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Review on :- Computer System Validation In Pharma Industry

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ABSTRACT
Computer Systems Validation (CSV) is a process that ensures computer-based systems produce information or data that meets defined requirements. Quality is crucial for customers, especially in life-saving products like pharmaceuticals. The Food and Drug Administration introduced good manufacturing practice (GMP) to maintain and improve the quality of pharmaceutical products. GMP requires that all critical manufacturing equipment, utilities, and facilities in the pharmaceutical industry be properly qualified and validated before production. Validation assessment programs are essential in the pharma industry to ensure adherence to cGMP guidelines and maintain consistent quality. The same principles apply to computer systems and information technology systems. Maintaining quality standards in the pharmaceutical industry is crucial, as nonconformance can have severe consequences. CSV checks the effectiveness and efficiency of a system's purpose. This study aims to identify the needs of computer system validation in the pharmaceutical industry, focusing on the instrument/equipment used in the pharmaceutical industry.

I. INTRODUCTION

Validation, first proposed by Ted Byers and Bud Loftus in the mid-1970s, is crucial in the pharmaceutical manufacturing industry for producing high-quality products that meet good manufacturing practice (GMP) guidelines. It is a requirement imposed by authorities worldwide to regulate the production of pharmaceutical and medical devices. The Food and Drug Administration (FDA) requires validation, which involves collecting and evaluating data to draw scientific evidence that an equipment, utility, or facility is capable of consistently delivering quality products.

In the pharmaceutical concept, validation refers to establishing documented evidence that an equipment, utility, or system can effectively produce a medicinal product that meets predetermined specifications when operated within established parameters. Validation of software and computer systems follows the same principle as the qualification of instrument hardware. Software can be divided into three categories: integrated firmware, software for instrument control, data acquisition, and processing, and standalone software, such as a Laboratory Information Management System (LIMS) package. The most valuable statement about firmware is that it is considered a component of the instrument itself, and qualification of hardware is not possible without operating its firmware. When the hardware is qualified at the user's site, the integrated firmware is also essentially qualified, without the need for separate on-site qualification.

General Concept

Product quality assurance relies on factors like selecting quality parts and materials, designing a proper product, controlling the process, and conducting in-process and end product testing. Routine end-product testing may not be sufficient for medical products due to their complexity and limited sensitivity. In cases where end-product testing fails to identify all variations, destructive testing may be necessary to ensure the manufacturing process is adequate.

CSV Requirements

The following FDA regulations contain the requirements for computer system validation: a. FDA 21 CFR part 820.70 b. FDA 21 CFR part 11.10 c.

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FDA 21 CFR part 11 d. FDA Guidance Document about Software Validation (including addressing process software). Pharmaceutical producers can improve their computer systems' validation. e. GMP directives f. ISO 13485, clauses 4.1.6, 7.5.2.1, and 8.2.3 g. GAMP 5, for example, with reference to the "risk-based approach of testing GxP systems.

NEED OF VALIDATION, QUALIFICATION AND IT SYSTEM VALIDATION

Pharmaceutical facilities require accurate processes to ensure high-quality end products. Validation is a systematic approach that confirms that a process operates within specified parameters, ensuring consistent and repeatable results within predetermined specifications. It is crucial in pharmaceutical facilities to verify that quality standards and compliance are being met in real-time and that the facility meets current good manufacturing practice (cGMP) guidelines set by regulatory bodies. Validation is considered documented evidence of the process meeting predetermined specifications. No pharmaceutical plant is complete without an IT system, which controls, supports, and documents various processes. Validation is crucial for controlling the development, design, testing, and routine of the software used in the IT system's life cycle. Accurate computer system operation ensures the safety of stored information and reports. In GMP-regulated industries, stringent quality requirements must be implemented to control procedures throughout the Software Development Life Cycle (SDLC). Focusing on risk analysis and in-depth validation approaches is essential, and documentation must be applied to the computerized system, as it manages crucial data that impacts product quality. The components of computer system validation include activities involved in applying appropriate controls throughout the SDLC and procedures for creating documentation.

System Development Life Cycle

SDLC is a framework for developing computer-based information systems, involving a multi-step process from initial requirements investigation to analysis, design, implementation, and maintenance in various phases.

Figure 1: System Development Life Cycle.

Types of Validation.

1.Analytical Validation: Analytical validation evaluates product quality attributes through testing to ensure reliability throughout the product life cycle, ensuring precision, accuracy, strength, purity, and specification are not compromised.

2. Equipment Validation: Equipment validation is a process that involves assessing the performance of equipment. It can be divided into installation Qualification (IQ), Operational Qualification (OQ), and Performance Qualification (PQ). IQ documents static attributes of a facility or item, ensuring correct installation and meeting manufacturer specifications. OQ ensures equipment can deliver operating ranges as specified in the purchase order, while PQs verify the process's functionality.

3. Process Validation: Process validation is a well-documented procedure that guarantees reliable product manufacturing that satisfies established standards and quality criteria while providing high assurance.".

Process validation is divided into different types as follows:-

(a) Prospective validation: Validation is the process of establishing documented evidence that a system performs its intended function based on a pre-planned protocol. This validation is typically conducted before the introduction of new drugs and their

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manufacturing processes, ensuring the safety and effectiveness of new formulas, processes, or facilities before routine pharmaceutical formulation begins.

(b)Retrospective validation: The process of establishing documented evidence of a system's control through analysis of historical data, ensuring the process remains in control throughout manufacturing testing.

