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Review On:- Computerized System Validation: Process, Methods and its Implications

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ABSTRACT:-
Every pharmaceutical and healthcare industry's manufacturing process starts with the most crucial requirement: quality. All medications must be produced with the highest level of quality. Testing the final product is insufficient to ensure quality; instead, we must closely monitor each crucial stage of the manufacturing process. To ensure the quality of the finished product, this qualification and computer system validation play a crucial part in regulating each crucial application phase. The life cycle of processes involves a number of tasks that are included in computer system validation.The qualification and validation of the software and applications used in the manufacturing process must also be carefully planned, and all work must be done in a systematic manner in accordance with established working norms. Overviewing the qualification and computer system validation of instruments and equipment used in the pharmaceutical sector is the goal of this work.

Keywords:- Computer System Validation, Installation Qualification, Operational Qualification, SDLC, V-Model.

I. INTRODUCTION

In today's technology-driven world, computer systems serve as the backbone for countless industries. From healthcare to finance, these systems are designed to collect, store, process, and transmit large volumes of data both reliably and efficiently.[1] One critical aspect in ensuring these systems can perform their intended functions without deviation is computer system validation (CSV). In this article, we will delve into the crucial aspects of computerized system validation, discussing its importance, methods, and regulatory compliance.[2]

II. DEFINITION

According to 21 CFR part 820; validation means confirmation by examination and provision of objective evidence that the particular requirements for a specific intended use can be consistently fulfilled.[3]

III. WHAT IS COMPUTER SYSTEM VALIDATION?

Computer system validation (CSV) is a documented process that demonstrates a computer system can consistently meet specified requirements and intended user needs. Validation activities involve planning, writing protocols, executing tests, documenting results, and managing deviations or discrepancies. The primary objective of CSV is to provide objective evidence that the designed system can perform its intended function reliably and securely while maintaining data integrity.[4]

IV. IMPORTANCE OF COMPUTER SYSTEM VALIDATION

1. Regulatory compliance: Many industries have strict regulatory requirements surrounding computer systems and electronic records. Compliance with standards like GxP (Good Manufacturing Practices) or 21 CFR Part 11 guidelines necessitates thorough validation of all systems managing electronic data.
2. Data integrity: Validating a computer system is integral to ensuring data integrity throughout its entire lifecycle. This includes protection against loss or corruption of data and guaranteeing accurate and reliable results.
3. Risk management: CSV helps manage potential risks associated with implementing new technologies by identifying possible issues before they become detrimental in the operation phase.
4. Cost reduction: Valuable resources are saved by identifying potential problems early on through collaboration across multidisciplinary teams during validation.[5]

V. REGULATORY COMPLIANCE

Maintaining compliance with data security and integrity regulations is an ongoing effort. To

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ensure a high level of compliance, CSV should adhere to guidelines established by regulatory bodies such as:

1.1 U.S. Food and Drug Administration (FDA)

The U.S. Food and Drug Administration (FDA) is one of the most influential regulatory bodies globally. It oversees food safety, drugs, medical devices, biological products, cosmetics, veterinary products, tobacco products, and electronic products emitting radiation. Under Title 21 Code of Federal Regulations (CFR), Part 11, the FDA established requirements for electronic records and signatures related to CSV.

Key guidelines issued by the FDA that regulate CSV include:

- General Principles of Software Validation;
- Guidance for Industry: Part 11
- Electronic Records: Electronic Signatures.

1.2 European Medicines Agency (EMA)

The European Medicines Agency (EMA) plays a significant role in protecting public health within European Economic Area member states through the evaluation and supervision of human and veterinary medicines. The agency has issued guidance on computerized systems validation under Annex 11 of the European Union Good Manufacturing Practice (EU GMP) guidelines.

Key guidelines by EMA pertaining to CSV include:

- EU GMP Annex 11: Computerized Systems;
- EU GMP Annex 15: Qualification and Validation

1.3 International Society for Pharmaceutical Engineering (ISPE)

ISPE is an international industry association that promotes the development and sharing of best practices around CSV. Although not a regulatory agency, ISPE works closely with regulators such as the FDA and EMA to provide guidance and recommendations on CSV-related topics.

ISPE's Good Automated Manufacturing Practice (GAMP) framework is widely accepted by pharmaceutical companies and regulators worldwide. This framework serves as a critical resource in guiding organizations on how to implement CSV efficiently and consistently.

