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Incloud Validation
- Trial on Life Science Regulation

White Paper

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Abstract

The validation of the cloud based solution for a life science domain is highly challenging as it involves following software development life cycle along with regulatory guidelines and satisfying "Good Manufacturing Practices". The product considered for validation is a Learning Management System and its service is based on the SaaS model. Since it is cloud based product and is used as a service from the vendor, there is not much availability on the background of the product to the client. The validation responsibilities are also split between the vendor and client. Considering the minimal availability of details and adherence to the regulatory guidelines, the validation activity discussed in this paper delivers an effective knowledge on reducing the validation timelines and using a quality product. This validation process discussed here certainly stands out as a best practice and reference for the testers who are involved in similar testing activities.

Introduction

Cloud computing adoption is growing at steady pace. Leading information technology research company Gartner says by 2020, a Corporate "No-Cloud" Policy Will Be as Rare as a "No-Internet" Policy Is Today. More and more organizations are moving their storage, services, product and collaboration to the cloud. This technology is one of the most disruptive forces of IT spending, which will have effects directly and indirectly to the organizations. Cloud computing is mainly suitable for organizations which are in need of a convenient model which is accessed on demand with less management effort. Cloud computing has four key technological elements such as High speed access, Data centers, Storage and Virtualization through which the consideration will happen. The amount spent on IT is accelerating from traditional IT offerings to smarter cloud computing. The Cloud computing model has been categorized into various models (Service Models – SaaS, PaaS and IaaS; Deployment Models - Public Cloud, Private Cloud, Hybrid Cloud and Community Cloud) The graphic representation below shows the usage of cloud by the industries and the pattern of how the shift is happening over the last two years.

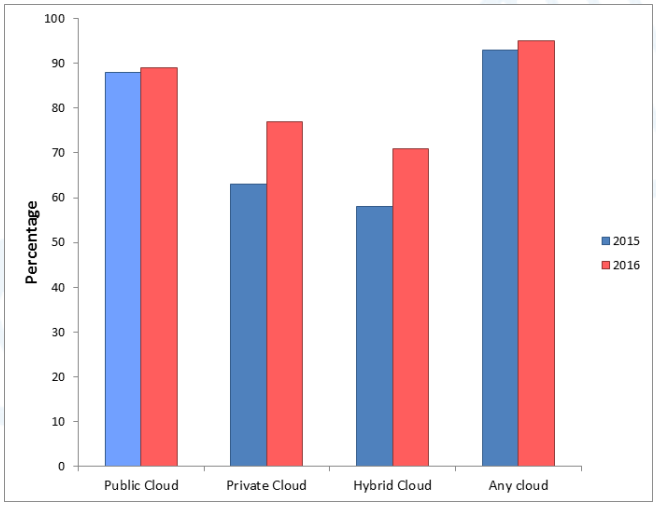


Fig 1: Cloud usage (Source: Right Scale 2016 State of the Cloud Report)

Challenges – Life Sciences and Cloud

The main challenge in cloud computing is on the security, control and compliance. According to a survey, there are few other challenges related to cloud systems. The risks that are associated with the cloud computing requires assessment and mitigation to overcome the challenges. Below is the chart representing various challenges that industries faced in the year 2016.

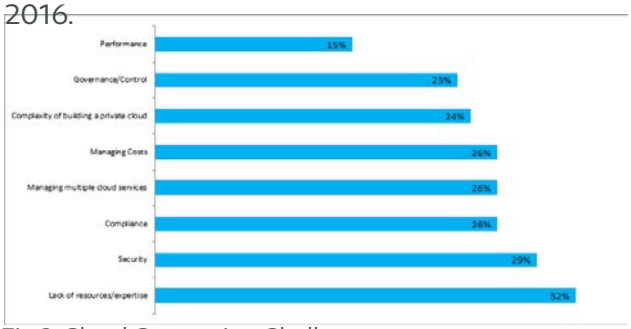


Fig 2: Cloud Computing Challenges
(Source: Right Scale 2016 State of the Cloud Report)

Research and Development is the key and expansive area when it comes to life science domain, along with many other phases like long product development, approvals, patent, marketing and many more. There are a lot of areas where cloud computing can bring in improvements and speed up the processes. Life Sciences need application based solutions in the fields of Analytics, Infrastructure, Manufacturing, Marketing, Data Management, Sales, Safety, etc. Cloud adaptation reduces the IT costs and complexities which allow the organization to focus on other process and thus creating a more flexible operating model. The main benefits for industries in moving to cloud solution are reducing the risk, improving operation efficiency and compliance.

