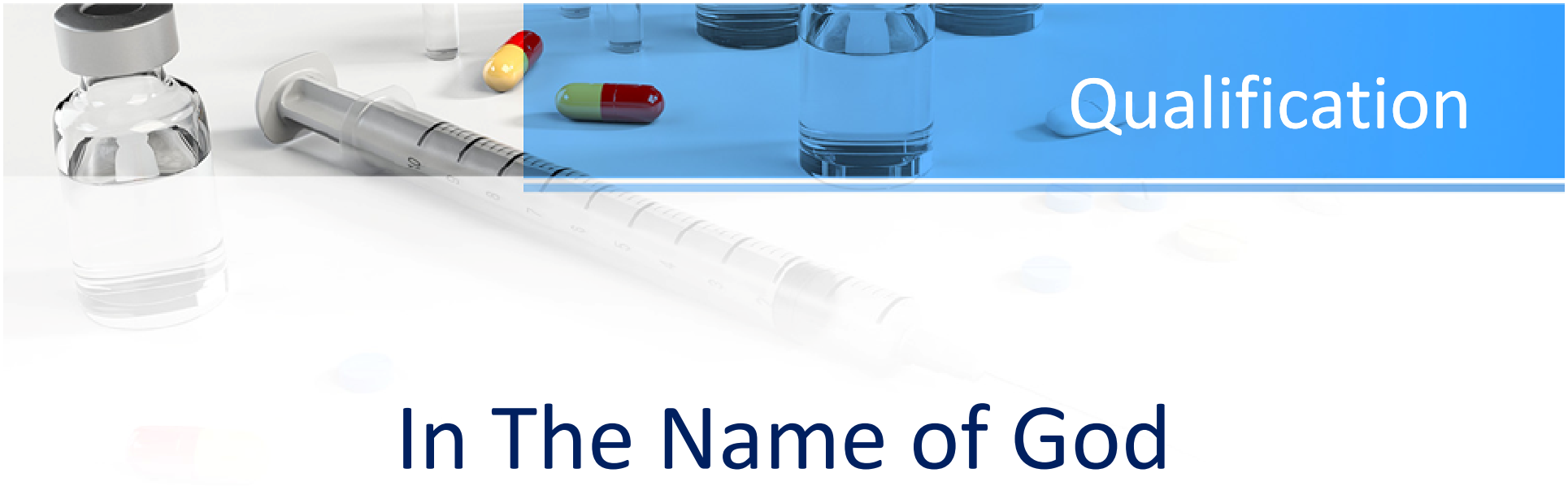


Qualification

In The Name of God

Qualification

Definition:

- Essential part of GMP
- Validation/ Qualification is the process of establishing documented evidence that a process, system and/or equipment when operated within established parameters, can perform effectively and reproducibly to meet pre-determined specifications and quality attributes.
- Documented evidence of suitable operation and performance of equipment, utilities , …
- Validation
- Calibration

Qualification

- The purpose of qualification is to gather documented evidence demonstrating that critical process equipment, critical supporting utility services, and processes are reliable and reproducible.
- A complete qualification package will consist of a Qualification/Validation Master Plan, Installation Qualification (IQ), Operational Qualification (OQ) and, as appropriate Performance Qualification (PQ) Protocols.

Qualification

- A master plan will be prepared for each new facility. An IQ and OQ will be prepared for all services and equipment, while a PQ will be prepared only for those systems or processes that require performance data for verifying proper operation.

Qualification

- All facilities, equipment, and services will be tested using methodologies and acceptance criteria described in pre-approved Validation Protocols. A sequential approach will be taken to ensure timely start-up and effective process implementation.

Qualification

- All activities impacting facility start-up will be scheduled to prevent the need for repeat studies, or invalidation of subsequent studies.
- The sequential approach requires that services and equipment scheduled for qualification/validation are mechanically complete.