Key resources provided by ISPE include:

GAMP 5: A Risk-Based Approach to Compliant GxP Computerized Systems.

1.4 International Organization for Standardization (ISO)

ISO is an independent, non-governmental international organization that develops voluntary technical standards for various industries, including healthcare. Among its numerous published standards, ISO has several relevant to computer system validation in the regulated sectors.

Key ISO standards related to CSV include:

- ISO 9001: Quality Management Systems;
- ISO/IEC 27001:InformationSecurity Management System.[6-13]

VI. GOAL OF VALIDATION

Since such validation activities will frequently involve training on the production process and operating procedures, training of people involved, and monitoring of the system while in production, the main goal of any regulatory agencies is to ensure that quality is built into the system at every step, and not just tested for at the end. In general, before a specific object inside a process is verified, the entire process should be validated or verified. The standards also outline a requirement that the various steps in the manufacturing process be well specified and under strict supervision, ensuring that the output won't fluctuate significantly over time. This includes the design, implementation, use, and maintenance of computer systems as well. "The software development and validation process should be sufficiently well planned, controlled, and documented to detect and correct unexpected results from software changes," the software validation guideline (GAMP-5) states.[14-15]

VII. VERIFICATION AND VALIDATION OF INSTRUMENT

Verification and validation are essential steps in ensuring the accuracy, reliability, and quality of an instrument, particularly in scientific research and industrial applications. These processes aim to ensure that the instrument meets its intended purpose and performs to its expected specifications. In this article, we will explore the concepts of verification and validation of instruments.

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Verification: Definition and Purpose

Verification is a process that involves checking whether an instrument or system meets its design requirements, specifications, and regulations. In other words, it confirms that the instrument has been designed and built correctly according to its intended purpose. Verification focuses on the following aspects:

1. Design Review: Assessing the design against a set checklist to ensure it meets specified performance requirements.
2. Inspection & Testing: Evaluating the performance of the instrument or system in a controlled environment to ensure it operates as expected.
3. Documentation Review: Checking if required documentation (e.g., design history files, standard operating procedures) is accurate, complete, and compliant with applicable standards.

Validation: Definition and Purpose

Validation is a process that ensures an instrument performs correctly in its intended use or application. It demonstrates that the instrument consistently produces accurate results when used within specified operating conditions. Validation usually includes three key stages which are:[14-15]

1. Installation Qualification.
2. Operational Qualification.
3. Performance Qualification.

Table 1: Difference Between Verification and Validation[14-15]

Verification	Validation
Done in house	Done at the Production site
Done by Developers and Testers	Done by customers, owners, vendors, and operation team
Includes unit, integration, and system testing	Done by customers, owners, vendors, and operation team

VIII. PHASES OF VALIDATION PROCESS

The validation process for any product, in general, relates to the entire life cycle of a product, from development to use and maintenance. Consequently, the validation process is divided into 5 phases, which are as follows:

1. Design Qualification.
2. Installation Qualification.
3. Operational Qualification.
4. Performance Qualification.
5. Maintenance Qualification.

Many industries, including manufacturing, healthcare, and pharmaceuticals, use this five-phase validation process approach.

To that purpose, before purchasing the programme, instrument/equipment, or product, the end user will validate and qualify the computer system.[16]

Table 2: Different Phases Relevant for the User in the Qualification.[16]

Qualification	Phase	Responsibility of	Activities
Design Qualification	Evaluation of the instrument	User	Provide documentation demonstrating that the instrument satisfies the functional and operational requirements.
Installation Qualification	Evaluation of the instrument	User	Evidence in writing demonstrating the instrument's correct installation in the chosen setting. Functional Check

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Operational Qualification	Putting the instrument into operation	User	Documentation in writing demonstrating that the instrument performs in accordance with operational requirements in the chosen environment.Performance check.
Performance Qualification	Check the performance of the instrument for its intended uses	User	Documented evidence that the instrument operates consistently and as intended when used in a typical working environment. Periodic checks of: • Specification • Specific system suitability tests • Analysis of control samples

IX. COMPUTER SYSTEM VALIDATION METHODS

There are several methods for validating a computerized system:

1. Installation Qualification (IQ):

This phase entails verifying that the installation of hardware, software, and other components conforms to manufacturer specifications and pre-defined requirements.

2. Operational Qualification (OQ):

Operational qualification documents that the system operates correctly and consistently under normal operation conditions. This phase typically involves testing system functions, features, and user access controls.

