COMPUTER SYSTEM VALIDATION IN PHARMACEUTICAL INDUSTRY

Swarupa Vijay Jadhav[1], Swamini Subhash Waghchaure[2], Dr. S. Z. Chemate[3].

Dr. Vithalrao Vikhe Patil Foundation's college of Pharmacy, Ahmednagar

Abstract:

Computer Systems Validation (CSV) is a procedure used to secure (and document) that a computer based systems will produce information or data that meet a synchronize defined requirements. If a system match these requirements, it can be accept that it is consistently presenting in the way it was intended. Quality is an critical for customers whenever they consider a product or service. It is also major as it relates to life-saving products such as pharmaceuticals. In this consider, the Food and Drug Administration introduced good manufacturing practice (GMP) to maintain and better the quality of pharmaceutical products. GMP ensures that products are continually produced and controlled according to the quality standards suitable to the intended use and as required by the marketing approval. One of the major GMP requirements is that all of the critical manufacturing equipment, utilities, and facilities in the pharmaceutical industries must be properly certified and validated ultimely to production. Currently, this practice forms the key of the regulations that are strictly followed by pharmaceutical companies worldwide. A validation judgement is a necessity in the pharma industry to ensure attachment to pharmaceutical cGMP guidelines, and to help companies maintain consistent quality. The same principles are applied in computer system validation to a computer system or an information technology system. It's important to maintain quality standards in pharma since non-conformance can have far-reaching consequences. Computer system validation checks the effectiveness and the efficiency with which the system is meeting the purpose for which it was designed. This study aims to identify needs of computer system validation of instrument/equipment practiced in the perspective of pharmaceutical industry.

Keywords: Computer system validation, Validation, Qualification, GAMP

Introduction

Computer system validation is the documented process assuring that computer based system will produce information or data that meets a set of predefined requirement. Validating computerized systems that help to improve handling complications and system performance in pharmaceutical companies and medical devices.

The main purpose of computer system validation is that to assure accuracy, consistency, reliability and consistency performance of the system in accordance with predetermined specifications. Computer system validation play important role in pharmaceutical industry to improve product quality, to accelerate performance of process, and support for high quality product. The major benefit of validation c computer system is that supporting the quality controls to ensure that the process is followed correctly, to reduce manual error. European Medicines Agency (EMA) and Food and Drug Administration (FDA) both produced guidelines for csv Practices.

In pharmaceutical industry, computer system validation is an unique process that maximize the effectiveness and enhance quality. Computer system validation save cost as well as time.

There are different industries like pharmaceutical, cosmetics, food and beverage that are regulate by Food Drug Administration (FDA). This industries have responsibility to ensure their products are safe and data are secure. Computer system validation in United States comes from the code of Federal Regulations (CFR), most specifically 21CFR Part 11 dealing with electronic record and signatures.

Software validation is part of computer system validation. Any computerized system include software, hardware and other devices which are important for proper functioning of the system.

Computer system is directly affect the quality of pharmaceutical and medical device product and should be checked to GMP and GAMP principles and standards.

If any defect in system that may cause data integrity. Computer system validation find out time to time error Flaws and mistakes (software bugs).

Need of Computer System Validation in pharmaceutical Companies

The need of computer system validation in pharmaceutical industry should be safe for distribution and sale. Computer system validation is one of those observance requirements and it is also part of quality management system in pharmaceutical manufacturing.

Computer system validation deliver accuracy, security, reliability and consistency to pharmaceutical industry.

COMMON COMPUTER SYSTEM VALIDATION PROBLEMS

Computer System Validation (CSV) in the life sciences was focused on software validation and infrastructure and computing platform qualification for systems that supported FDA-regulated activities and records. Today, organizations are increasingly focusing on overall, global IT compliance, to satisfy 21 CFR Part 11 but also equivalent laws in other countries, Sarbanes-Oxley (SOx), HIPAA, export and shipping regulations, and much more. To meet

these varied and global needs, pharmaceutical manufacturers must:

Challenge I. Standards: Various standards exist across the organization. Policies, plan of action, work instructions, and layout vary by business, department, or site. Remarkable costs result from overlying SOPs and incompatible standards, which make sharing of assets difficult. Industry-wide standard methodologies, guidelines, and tools have been issued by global organizations, such as ISPE and ICH, but in order to make the assets applicable to a wide range of companies, processes, systems, and products, they did not replace the more detailed, localized standards

Challenge II. Interpretation: A significant cost to validation projects is caused by long debates among the various authors and reviewers, rework, and inconsistent interpretation of standards and requirements. Most regulations include very high-level statements that set objectives, but don't specify how to implement the controls or how much is good enough. For example, 21 CFR Part 11 (11.10 (d)) requires "Limiting system access to authorized individuals." This one statement can be expanded to varied requirements for technical security controls and procedural controls for managing access.