What does cloud specially offer to the life science domain?

- Pre validation already done in platforms, functions and configurations.
- Avoids complications in customization and configuring systems.
- Less validation effort.
- Regulatory compliance covered.

Testing Challenges in Life Sciences

Validation on cloud for Life Sciences has lot of challenges unlike the regular testing done for other domains. In cloud validation, analysis should be done to understand what type of cloud service (PaaS, IaaS and SaaS) is opted by the organization. Depending upon the service, the controls under cloud infrastructure are considered for validation from the client's end. The validation team should develop a strategy and process for validation such that it is as per the major regulatory guidelines and verify the product is falling under the Good Manufacturing Practice (GMP).
There are several critical documents that should be created and maintained as a part of the overall validation package. This is termed critical because the documents will be reviewed by the FDA and other global regulatory agencies when audited.

Three main questions should be answered as a part of Installation Qualification (IQ), Operational Qualification (OQ) and Performance Qualification (PQ).

- Is the system installed correctly?
- Is the system operating correctly?
- Is the system performing correctly to meet the stated user requirements?

To prove that the system is validated as per the guidelines, each individual item under the IQ, OQ and PQ phase must be tested thoroughly, proper evidences should be captured, each procedure must be documented and signed.

Software Testing vs Validation

Testing basically focusses on finding and destroying the mission whereas validation goes further with adding quality into it. Validation follows rigorous documentation processes which is forced by FDA going by the term "If you didn't document it, you didn't do it". Validation doubles the schedule and other process comparing to the project done without validation. Three major focus area of validation are Quality, Regulatory affairs and Legal. To put it simply, Validation is double the effort of the Software testing.

Process

The process of validation carried out for this case study involves shared responsibility between client and the vendor. The V model outline represented below helps to understand how the responsibility is shared and what the client focus area is during the validation process. Unlike the regular software testing process, this validation process requires more attention and many references are not available to follow. Validation according to the FDA means establishing documented evidences, a need of high degree of assurance in system quality and system must behave consistent following the standards.