3. Performance Qualification (PQ):

PQ demonstrates that the system performs according to its intended purpose under real-life or simulated conditions. This step verifies how the system handles varying data volumes, as well as adverse conditions and exceptions.

4. Risk Assessment:

This validation method involves identifying potential risks posed by the system across all areas of an organization. It evaluates the likelihood, severity, and impact of each risk, prioritizing them for remediation during validation. Risk assessments are crucial in determining the depth and extent of validation activities.[17-22]

X. SDLC (SYSTEM DEVELOPMENTLIFE CYCLE)

A life-cycle development model (SDLC) is used in software development. A stage in computer validation can be linked to eachstep in the software development process. As a result, this model may be used to explain each step in the validation process for computer systems. This makes it possible to efficiently document the development process.[18-19]

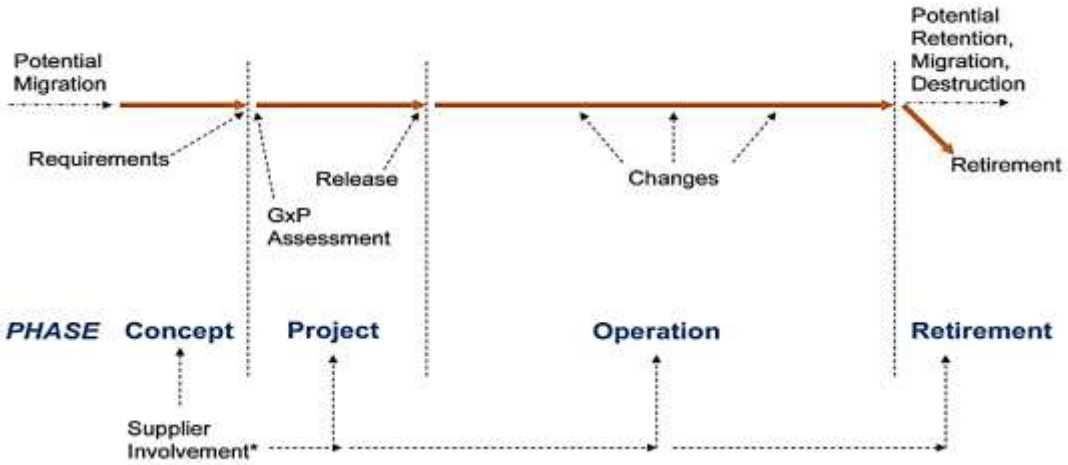

Fig. 1: A Risked Based Approach to Compliant Computerized System[18-19]

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XI. V – MODEL

A step in the life-cycle model is semantically equal to each level of the V-model. If the validation process also involves software development, the V-model performs pretty well. However, several crucial procedures, such as vendor assessment, are not covered. For a truly commercial off-the-shelf system that does not require custom coding, it also appears to be rather complex. It is not necessary to go through phases like design specification, code development, and code testing. User requirement specification (URS), design qualification (DQ), installation qualification (IQ), operational qualification (OQ), and performance qualification (PQ) are all included in this approach.[20-21]