Challenge III. Organization and Governance: Many companies still have decentralized governance and uncontrolled execution. The ownership and management of validation activities vary from project to project and from one department to another. Projects are not handled consistently with clear roles and responsibilities. Some are led by IT, other by users or quality.

Challenge IV. Efficiency Across Sites and Departments: Site-to-site efficiencies have not been achieved due to site- and department-specific procedures, templates, and interpretation. We've seen many cases where multiple sites develop complete validation packages for the same system that they use the same way, because there is no sharing of inventory and project information.

Challenge V. Execution: As stated earlier, we see excessive rework being done by validation teams. Most often, the rework is a result of different opinions and styles of project team members and inconsistent quality of work that is done by unqualified individuals. A common scenario is that individuals perform work that doesn't align with their level and skills. Junior quality reviewers, who are qualified to review documents and identify incomplete or inaccurate information and deviations from standards, end up determining the course of action to remediate the problems. The solution is often redoing the work. On the other hand, we see highly-

qualified, expensive resources performing low-level mechanical tasks, because a fixed team is assigned to the project and must share the workload.

Challenge VI. Tools: System life cycle assets, such as templates, outlines, forms, and guidance documents are often inconsistent across departments and are not targeted to drive value. They are put in place to minimize the risk of project team members taking shortcuts and skipping sections, but are not flexible and drive unnecessary efforts with minimal value to quality or compliance. We've seen cases where an extensive validation package was prepared for a new CD writer, or complete detailed Installation Qualification protocol, scripts, and report were produced for the installation of utilities such as WinZip and virus
scan.

Challenge VII. Training: Training is usually conducted within each business on standards and processes; however, there is minimal coaching and guidance. The short training that is usually provided is rarely enough to qualify individuals without coaching and support until they gain hands-on experience. Often multiple training sessions have to be taken in a very short period of time, where the individual's ability to absorb, understand and retain the materials is in question.

Challenge VIII. Personnel: Working with many life science companies shows that usually there are capable, knowledgeable central validation groups, but weaker decentralized execution groups. CSV standards are often deployed without the appropriate training and coaching and without assurance of consistent interpretation. Organizations believe that simply reading standard operating procedures (SOPs) and receiving a few hours of training enable individuals to follow a consistent approach
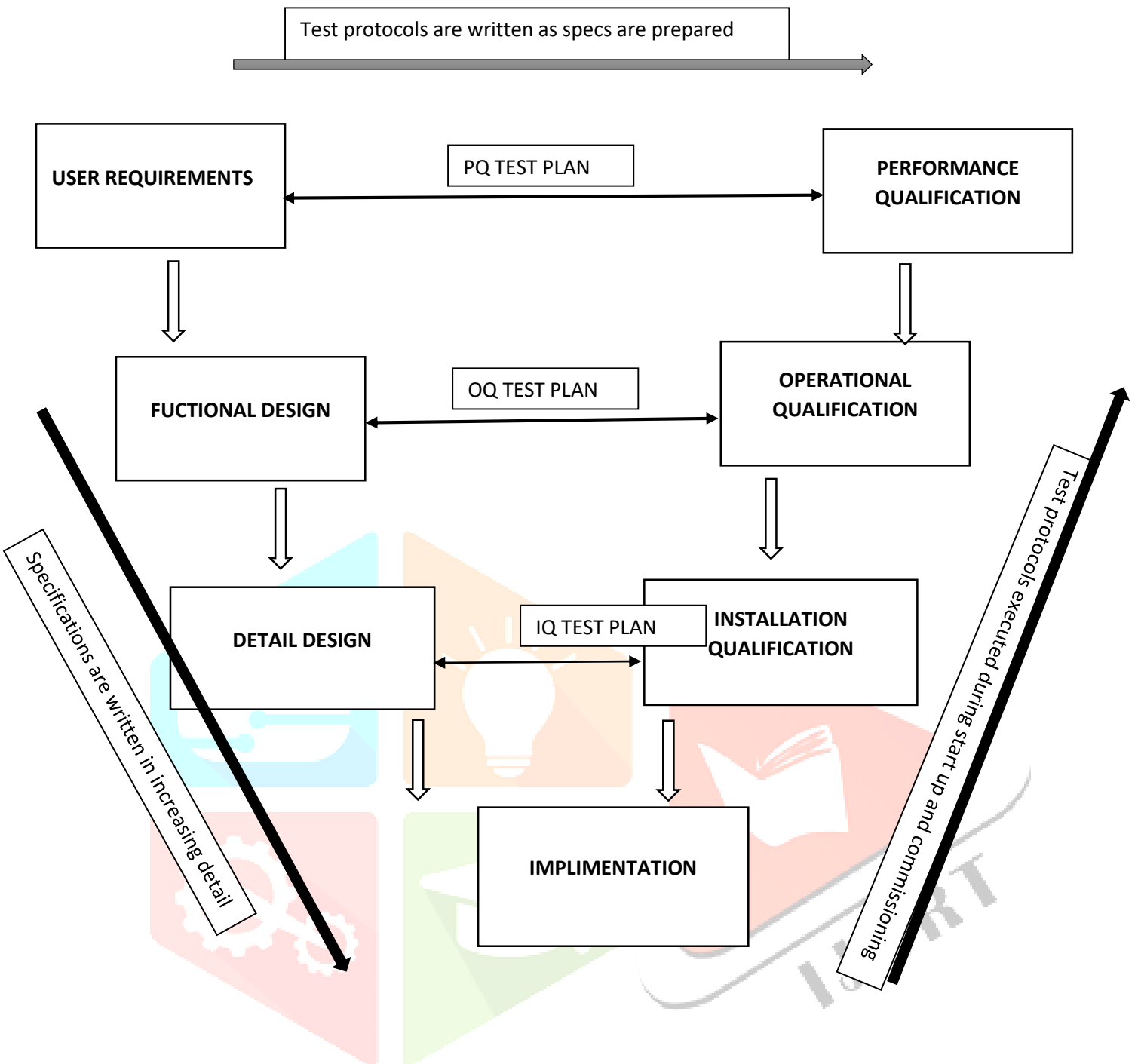
Test protocols are written as specs are prepared