(c) Concurrent validation:The operating firm sells the product during qualification runs to the public at its market price, involving process monitoring and product testing. This validation process repeats when formulation, equipment, and plant or site location changes or replacements occur.

(d) Revalidation: Batch size and in the case of sequential batches that do not meet product and process specifications.

GOOD AUTOMATED MANUFACTURING PRACTICE (GAMP)

GAMP, or Good Automated Manufacturing Practice, refers to the GAMP-5 guidance document, which focuses on a risk-based approach to compliant GxP computerized systems. The approach is summarized by the V-model diagram and includes five software categories.

GAMP CATEGORY
Category 1: Operating systems
Category 2: Firmware
Category 3: Standard software
Category 4: Configured software
Category 5: Custom software

Fig.2. GAMP Categorization

- Category 1: Operating systems
- Category 2: Firmware
- Category 3: Standard software
- Category 4: Configured software
- Category 5: Custom software

The debate over commercial software packages' classification has been ongoing, with some spectroscopists arguing for category 3 classification. GAMP 5 addresses this debate by revising software categories, resulting in four categories: category 3, category 4, and category 5. This evolution of software classification approach aims to simplify validation and avoid classification errors.:

- Category 1: Infrastructure Software
- Category 3: Nonconfigured products
- Category 4: Configured products
- Category 5: Custom applications

Software classification provides a built-in risk assessment, with category 1 being the least risky and most widely available software. This category includes operating systems, databases, office software, and other widely available software. As the software progresses through the categories, it becomes more specialized in its function, ranging from general office applications to data processing software. Users' ability to change software operations and process results increases until category 5. Category 5 is a unique solution that is conceived, specified, written, tested, and maintained by users or organizations, with the greatest risk. By examining each software category, it becomes clear what has changed and if there are any problems that need to be discussed.

Category 1: Greatly Expanded Scope-Infrastructure Software has evolved from operating systems to infrastructure software, divided into two subcategories: Established or commercially available layered software and Infrastructure software tools. This category provides a computing environment for regulated and non-regulated applications within an organization. All software must be controlled and qualified to avoid dual standards being applied by the IT department. The subcategory includes databases, programming languages, middleware, office software, ladder logic interpreters, statistical programming tools, and spreadsheet packages.

Category 3: Nonconfigured Products: Products that are off-the-shelf and cannot be customized to meet business procedures; nevertheless, this category can also include software products that can be customized but only employ the default configuration.

Category 4: Configured Products: Configurable software products offer common interfaces and features that let the program be customized to fit user-specific business processes. However, configuration done through a scripting language provided by the manufacturer ought to be treated as bespoke components (category 5).

Category 5: Custom Applications: These programs were created to cater to the particular requirements of a regulated business. Visual Basic for

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Applications (VBA)-created spreadsheet macros and language modifications for LIMS are inherently included in this description. It will also contain macros created as shortcuts for carrying out a number of activities in various spectroscopic applications. The life cycle model must include adequate controls to guarantee that the software is properly defined, developed, constructed, and tested before release because this software carries the highest risk of having functional omissions, flaws, and errors.

COMMON COMPUTER SOFTWARE PROBLEM

The validation of Computer systems has a lot of problems associated with it. Some of the common problems are listed below:

1. Standard: Each organization works as per its own standard operating procedure. Even policies, procedures, work instructions and templates vary as per business, department or site. These overlapping SOPs and inconsistent standards make it difficult to maintain a standard for Computer Software Validation.

2. Interpretation: A significant cost to validation projects is caused primarily by inconsistent interpretation of standards and requirements by various authors and reviewers. Most regulations include very stringent guidelines but do know mention the procedures to follow them.

3. Organization and Governance: Many companies still have decentralized governance and uncontrolled execution. Thus, the validation tasks vary from project to project and one department to the other. Also, it depends on the team handling the projects.

4. Efficiency across sites and departments: Site-to-site and from one department to other, the efficiencies have been seen to differ. There are many cases where multiple sites using the same system and procedures have been differed as there is no sharing of inventory and project information.

5. Execution: Most of the times excessive rework is done by the validation team in order to get consistent results. This leads to inconsistent quality of work as different opinions and styles are involved. Also, junior as well as well experienced senior reviewers bring a lot of change in the style of execution of a project.

6. Tools: System life cycle asset such as documents, templates, outlines, forms, etc are often inconsistent across departments, sites and organization. Differences in these systems are majorly because these tools are not targeted to drive value.

7. Training: Training in the pharmaceutical company regarding the approaches to the validation is usually conducted in a timely manner. But the standard and processes regarding the procedure requires coaching and guidance which is minimal. The short training provided is rarely enough to qualify individuals without coaching until they get hands on training.

8. Personnel: Many pharmaceutical companies have capable, knowledgeable central validation groups but weaker decentralized execution groups. Organization believes that simply reading the Standard Operating Procedures and receiving a few hours of training can build the gap to a consistent approach .

II. CONCLUSION

Pharmaceutical manufacturers can enhance their validation projects by addressing computer system validation deficiencies, promoting collaboration, prioritization, planning, oversight, and clarity of purpose. Research on existing validation frameworks can identify positive elements that can eliminate pitfalls. A simple, systematic, easily understood, and flexible framework should be developed, applied in case studies conducted in pharmaceutical companies. Conducting case studies in three different backgrounds can confirm the framework's flexibility, robustness, and validity. This approach can help future implementers achieve significant improvements in validation scope, saving manufacturers time, effort, and money spent on validation projects.

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