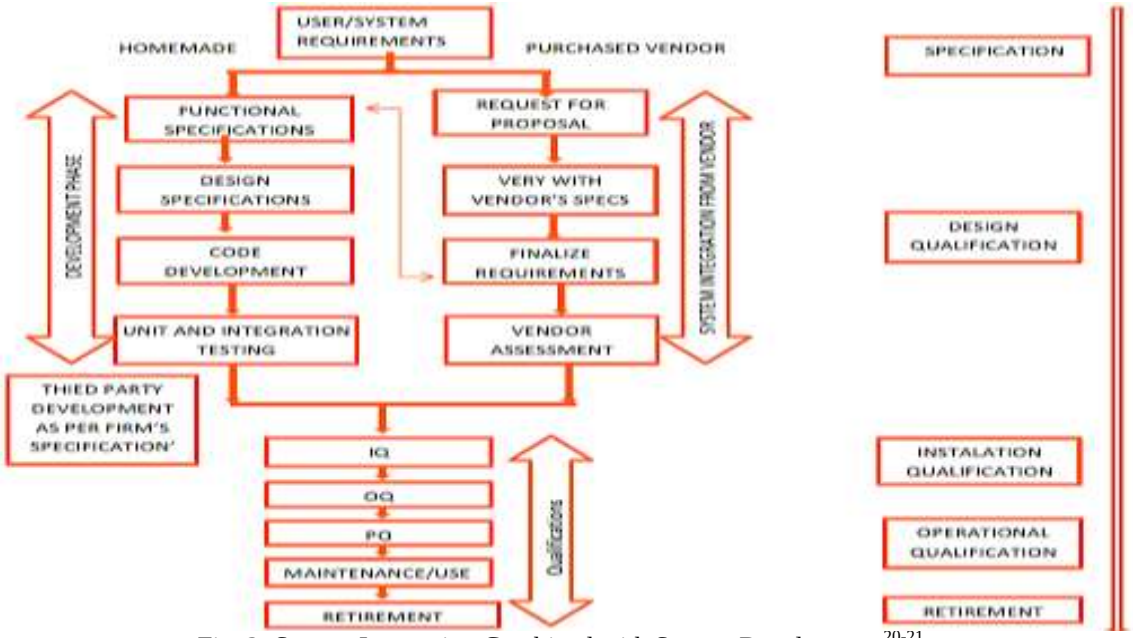

Fig. 2: System Integration Combined with System Development[20-21]

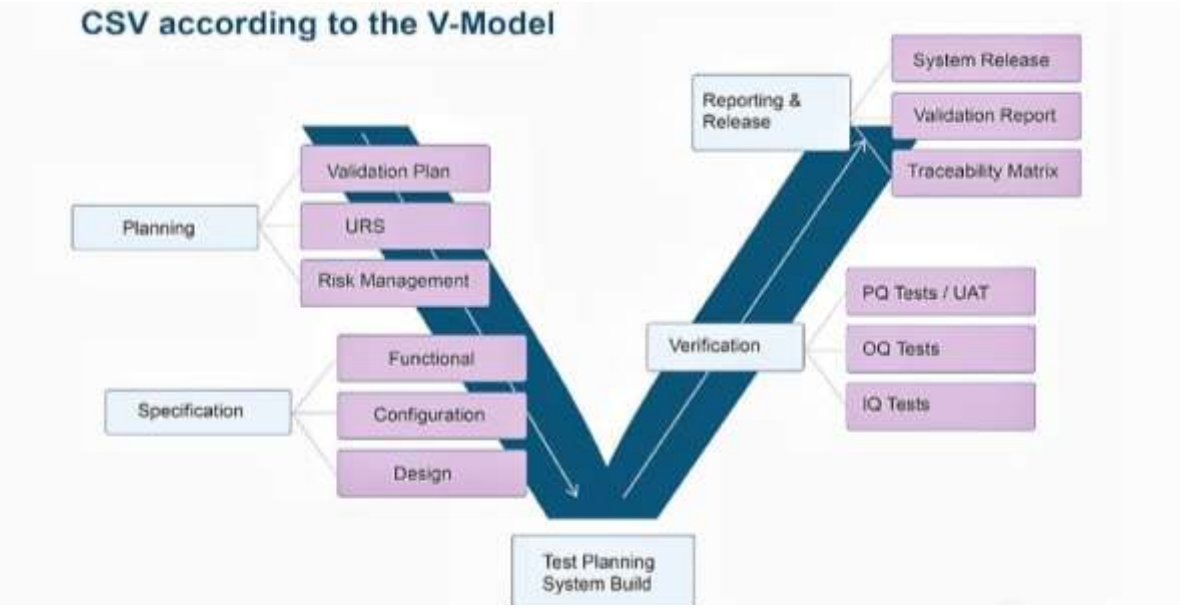

Fig. 3: V-Model

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1.5 Installation Qualification:-