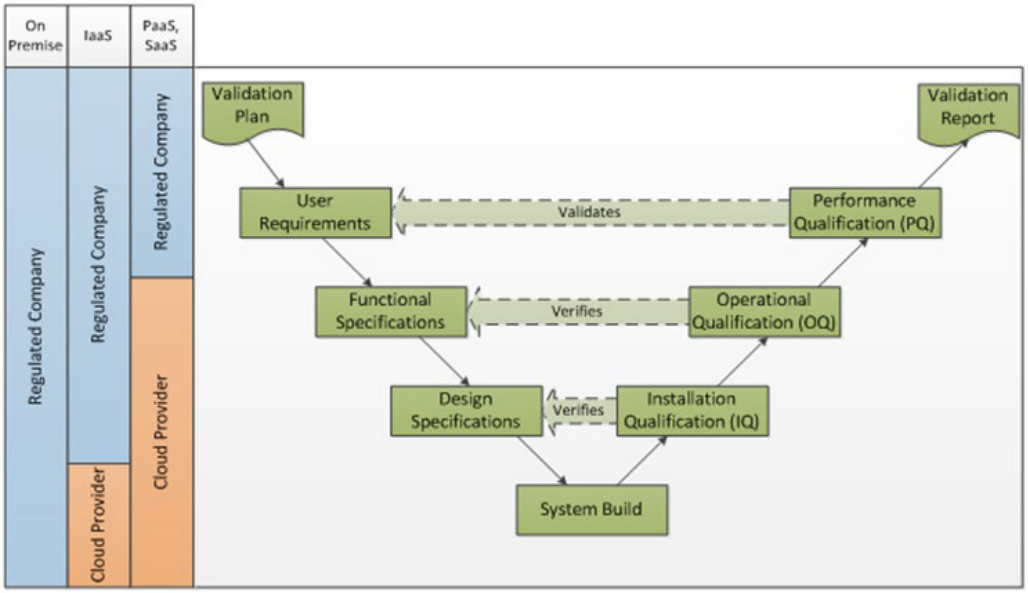


Fig 3: Validation work flow

Fig 4: Validation framework

Validation Plan

There is no specific format of Validation Master Plan (VMP) followed throughout the industry practice or framed by the FDA. But there should be certain requirements that should be met in a VMP. It should include what will and what will not be added for the validation process because of using cloud computing. Considering the SaaS cloud model, things such as training records, change control, security procedures and Audits should be added to the plan. Below are some of the must have items.

- Validation Activities - prospective, concurrent and retrospective
- References to documents - Policies, SOP's, Protocols and Reports
- Authorization from Management – List of personnel with roles and responsibilities
- Scope of operations - Details on facilities, processes and products
- List of relevant validation documents
- General Acceptance criteria

The VMP must include clear details on the deliverables that is to be generated in the validation process, timelines for completing each qualification phases, Individuals participating, Acceptance criteria for meeting requirements and details on validating the compliances as per regulatory guidelines and good manufacturing practices.

Risk Assessment

Performing a risk assessment for cloud based solutions are quite challenging where lots of effort is needed for analyzing the background of the product and the model used for implementing it. Some of the components to be considered while assessing the risk are Business, security, location, performance, regulatory compliance and change management.

Below are the risks that were considered for the product specified in the case study. Each risk is clearly analyzed and depending upon the severity, suitable mitigations are proposed.

- Business Risk – Data lock-in, Application lock-in
- Security Risk - Data Confidentiality and integrity, Data disposal, Data backup, Data viability, Privileged user access
- Resilience Risks - Continuity Management
- Performance Risks - Network Failure
- Regulatory Compliance Risk - Regulation and legislation
- Organizational Risk - Change Management
- Application Risks - Roles and responsibility configuration, Certificate Management, Auditing and tracking, Reports, Import & Export, Scalability & Configurable solution

Installation Qualification

In the Installation Qualification (IQ) phase, verification of proper installation and system configuration are performed. This mainly evaluates the means of accommodating the new product and testing it completely for acceptance. In this case study, the product is a SaaS model and hence the IQ phase is the responsibility of the vendor. But the client is still expected to understand the Installation processes and make sure all the necessary documents are available. In the IQ phase, details on the Compliance and Infrastructure Management, Release Management and Security Enforcement are to be shared with the client. Knowing these details is very essential in answering the queries raised by the regulatory organizations.

With reference to the auditing in the vendor's end and the availability of IQ reference documents, the IQ phase is considered to be completed. The reference documents are available with the vendor and should be submitted during audit. The details of the documents are shared with the client helping them in easier in answering the FDA Audit.

Operational Qualification

The Operational Qualification (OQ) phase starts with the successful completion of Installation Qualification. A protocol which specifies the plan for this phase is drafted with necessary details. This protocol should be approved by the owner of the document and Quality Assurance. An unexecuted copy of this protocol should be readily available in the validation package. The Functional requirement specification serves as the blue print for the OQ test design. Each functional requirement is analyzed well, test scenarios are identified and against each scenario, test cases are written. The overall test coverage must be ensured while designing the test cases. If the application requires testing with multiple roles, then each of it must be tested individually while considering the respective functionality. Every step used in OQ validation includes an instruction to perform, an expected result and the actual result. Any deviations observed during this process is also captured and raised as defects. The Dev team works on the defects and further before completion of the OQ phase all the defects should be resolved.

The main challenge in this phase is that each and every test step must be captured as evidence and must be made available with the validation package which is more time consuming for the validation team. Since this is the most important phase of the validation, more efforts are spent during this phase.

In a SaaS based model, usually the vendor is responsible for the Operational Qualification. But it is always better that the client validates at their end ensuring all the functionalities are working as intended and all necessary documents are available for Audit.

After the successful completion of the OQ phase, the trial at the user end is necessary. The UAT is termed as performance Qualification where the product is put to final test.