Qualification

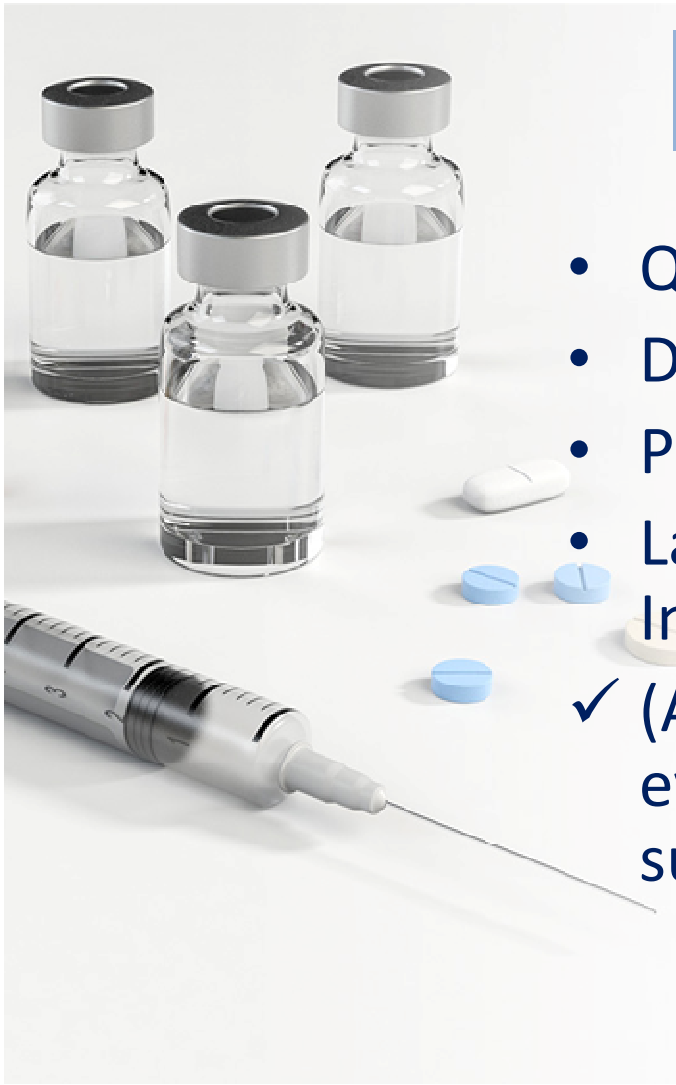
- The documentation will be generated in a sequential manner that is compatible with the execution of the qualification/validation program.
- Some tasks may be undertaken simultaneously while others must be completed prior to undertaking subsequent tasks.
- Deviation or Discrepancy reports will be prepared to document failures to met specifications.

Qualification

- A final report will be prepared to summarize the qualification effort.
- Qualification/Validation is not a "one time" exercise.
- After initial qualification, the system will be under scrutiny in the Change Control system.

Qualification

- Revalidation of all critical systems and equipment is required on a routine basis, as well as after significant maintenance or modification.
- The frequency of revalidation will be based on equipment, system, or process performance, a periodic revalidation schedule, and change control records.



Qualification

- QMP (Qualification Master Plan)
- DIOPQ
- Personnel (QP)
- Lab Instrumentation (Analytical Instrument Qualification) (AIQ):

✓ (AIQ is the collection of documented evidence that an instrument performs suitably for its intended purpose).