USER REQUIREMENTS

PQ TEST PLAN

PERFORMANCE QUALIFICATION

FUCTIONAL DESIGN

OQ TEST PLAN

OPERATIONAL QUALIFICATION

Specifications are written in increasing detail

DETAIL DESIGN

IQ TEST PLAN

INSTALLATION QUALIFICATION

Test protocols executed during start up and commissioning

IMPLIMENTATION

Fig: V- model of computer system of validation

Process of computer system validation

There are five step involve in computer system validation

1. Validation Master plan
2. Project plan
3. Installation Qualification (IQ)
4. Operational Qualification (OQ)
5. Performance Qualification (PQ)

1. Validation master plan: Master plan is the process of preparing blueprint for entire Computer system validation. This process is the main process of validation hence it covers complete setup such as hardware, software and also validate processes such as reduction of risk.

2. Project plan: For evaluation of validation program each step require Standard Operating Procedure (SOP) and also require validation master plan.

3. Installation qualification: This stage delves deeper into installation process and creates checks and balance for any new component that may have been purchased or any new hardware or software that may have been installed

4. Operational qualification: Operational qualification check the security process like software security, physical security) and OQ also check the accuracy of operational function.

5. Performance Qualification: Performance qualification test specific applications and enterprising engage in maintenance and conduct performance test.

All the processes give to effectively meeting pharmaceutical cGMP and all these technical processes are help to require product quality standard.

Aspects of healthcare

- Services
- Equipment
- Computer system
- Processes

FDA compliance software

Every computer based control system being used in medical devices should comply to following requirements

- Information security
- Information backup
- Information restore
- Information recovery capabilities in cases as "disaster"
- Periodic Maintenance

Basic requirement of CSV

- To develop validation plan.
- Usage of standard operating procedure.
- Documented training on SOPs.
- Development of detailed specification.
- Development of test plan

Validation HPLC-

Validation is demanding tool to assure the quality of computer system performance. Computer system software system validation increases accuracy of system, and cause less risk to process and data integrity. Major benefits of computer system validation are decrease long term system and cost of project by minimizing cost of maintenance and rework.

Validation of HPLC system is most demanding and important because all regulatory authorities focusing on this instrument and data integrity problems are found during FDA inspections therefore, validation of HPLC is important example in computer system validation.

This system updating all requirement which is used in HPLC like injection volume, flow rate, column temperature, wavelength etc.

Benefits of Computer system validation

1. Legal observance with FDA

2. Reduces risk associated with pharmaceutical industries

3. Find out fault before a system build goes live.

4. Continuous improvement of pharma industries

5. Reduces operating as well as labour cost.

6. To maintain consistency in final product.

Conclusion of computer system validation

The main conclusion of computer system validation is it maintain consistency and accuracy in final product. It also prevent from data integrity due to the fault in computer system. It find out time to time error in software that's why it prevent data integrity issues which are happens during FDA inspection.

Reference:

1.Agalloco, J, Carleton FJ, Validation of Pharmaceutical Process, 3rd Edition, USA, New York: Informa Healthcare, 2008.

2. Sangeetha NKD, Bala krishna P, Development and validation of a UPLC method for the determination of duloxetine hydrochloride residues on pharmaceutical manufacturing equipment surfaces, Pharmaceutical Methods, 2011; 2 (3):161–166.

