Honeywell

Managing Validation

Paperless Recorders

Multitrend Plus

Validation Background

The past five years has seen an increase in the use of computerized systems and products in the pharmaceutical and bio-pharmaceutical industries that incorporate electronic data recording. Computer controlled instruments, which operate in regulated environments, must comply with requirements of good practices such as Good Manufacturing Practice (GMP) and FDA guidelines for Electronic Records and Electronic Signatures (21 CFR Part 11). However, the ultimate responsibility for ensuring compliance to current regulations lies with the end user and involves going through the steps of doing a process validation.

Validation is defined as: *the procedure of establishing documented evidence that provides a high degree of assurance that a specific computer related system will consistently operate in accordance with a pre-defined specification*.

Validation is a complex, time-consuming procedure involving different qualifications of equipment. It is a compilation of standard operating procedures and standard test procedures, which are complementary to each other; with each consisting of a number of sub-procedures:

Standard Operating Procedures (SOP)

- Installation Qualification (IQ)
- Operational Qualification (OQ)
- Performance Qualification (PQ)

Standard Test Procedures (STP)

- Process Description
- Risk Analysis
- Data Evaluation and Documentation

Processes are validated and equipment is qualified. The user is responsible for documenting all levels of qualification.

One of the inherent problems in developing a plan for process validation is that various stakeholders of the process can have different views and objectives. The key issues typically encountered with validation center around reproducibility and performance.

Process Validation

In essence, process validation should provide evidence of control (i.e. the process does what is intended given a known stimuli). Qualification assures that an instrument performs its task consistently according to specification and within the process environment where it is being used. Validation goes beyond just the instrumentation level and includes the validation of the process to insure that the process delivers a safe and effective product to the market. Instruments can be supplied as "validated", in the sense that the vendor has verified in-house that his instrument conforms with and functions according to its specification. Regardless of how the equipment is qualified, the FDA expects the pharmaceutical producer to take on the ultimate responsibility for the instrument and system validation, and uses this documentation to gain approval of the acceptance of the end product. This is one of the important ways to assure the safety and effectiveness of a drug or pharmaceutical product. From a regulator's perspective, time and money are of little or no importance – the focus is on the quality and safety of the product when used by the consumer. From a pharmaceutical company's perspective, these issues are critical to them for the same reasons, however time and money are key business drivers.

Equipment Qualification

Equipment qualification is the process of ensuring that an instrument (or system) such as a paperless recorder is appropriate for its intended use. Systems cannot be delivered "pre-approved", because of the unique characteristics of each production site environment. Slight variations in temperature, humidity, voltage, as well as different operators, can affect the equipment's performance. Qualification is commonly broken down into design, installation, operational and performance qualification.

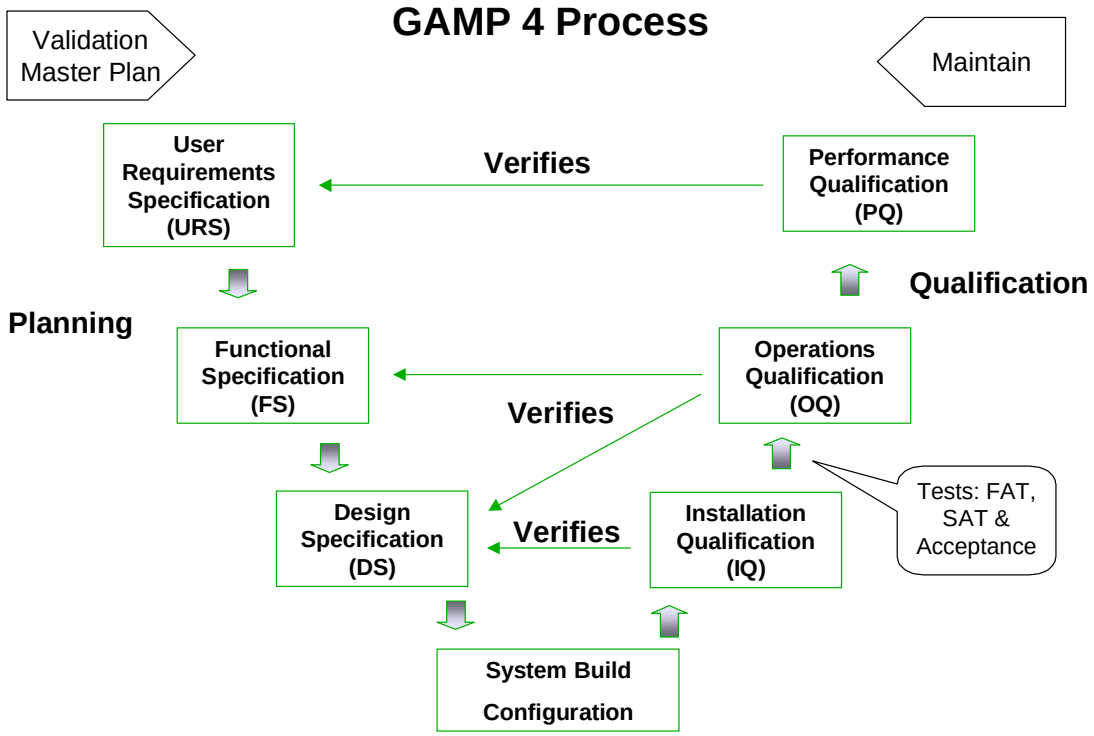
A well-organized approach to equipment qualification projects is crucial for success. A well-defined strategy should include:

- a validation plan
- defined responsibilities for documentation and procedures
- cross-functional teaming
- user (operator) input in the qualification protocol

It is critical to have a consistent approach to the overall project execution at the highest level of the company, meaning that there is a specific quality management system in place that supports the qualification process. This ensures consistency and efficiency when carrying out the development and execution of validation projects.