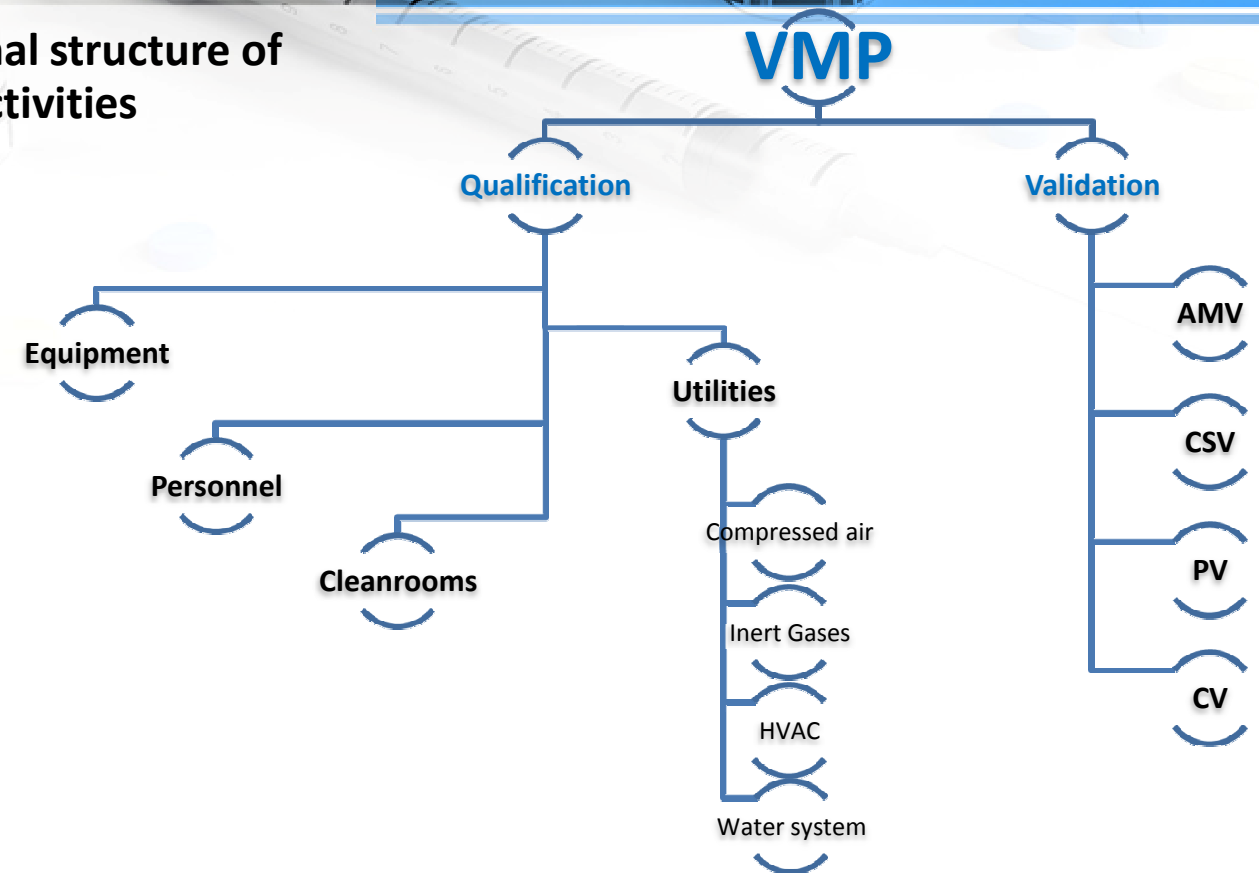
Qualification

- Critical Utilities (HVAC & Water System)
- Equipment
- Utilities (CA, IG,…)
- Clean Rooms

Qualification

- Stability Chambers, Refrigerators, Freezers, Autoclaves,…
- Software (ERP, MRP, MRP2)
- Suppliers
- Temperature Mapping
- Packaging
- Shipment (Shipping Qualification)
- Monitoring (EMS)