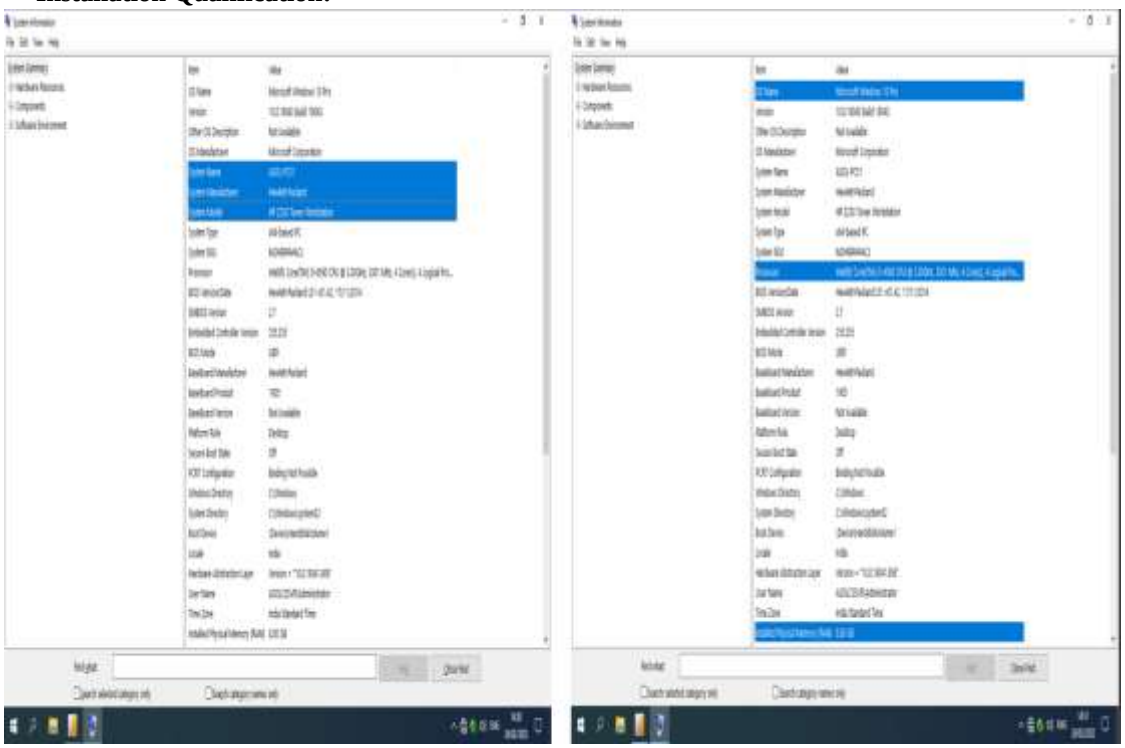

Fig. 4: Hardware and Software Evidence

The purpose of this document to verify that System Installation and Setup includingHardware and Software is performed in line with the recommendation from the application vendor. This document covers the retrospective verification of installed software and hardware through qualification scripts like component verification (e.g. PC configurations), document verification, Hardware Components and Software Components, Backup Configuration, Security policy configuration, and Date & Time synchronization.[22-23]

- Test Scripts to be executed are identified in the table below:

Sr. No.	Test Title
1.	System Identification
2.	Document verification
3.	Hardware Components and Software Components.
4.	System network connection & Date and time format
5.	Security policy configuration
6.	Date & Time synchronization

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1.6 Operational Qualification:-

The purpose of this document is to verify that system operational qualification performed in line with the functional requirements specified in the User Requirement Specification. The operational qualification will be performed according to the validation document adherence to functional requirements specified in the URS. Pre-approved operational qualification document will be created and used to document the execution of the operational steps. Any exceptions to the operational qualification will be documented.[22-23]

- OQ Test Scripts to be executed are identified in the table below:

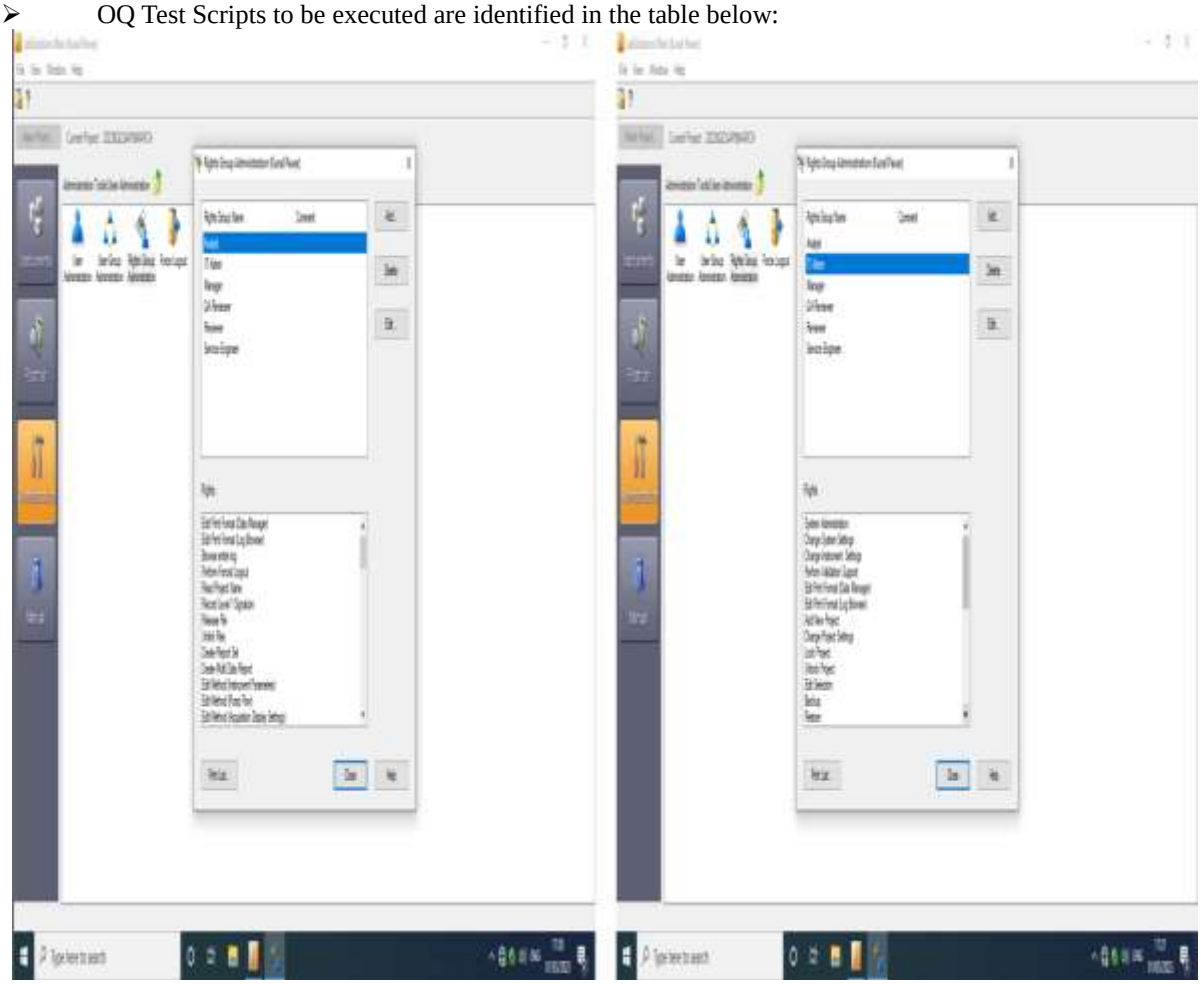

Fig. No:5 Access Control Evidence

Sr. No.	Test Title
1.	User Access and Privileges.
2.	Security Requirements.
3.	Method creation, run sequence and reporting
4.	Audit Trail
5.	Backup and Restore