The Master Validation Plan should be an overview of the entire validation operation, including its organizational structure, content and planning.

The most recent version of GAMP 4 provides the following guideline for the overall validation process:



FAT = Factory Acceptance Test
SAT = System Acceptance Test

The Master Validation Plan should include: a statement of the validation policy, definition of the scope of the validation, identification of key acceptance criteria, description of the plant/process/product, identification of resource planning and information on the validation organization, description of the change control process, training needs, schedule, and a risk analysis. Keep in mind, the failure to build a plan is planning to fail!

The Validation Plan elements include:

User / Functional Specification (URS and FS)

- description of system functionality
- describes the "What" of the system
- enables ease of system change control (impact of change)
- guidelines for product additions or deducts
- enables traceability

Design Specification (DS)

- provides detailed design of the individual system (as well as global system)
- describes the "How" of the system
- serves as the enabler for Operational Qualification and testing
- provides for ease of system change control

Installation Qualification (IQ)

- detailed commissioning procedures to enable repeatable process
- clear identification of calibration, SOP and training needs and Maintenance Guidelines
- serves as procedure and documented proof for qualifying the entire system

Operational Qualification (OQ)

- documented procedures for key operational function tests, including security
- documented procedures for system integrity tests to functional and detailed design specifications
- documented procedure for alarms and global system functionality

Performance Qualification (PQ)

- defines standard operating procedures (SOP) for setting-up trend logs to monitor system performance
- SOP for logging alarms and taking corrective actions to maintain system performance
- Supports ongoing performance tests to ensure that the system is maintained in a validated state

Installation and operational qualification phases are performed at the user's site. The installation qualification verifies that the product was installed correctly. For operational qualification, the product is tested in the specific application in which it is used.

In general, regulatory authorities (i.e. FDA) do not approve the system or instrumentation, but inspect the application in which the product is used and offer an opinion. Any data that is submitted to the FDA for review must be from a validated system. They serve as a watchdog to protect the safety of the consumer.

Honeywell's Participation in the Validation Solution

Pharmaceutical companies must satisfy their own management's requirements for cost-efficient validation, production and analysis while assuring the FDA that they are producing safe product for consumption. The validation management strategy must cover all stages of the process, from the concept phase to full-scale production. Without vendor input on how their instrumentation performs, qualification protocols can end up being too general – details are missing due to missing links in the knowledge base of product operation and performance. Instrument vendors, such as Honeywell, can provide system knowledge and installation and maintenance experience, which help the end user achieve cost efficiency, reduce validation project time, and help accelerate start-up and time to market.

Honeywell provides an Installation and Operational Qualification Protocol product *(part #51452180-501)* for its Minitrend and Multitrend Plus paperless recorders to aid this process. This protocol document serves as an IQ/OQ template and provides documented verification that all aspects of the equipment installation adhere to the manufacturer's recommendations, appropriate safety codes, and approved company specifications and design intentions.

To ensure proper installation of the paperless recorder components, Honeywell's IQ/OQ Protocol documentation establishes the test procedures, specific responsibilities, and acceptance to provide evidence that:

- hardware has been installed according to manufacturer specification
- hardware has been configured in accordance with user requirements
- software has been installed according to the manufacturer specifications
- software has been configured in accordance with user requirements
- recorder operates in accordance with manufacturer and user specifications

Honeywell can also provide Validation and Conformance Services, which can help manufacturers of pharmaceutical and bio-pharmaceutical products establish evidence that their systems perform as expected. Honeywell's globally qualified and experienced personnel deliver Validation consulting, System Design, Engineering, System Maintenance and calibration. Validation services can include all or parts of the following:

- assistance with Master Validation planning
- vendor qualification
- gap analysis for validation and 21CFR11 compliance
- development of validation protocol, which includes;
  - writing the user Requirements Specification
  - writing the Functional Specification
  - writing the Detailed Design Specification
  - Installation Qualification and Operational Qualification
  - Performance Qualification
  - Change Control guideline development
  - Backup and Recovery plan development
  - Training Requirements and Testing Procedure development
  - Maintenance plan development

It is extremely important to have a strict validation management strategy in place, which addresses all of the important issues – supplier, compliance with regulations, and staff training. All of these directly affect the end product's development cost and quality.

For information about Honeywell:

- Validation support/services: 800-223-8947 or email servicesales@honeywell.com

- Paperless recorder information can be found at: www.honeywell.com/imc/pi/recorders