Organizational structure of validation activities



Qualification

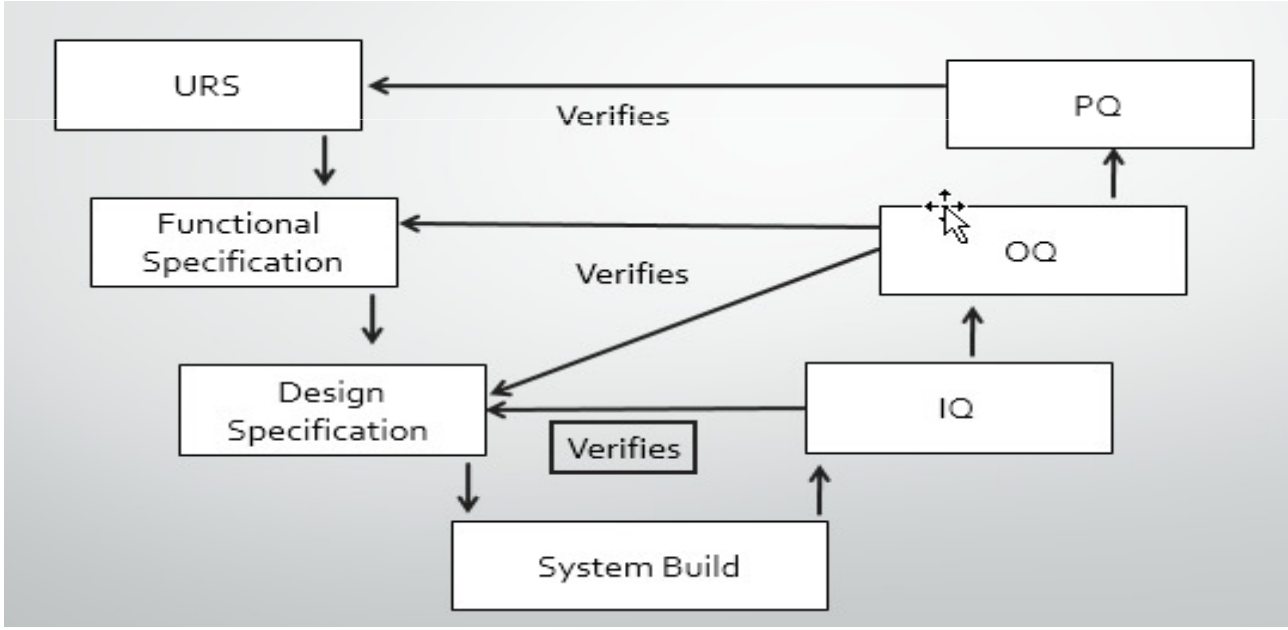
- **Qualification = Project management**
- Define good Team-Members, experts where needed
- QA, Engineer, technician, system owner
- The team determines your success
- Approach: planning, doing and reporting
- Using professional project management Tool (MS-Project)
- Define milestones
- Arrange periodical status-meetings

Qualification

URS

- Is generated by the purchaser for the purpose of specifying the user requirement for the equipment.
- Provides the user through the important components, variables and options necessary to purchase the equipment that meets the user's need.
- The URS is provided to the supplier to provide a price quotation.

Specification And Qualification



Qualification

Critical role in all project phases

Factory Acceptance Testing

- Takes place within the supplier's facility
- The goal is to identify deficiencies, variances, or changes that require correction before the unit leaves the supplier.
- Benefit – the purchaser knows that the equipment is constructed and/or functions as intended within the factory environment.
- Due to the complexity of the equipment, FAT may cover a fraction of the desired tests. (Dry test only).

Site Acceptance Testing

- SAT takes place at the production site
- It can be more extensive that FAT
- Wet tests will be performed during SAT
- During SAT, many of the operational tests must be moved to the site due logical concerns: for example; a mismatch or insufficient utilities between the supplier and the site.

Commissioning

- Is the final step before the equipment is turned over to an owner
- Is completed and documented via GMP documents – The SAT not
- It is more appropriate that simple mechanical changes to be done outside of the validation chance control process.

IQ and OQ

The basic principles are:

- equipment be correctly installed in accordance with an installation plan
- requirements for calibration, maintenance and cleaning be covered in approved SOP's
- OQ tests be conducted to assure that equipment is operating correctly, under normal and "worst case" conditions
- Operator training requirements pertaining to new equipment be conducted and documented.

Installation Qualification (IQ)

- I.Q. is the method of establishing with confidence that all major processing, packaging equipment and ancillary systems are in conformance with installation specifications, equipment manuals, schematics and engineering drawings. This stage of validation includes examination of equipment design, determination of calibration, maintenance and adjustment requirements.

Installation Qualification

- Material of Construction
- Spare Parts List
- Instrument List
- Design Features
- Configuration of Components
- Installation Requirements
- Codes
- Drawings
- Peripheral Equipment

Operational Qualification (OQ):

- The conduct of an Operational Qualification should follow an authorized protocol. The critical operating parameters for the equipment and systems should be identified at the O.Q. stage.
- The plans for the O.Q. should identify the studies to be undertaken on the critical variables, the sequence of those studies and the measuring equipment to be used and the acceptance criteria to be met.