Performance Qualification

In this stage of validation, the system is intended to be tested at the user end to verify whether all the user requirements are working as expected. The User Requirement Specification serves as the key behind this process. Some of the main scope of the performance qualification is:

- Verifying whether there is no system lag is observed multiple user access
- Performance of the application on producing large quantities of data and queries
- Workflow is correct and working as expected without affecting each other
- System works as per the requirement and processes within the specified limits

In the Quality perspective, the performance qualification is important in implementing the system to the real users. The successful completion of PQ phase establishes the confidence on the finished product satisfying all the essentials the project requires.

Regulation Guidelines – 21 CFR Part 11

In this phase of validation, the application is validated to prove that it is developed as per the regulation guidelines framed by the FDA. It ensures that the electronic records and electronic signatures in the application are considered trustworthy, reliable, and equivalent to paper records. As a part of this validation phase, the following activities were performed.

- Identify the relevant portions of the regulations applicable to application
- Design the 21 CFR Part 11 Checklist
- Design and execute 21 CFR Part 11 test scripts
- Generate Test Evidences

Clause Category
11.10 - Controls for closed systems
11.50 - Signature manifestations
11.70 - Signature/record linking
11.100 - Electronic Signature General requirements
11.200 - Electronic signature components and controls
11.300 - Controls for identification codes/passwords

Table 1: 21 CFR Part 11 Clauses

Auditing the Vendor

In order to maintain the quality of the software, an audit should be conducted at the vendor's location at regular intervals. The client validation team's responsibility is to understand the design, development, testing and maintenance of the application at their end. In addition to getting familiarize with basics of life cycle, reviewing of the QA documentation, project files, security procedures should be typically reviewed. The client should ensure that the vendor is following a good standard practice which demonstrates effective planning, operation and controlling in all process and documentation.

Validation Summary Report

This report summarizes all the activities performed under validation with results. This document is created, reviewed and approved by individuals responsible for the respective actions. In Life sciences companies specific SOP's for validation process, coverage of validation package, roles and responsibility of individuals are maintained. Along with this the procedures for controlling documents, change management, auditing procedures and access controls are carried out. It can also suggest recommendation and activities that are to be performed in the future.

Case Study

The case study to be discussed here is for validating a cloud based solution for a leading pharmaceuticals company. As it is in line with the life sciences industry, testing within the regulatory validation guidelines is the most important aspect of the story.

The success of the story is to be uncovered further with interesting notes and data points.

Background

Organization	Biopharmaceutical Company
Domain	Life Sciences
Product Type	Learning Management System
Service Model	Software -as -a-Service (SaaS)
Cloud Type	Private
Team Size	2
Duration	60 Days
Regulation	FDA

Table 2: Case Study background

The scope of this assignment is to validate the Learning Management system and being a SaaS based application, the vendor and the client are responsible for splitting the validation efforts. Both vendor and the client validation teams should make sure that the necessary documents are available for audit. Below is the list of responsibilities that was considered during the validation activity.