3. Giridhar A, Hamdan I, Joglekar G, Venkata subramanian V, Reklaitis GV, Real-time process management in particulate and pharmaceutical systems, Computer Aided Chemical

Engineering, 2011; 29:1035–1039.

4. Bedson P, Sargent M, The development and application of guidance on equipment qualification of analytical instruments, Accreditation and Quality Assurance, 1996; 1(6):265-274.

5. Coombes P, Laboratory Systems Validation Testing and Practice, DHI Publishing, LTD, Raleigh, USA 2002.

6. US Food & Drug Administration - Guidance for Industry Quality Systems Approach to Pharmaceutical Current Good Manufacturing Practice Regulations, September 2006.

7. US Food & Drug Administration - Guidance for Industry Process Validation: General Principles and Practices – Revision 1, January 2011.

8. US Food & Drug Administration - General Principles of Software Validation; Final Guidance for Industry and FDA Staff, January 2002.

9. US Food & Drug Administration - Guidance for Industry: 21 CFR Part 11 - Electronic Records and Electronic Signatures: Scope and Application, August 2003.

10. PIC/S Good Practices for computerized systems in regulated "GxP" environment, Pharmaceutical Inspection Co-operation Scheme guidance, September 2007.

11. GAMP Forum – GAMP Guide, A Risk-Based Approach to complaint GxP Computerized Systems - Ver. 5.0

12. GAMP Forum – GAMP Good Practice Guide, Testing of GxP Systems.

13. GAMP Forum – GAMP Good Practice Guide, A Risk-Based Approach to Compliant Electronic Records and Signatures.

14. GAMP Forum – GAMP Good Practice Guide, Global Information Systems Control and Compliance.

15. GAMP Forum – GAMP Good Practice Guide, A Risk-Based Approach to Operation of GxP Computerized Systems – 2010.

16. FDA, "Guidance for Industry: Regulatory Submissions in Electronic Format for New Drug Application (NDA)," http://www.fda.gov/cder/guidance/2353fnl.pdf.

17. FDA, "Guidance for Preparing Data for Electronic ANDA Submission," http://www.fda.gov/cder/guidance/3223fnl.htm.

18. FDA, "Revised Guidance for Providing Regulatory Submissions to CBER in Electronic Format," http://www.fda.gov/cber/gdlns/ebla.pdf.

19. FDA, "Enforcement Policy: 21 CFR Part 11, Electronic Records, Electronic Signatures" (CPG 7153.17, 13 May 1999), http://www.fda.gov/ ora/compliance_ref/cpg/cpggenl/cpg160-850.htm.

20. FDA, "Public Docket Index for 21 CFR Part 11 (E-Rec/E-Sig Rule)," http://www.fda.gov /ora/compliance_ref/Part1 1/dockets_index.htm.

21. FDAMA, SEC. 410, "Mutual Recognition Agreements and Global Harmonization," http://www.fda.gov /cder/guidance/105-115.htm#SEC.

22. CDER Warning Letters Web site: http://www.fda.gov/foi/warning_letters/m5056n.pdf and http://www.fda.gov/foi/warning_letters/m5057n.pdf.

23. FDA Cyber Warning Letters Web site: http://www.fda. gov/cder/ warn/cyber /cyber 2017.htm.

24. GAMP and ISPE Web site: http://www.gamp.org and http://www.ispe.org.

25. PDA Web site: http://www.pda.org.

26. PIC Web site: http://www.picscheme.org/index.htm.

27. Information Society Standardization System Web site: http://www.cenorm.be/isss/

28. International Biometric Industry Association Web site: http://www.ibia.org.

29. ComputerValidation.com Web site: http://www.computervalidation.com .

30. GAMP 5, A risk based approach to compliant GxP computerized systems by ISPE, http://www.ispe.org/gamp5.

31. Keith Williams CEO GxPi, GAMP®5 as a Suitable Framework for Validation of Electronic Document Management Systems 'On Premise' and 'In the Cloud'. 3.Stephen Shields, GAMP 5, A Risk-Based Approach to compliant GxP computerized Systems, 10 September 2013, ASQ –Orange Section Meeting –Part 1.

32. Kevin C Martin and Dr. Arthur Perez, (2008), GAMP 5 Quality Risk Management Approach, Pharmaceutical Engineering, the Official magazine of the ISPE. 5.Components and Tools of SAP Net weaver: SAP Solution Manager, http://www.sap.com/usa/platform/netweaver/components/solutionmanager/index.epx.

33. https://performancelabus.com/csv-benefits/#7

34. https://qedge.sarjen.com/computer-system-validation-pharmaceuticals/

35. https://www.reutersevents.com/pharma/column/pharma-and-computer- system-validation

36. https://qbd.eu/en/a-complete-guide-to-computer-system-validation

37. https://validationcenter.com/why-computer-system-validation-required/