Operational Qualification

- Standard Operating Procedures
- Cleaning
- Operation & Maintenance
- Calibration of Devices
- Peripheral Functioning
- Chart Recorder
- Mixer
- Computer Software/Hardware
- Alarm Verification
- Controls Operation Verification

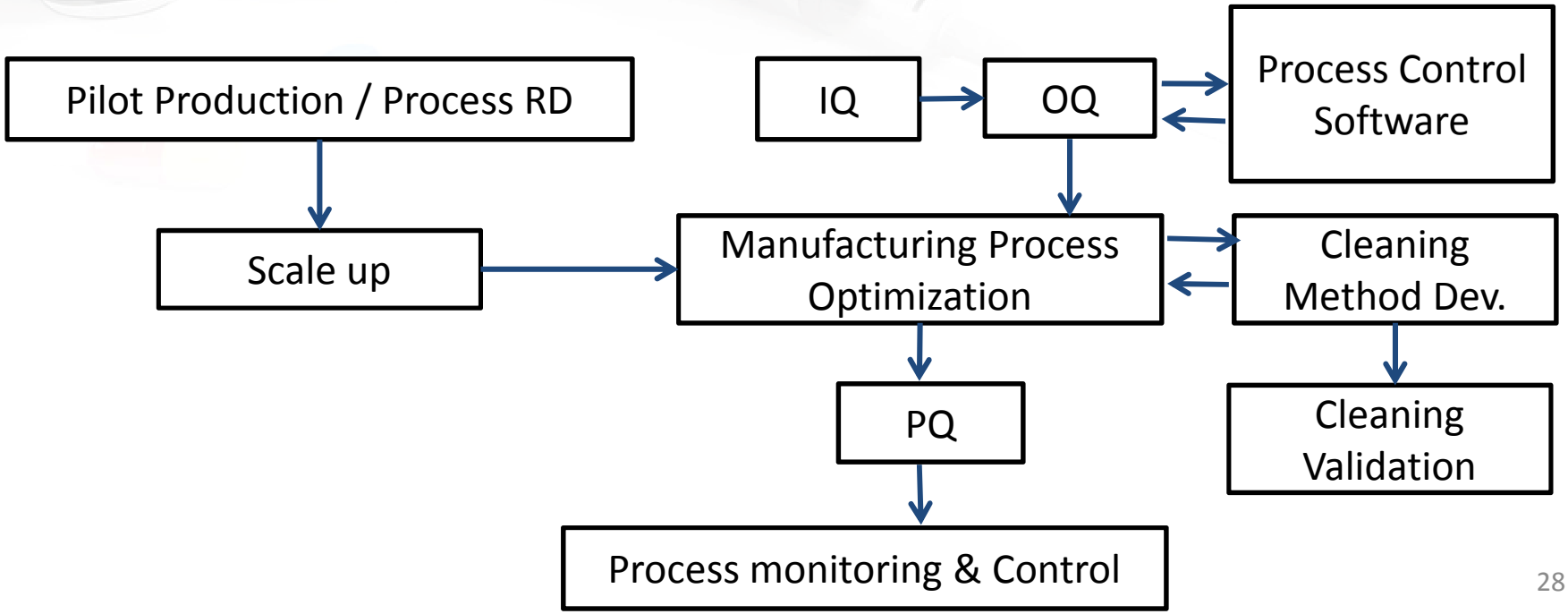
Performance Qualification (PQ)

- PQ is a documented plan for the execution of tests to demonstrate the effectiveness and reproducibility of a system/process as a fully integrated functional entity.