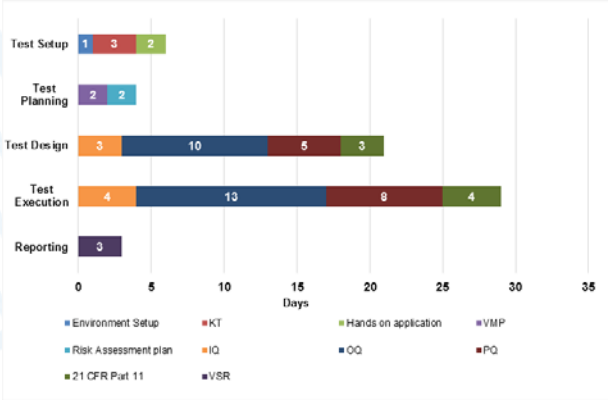


Fig 5: Project plan

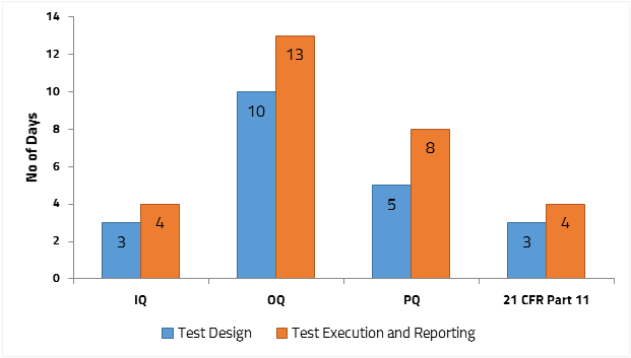
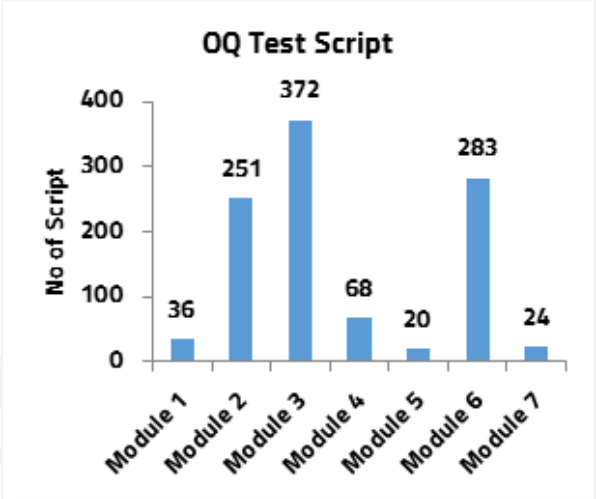


Fig 6: Effort across each qualification phases

In the case study, around 38% of effort was spent during the OQ phase. All defects were captured in a defect management tool and resolved in coordination with the development team. Around 75 defects were submitted with severity classification as Critical, High, Medium and Low.



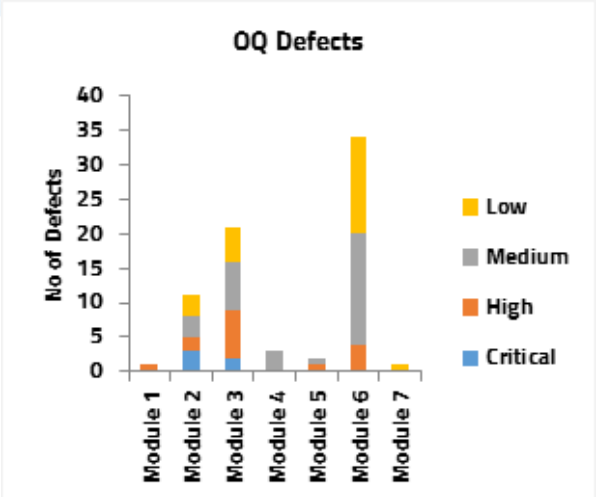


Fig 7: OQ Test Script and Defects

In the PQ phase, end users from various departments inside the organizations are invited and using the PQ test scripts written based on the User requirement are executed. As a part of execution, separate credentials were also created with specific roles and responsibilities for easy tracking and documentation. At the end of the PQ phase, the validation team ensures that no open defects were present while testing

the product against regulatory guidelines, a 21 CFR Part 11 check list was created and with this as a baseline, test scripts were written. A total of 57 test scripts were written and tested to prove that the product is developed and maintained as per the FDA guidelines.

Clause Category	Total Number of Scripts
11.10 - Controls for closed systems	35
11.50 - Signature manifestations	2
11.70 - Signature/record linking	1
11.100 – Electronic Signature General requirements	5
11.200 - Electronic signature components and controls	7
11.300 - Controls for identification codes/passwords	7

Table 3: 21 CFR Part 11 Test Script details

Finally the validation summary report was prepared with complete results and recommendations on the product. The validation framework showcases that the entire validation process is successful by reducing the testing effort with shared responsibility and delivering a quality product satisfying the organization.

Summary

Validation of the SaaS model has considerable restrictions and challenges while comparing it with the other models. But it potentially reduces the validation effort if planned and executed correctly. It certainly lowers the costs spent by the life science organization if the coordination is smooth between the validation team of the client and vendor. The primary focus of the Client should be more on understanding the details of the product background and making sure the necessary documents are maintained by the vendor which should fit within the regulatory guidelines and good manufacturing practices. The next most important element to be taken into consideration is the developing an efficient User Requirement Specification and the validation plan which is the heart of the validation process. The shared responsibility between the client and vendor as explained in the paper benefits the organization on spending less time in validation and using a quality product.

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