, periodic validation of the SaaS solution (revalidation) should occur as baseline software changes are made – particularly when regulated areas are impacted. Lastly, if tools are available within the SaaS solution that allow the customer or others to change application functionally – particularly in regulated areas – the tools themselves should also be included in the validation testing scope. In addition, appropriate warnings – either in the application itself or in outside documentation – should be available to the users of the tools that will warn them or prevent them from changing functionality that will take the solution out of a validated status.

Final thoughts

Validation is a critical activity that should be pursued and formally documented for all systems with regulatory implications. Validation activities provide the controlled testing conditions necessary to ensure proactive identification and resolution of operational, fiscal, and regulatory issues.

Validation can be a complex challenge for an organization; however, a clear consistent approach to achieving validated systems can ensure significant ROI for the system under test and can ensure regulatory compliance is consistently maintained.



Contact Cegedim Dendrite today for more information.

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