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EXPLORING IT INFRASTRUCTURE QUALIFICATION PRACTICES FOR GMP ENVIRONMENTS

Imagine this: you put in a new firewall for your good manufacturing practices (GMP) facility. A few months later, you realize it's not working as intended. Perhaps the firewall allowed traffic that was not part of the network. How long has this issue been going on, and what problems has it caused? Yikes! This is why we have qualification practices for GMP environments.

What is Qualification?

Qualification is the process of ensuring that an installed system is operating as intended and with a high degree of quality assurance. This ensures that the production process the equipment supports is of high quality and that the integrity of the data generated is maintained throughout the lifecycle of the product/process. It's required by the U.S. Food and Drug Administration (FDA) to verify that a system is operating as intended, quality standards are upheld, and the system is safe and secure. The FDA also validates that the system meets business and regulatory requirements when audited.

Below, we explore the importance of qualified systems, various requirements for an IT qualification, and how those requirements would play into the qualification process as a whole.

Qualification vs. Validation

Validation is a documented methodology to ensure that a specific manufacturing, packaging, or testing process for a product meets specifications and fulfills its purpose. When validating a product/process, the equipment, instruments, software, facility, and utilities that are part of that process must first be qualified to ensure all the components are functioning as intended before validation is performed. To put it simply, qualification is a subset of validation.

The Need for IT Qualification

An IT qualification ensures any computerized system and its associated components leveraged within a validated process function as expected and are maintained with controlled and repeatable processes.

As per 21 CFR Part 11 requirements, "*any decision to validate computerized systems, and the extent of the validation, takes into account the impact the systems have on its ability to meet predicate rule requirements (manufacture, package, test, store, transport; pharmaceutical, biological, medical devices, cosmetics, nutraceuticals products or derivatives, and to document or record data related to predicate rule requirements).*"

GAMP (Good Automated Manufacturing Practice), developed by the International Society for Pharmaceutical Engineering (ISPE), provides guidelines for regulated industries to ensure the proper use of automation and computerized systems in manufacturing processes.

Scope and Objectives of GAMP 5

GAMP 5 offers a standardized method for qualifying and validating automated systems, aiming to ensure compliance with regulatory standards, uphold data integrity, and consistently deliver top-notch products throughout the manufacturing process. Its scope encompasses various systems, ranging from manufacturing machinery and control systems to laboratory tools and software applications.

On the other hand, infrastructure devices fall under GAMP Category 1, designated as Infrastructure Software. These devices, similar to operating systems and database engines, pose minimal direct risk to patients. As Category 1 software, they undergo qualification rather than validation. The emphasis lies on demonstrating proper installation and configuration, safeguarding records, and maintaining them under controlled conditions.

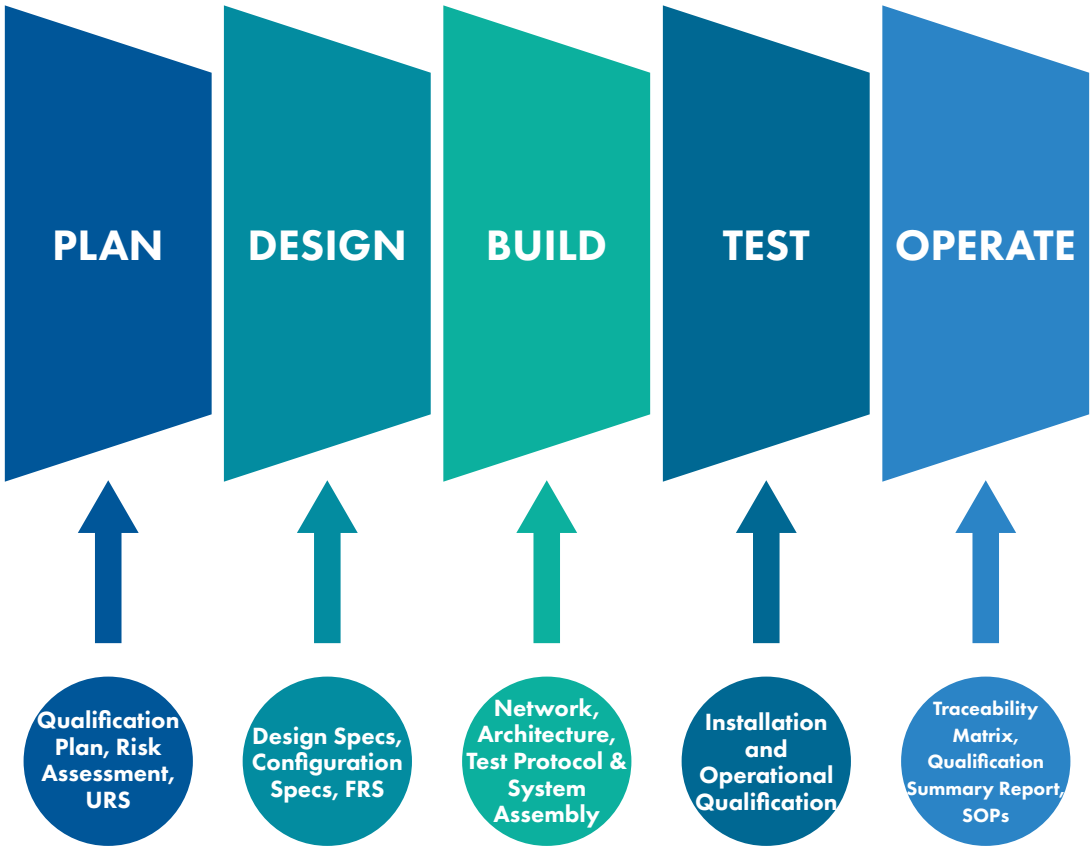
System and Devices

An IT infrastructure system may consist of devices like firewalls, routers, network switches, servers, virtual machines, operating workstations, monitors, etc., and the associated software application for operating those devices. Here are some key functions of the devices:

- **Firewall:** Monitors incoming and outgoing network traffic as set up by the organization's rules and rejects unauthorized network traffic based on IT, business, and GMP requirements.
- **Network Switches:** Receives network packets from the computing system, connects them to the firewall, and facilitates data exchange between network hosts.
- **Workstations and Monitors:** Displays using a specific operating system and processor, with the appropriate amount of RAM and storage space to support day-to-day operations.
- **Adaptors:** Appropriate physical connectivity to facilitate data exchange between the relevant devices.
- **Servers, Hypervisors, and Virtual Machines:** Accommodate simultaneous operations of multiple applications and store, archive, and retrieve data as required.

Phases Involved in an IT Qualification

Once you have identified the IT Infrastructure present in your system, it's time to start looking at the phases of an IT Qualification.



Planning Phase:

During the planning phase, the scope of the IT Infrastructure Qualification project is defined, a Qualification Plan is developed, and a complete risk assessment of the system is performed to identify the risk/impact of the system to the GxP process related to the system. Once the scope and the qualification plan are determined and risk is assessed, the next step in the planning phase is the requirement gathering. A key step in the qualification process is requirements and information gathering. The URS (User Requirements Specification) specifies, on a broad level, what activities the infrastructure system needs to be able to accomplish.

Design Phase:

The next step in the qualification process is the development of functional requirements specification during the design phase. The FRS (Functional Requirements Specification) goes into more detail about the needs of the system and encompasses the configuration, software, and hardware specifications that are required for the intended operation and functionality of the infrastructure system. Once the requirements are documented, the build phase of the qualification process is initiated.

Build Phase:

During the build phase, the system and its components are assembled and interfaced, and a testing environment and strategies are developed as part of the system life cycle. A network diagram is typically developed, intended to help the user understand the interactions of different devices. An IT network diagram usually maps the direction of data flow from one device to another; for example, the internet is routed through the firewalls and to the network switch, which connects to the devices in the network, such as the servers, platforms, and operator workstations.

Testing Phase:

During the testing phase, installation of the system and operationality are verified and documented through Installation Qualification (IQ) and Operational Qualification (OQ) protocols, respectively.

IQ: Installation qualification ensures that all crucial elements of system installation comply with design specifications and manufacturer's guidelines. It documents evidence confirming that the system aligns with design drawings, supplier recommendations, and internal system design and configuration requirements. Additionally, the IQ test verifies the availability of all primary features as intended, bringing the system closer to its operational state.

Examples of IQ activities pertaining to IT Infrastructure include:

- *System/device make and model verification*
- *System software application specifications verification*
- *Operating temperature of the system verification*
- *Hard disk space for storage of data verification*
- *Random access memory (RAM) verification*
- *Operating system, processor verification*
- *Physical dimensions of the system verification*
- *Manufacturer specifications of the system (such as the number and type of ports)*
- *System's high availability verification*
- *System's firewall, network switch, servers, configuration (access control list, VLAN features) verification*
- *Power supply requirements verification*
- *Devices interface verification*

OQ: Operational Qualification involves a series of procedures aimed at guaranteeing the functionality and dependability of installed systems. It's a methodical approach that verifies and documents the proper functioning of the system's software, hardware, and related devices, ensuring they perform as intended and satisfy user requirements.

Examples of OQ activities pertaining to IT Infrastructure include:

- *Software application functionality testing*

- *User Access Control and system security operations testing*
- *Devices interface, connectivity, and data exchange testing*
- *Ingress/egress data and network data integrity testing*
- *Network high-availability testing*
- *Network throughput testing*
- *Data backup and restoration verification*

Operation Phase:

The operation phase includes the following activities, which are the final steps to be completed before the system is allowed to be operated in the production environment.

- The Trace Matrix (TM) tracks the user and functional requirements and traces them to the installation and operational tests that are associated with the respective requirement. A robust TM is an indication that the requirements are tested and (or) verified during the testing phase.
- The Summary Report summarizes the results of the IQ execution. It will document any test failures and deviations and detail how these events are being resolved. It will also decide if the system is fit for use.
- Standard Operating Procedures (SOPs) are developed and implemented for the administration, use, and maintenance of the systems. Administrators and end users are trained in the system to ensure that the system is operated and maintained in a controlled manner.

Moving Forward

Though the principles and guidelines surrounding the IT qualification process are very robust, interpreting and implementing GAMP5 and 21 CFR PART 11 guidelines are where most projects falter. Emphasis on testing low-value attributes, focusing on too many testing activities, ambiguity during requirements generation, and producing unnecessary documentation are some of the key reasons for IT qualification not being effective.

IT qualifications are a necessary and important step to ensure your systems are safe and operating as intended. Focusing on the quality of the computer software/infrastructure qualification will contribute to a quality-focused culture. This allows compliance to become a by-product of the culture, embedding it into the organization.

Selecting a consulting partner who can support you through these quality-focused validation and qualification activities is a great way to get started. To learn more about Clarkston's validation and qualification services, please contact us today.