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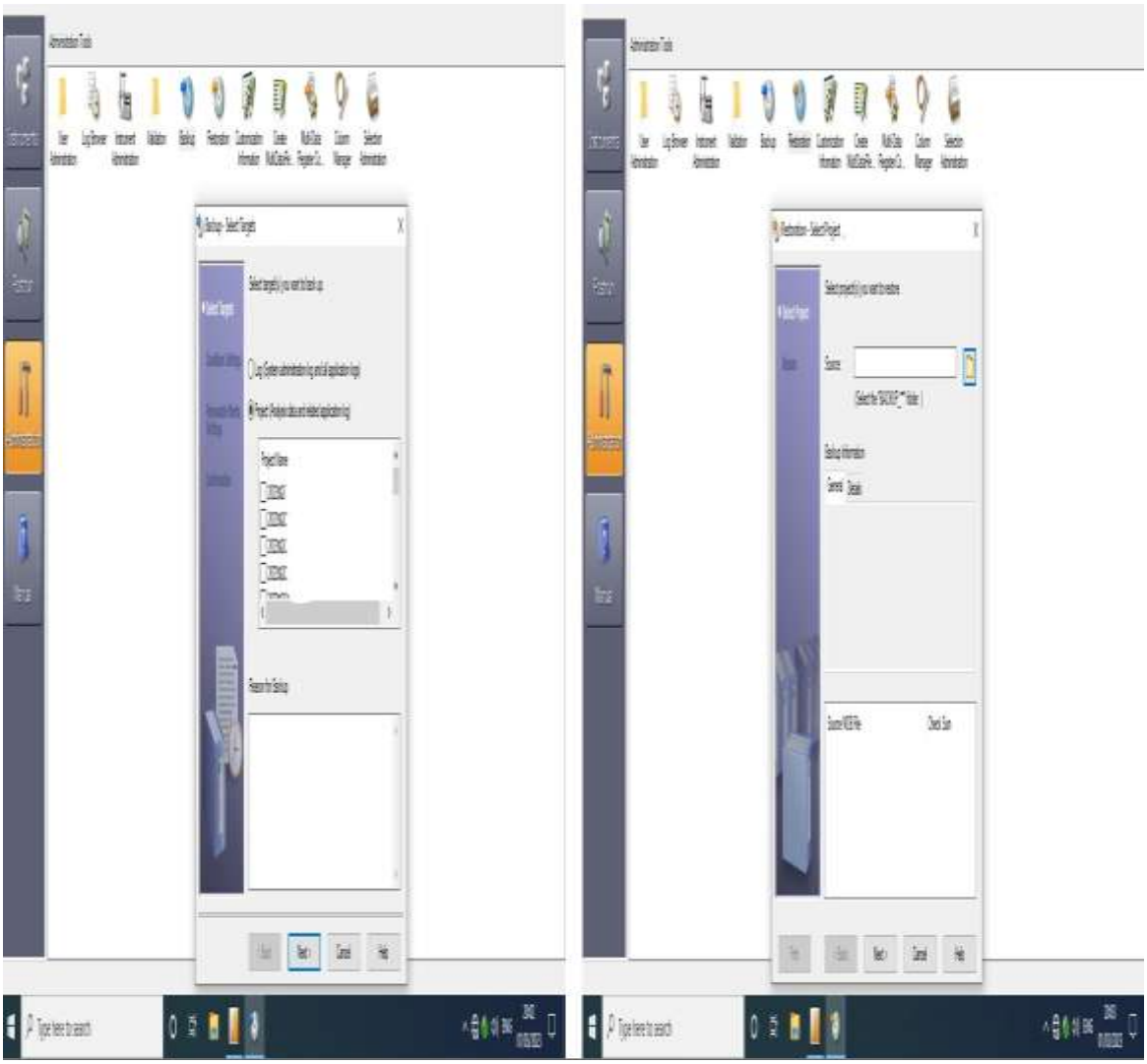

Fig. No: 6 Backup and Restore Evidence

1.7 Performance Qualification:-

The next step in the validation process, after the installation and operational qualification activity is successfully completed, is to confirm that the product/software satisfies the specified Performance aspects under the expected load consistently without creating any bottleneck in the production environment. Performance qualification's primary objective is to guarantee that software will function as expected when installed on the anticipated system. Performance qualification is carried out to make sure the given performance standards for software are met reliably over time and under varied load conditions, as is the case in the live environment.Since these tests must be performed daily to track the behavior of the software system, PQ won't be finished until the system's performance has been established. PQ Validation is best performed after OQ is finished, when the software's functioning is confirmed and it is possible to go on to confirming the product's or software's performance.

Based on the confidence in the proportion of OQ completion, PQ may occasionally begin concurrently with the OQ due to time restrictions. The Performance Qualification typically consists of the exams listed below. Additionally, the assessments available vary from software to software. [22-24]

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- PQ Test Scripts to be executed are identified in the table below:

Sr. No.	Test Title
1.	SOPs Verification
2.	Data Acquisition and Report Printing

XII. CONCLUSION

If the programme or product has passed all of the verification phases and it cannot pass any of the Qualification (Installation Qualification, Operational Qualification and Performance Qualification) and Validation stages, the outcome could be disastrous and would be extremely expensive to the firm. Therefore, the successful transfer of the product from the development site to the production site is solely determined by the completion of Installation, Operation, and Performance Qualification. Overall, the Client, Owner, programme Developers, and Testers feel at ease knowing that the qualification and validation processes have been successfully completed, which not only provides them confidence in the programme. Running installation, operational, and performance validation also lessens the danger of deploying it to live without testing, as well as the cost of failure and the risk of product recall.

We may infer that instrument qualification and software validation are key quality attributes for any manufacturing industry when instrument/equipment is employed for continuous, uninterrupted process from the aforementioned qualification and validation point of view.

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