PQ Requirements

- Standard Operating Procedures
- Utilities and Equipment Qualified
- QA Assurance Program In-place
- Raw Materials Qualified
- QC Test Methods Qualified
- Calibration Program
- Environmental Monitoring

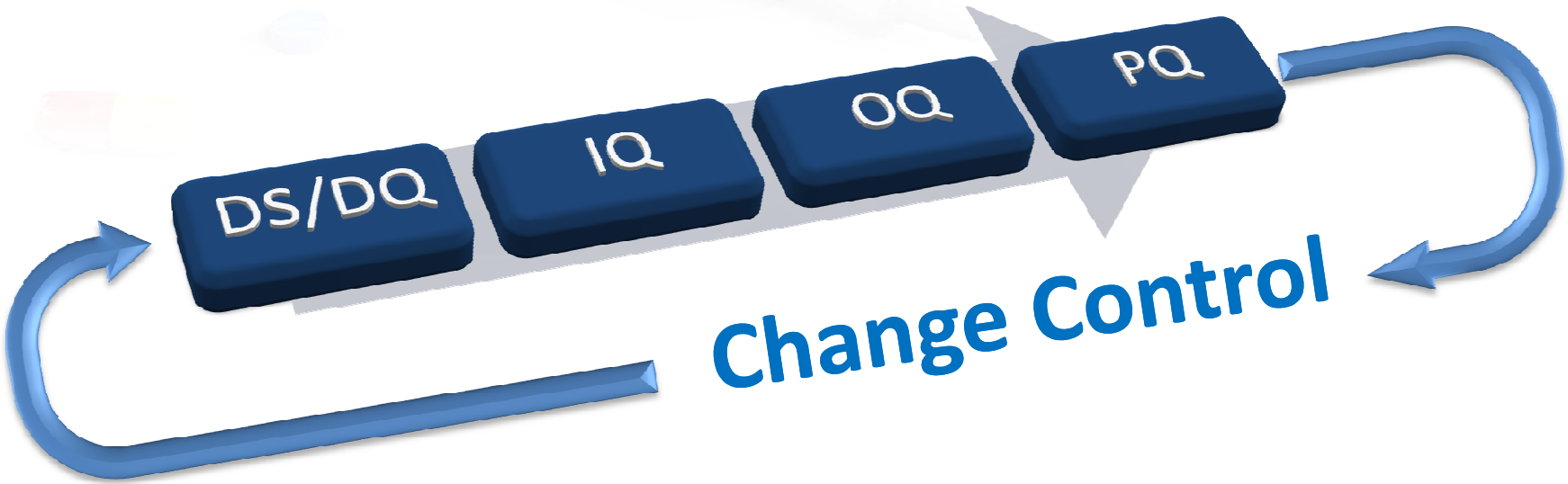
Process Qualification Flow



Re-Qualification:

- Modifications to, or relocation of equipment should follow satisfactory review and authorization of the documented change proposal through the change control procedure. This formal review should include consideration of re-qualification of the equipment. Minor changes or changes having no direct impact on final or in-process product quality should be handled through the documentation system of the preventative maintenance program.

Qualification



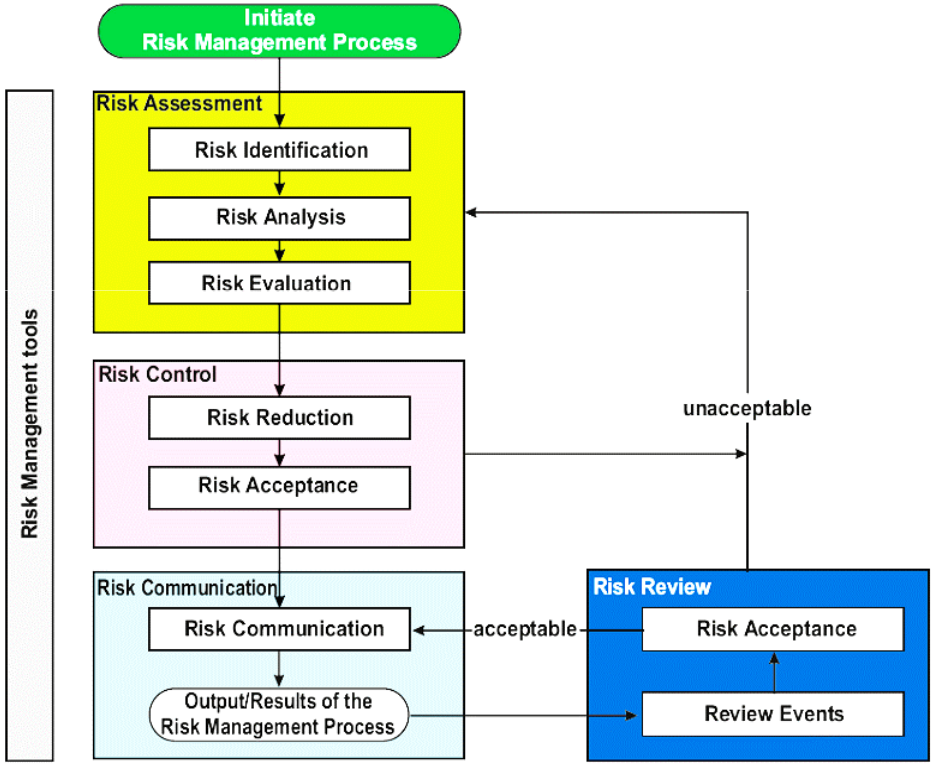
Qualification

- Validation/ Qualification incorporates good documentation practice, good engineering practice, and sound scientific analysis coordinated by effective project management practices.

Qualification

- Practical implementation of GMP requires a risk-based approach to validation and qualification.
- This will direct effort and resources to controlling the parameters that have the potential to have a significant impact on product quality.
- The validation/qualification requirements of each system and/or equipment should be determined by assessment of the potential impact of that system on the quality of the product and the inherent risk of system failure, in addition to requirements mandated by Regulatory Authorities.

QRM



ICH Q9: Quality Risk Management

QRM (Quality Risk management)

- Cause and Effect
- Fault Tree Analysis
- Hazard Analysis and Critical Control Point (HACCP)
- Failure Mode and Effect Analysis (FMEA)

Risk Assessment Tools

- **Cause and Effect:**
- Cause-and-effect diagrams are used to systematically list the different causes that can be attributed to a problem (or an effect). A cause-and-effect diagram can aid in identifying the reasons why a process goes out of control.

Risk Assessment Tools

Creating Fishbone Drawing

1. Identify a quality problem
2. Generate causes
   - brainstorming
3. Construct the fishbone Diagram
   - Use check sheets and Pareto charts to identify root causes (e.g. material, machine, measurement, methods, men) and secondary causes

Risk Assessment Tool

Fault Tree Analysis

- A fault tree analysis (FTA) is a deductive, top down method of analyzing system design and performance.
- It involves specifying a top event to analyze (such as a sterilization process), followed by identifying all of the associated elements in the system that could cause that top event to occur.

Risk Assessment Tools

Hazard Analysis and Critical Control Point (HACCP)

- HACCP is a management system in which product safety is addressed through the analysis and control of biological, chemical, and physical hazards from raw material production, procurement and handling, to manufacturing, distribution and consumption of the finished product.

Risk Assessment Tool

Failure Mode and Effect Analysis (FMEA)

- Potential Failure Mode and Effect Analysis (FMEA) have recently emerged as a powerful tool for avoiding costly product performance failures.
- Both product/design FMEA and process FMEA can help you improve product reliability and reduce design and manufacturing costs. FMEA is a bottom up approach to failure mode analysis .

Risk assessment Tool

Following are the basic steps required to do a FMEA:

1. Select a team and brainstorm
2. Create or review and update a flowchart
3. Set priorities - What's important?
4. Collect data
5. Analysis for effects, controls, occurrence, detection, and severity
6. Results – quantify
7. Measure and confirm
8. Repeat for continual improvement

Risk Assessment Tools

Types of FMEAs:

Design FMEA

- Design FMEA is used to analyze product design before they are released to manufacturing. A design FMEA focuses on failure modes caused by design deficiencies.

Process FMEA

- Process FMEA is used to analyze manufacturing processes.
- A process FMEA focuses on failure modes caused by deficiencies or potential problems with the actual process.


Thank You