QUALIFICATION OF AN ISOLATOR FROM A QUALITY PERSPECTIVE

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WHAT IS AN ISOLATOR?

Isolators are routinely found within the pharmaceutical industry for aseptic operations

They are designed to provide continuous and complete isolation of the inside of the isolator from the external room environment (including its operators). Only installed gloves or robotic arms are used to manipulate the product. This ensures that the environment is maintained as contamination-free to safeguard patients who will later be administered the drug. Isolators operate as positive-pressure devices, and use full wall separation and substantial overpressure to both physically and aerodynamically separate the interior from the external room environment.

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QUALITY ASSURANCE (QA) HAS AN INTEGRATED ROLE FROM INITIAL REQUIREMENTS TO SYSTEM IMPLEMENTATION

- Validation Program
- User Requirements
- Supplier assessments
- Design review
- Commissioning
- PQ of the system
- Periodic monitoring
- Lessons Learned

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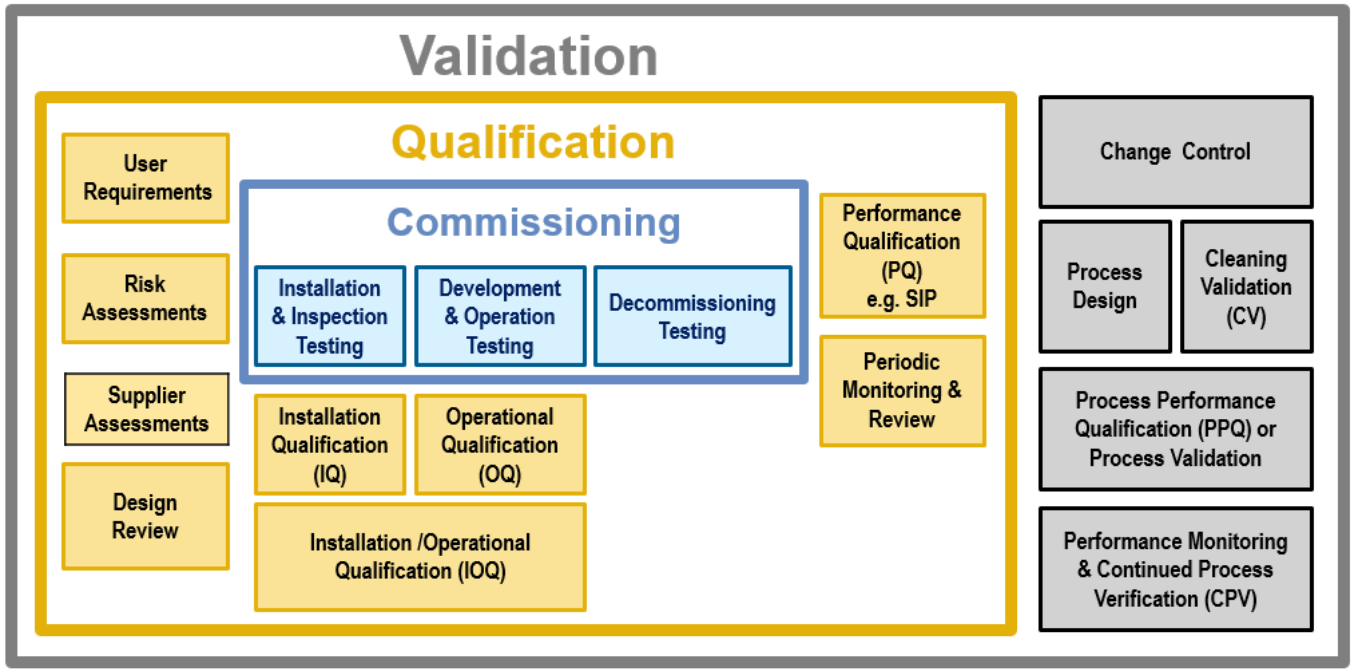
A STRATEGIC OVERVIEW OF THE COMMISSIONING, QUALIFICATION, AND VALIDATION (CQV) PROGRAM



- Engineering Owns Commissioning
- Manufacturing Owns Post-Commissioning Activities
- Process Development Provide Key Process Parameters
- Quality has Oversight Responsibilities

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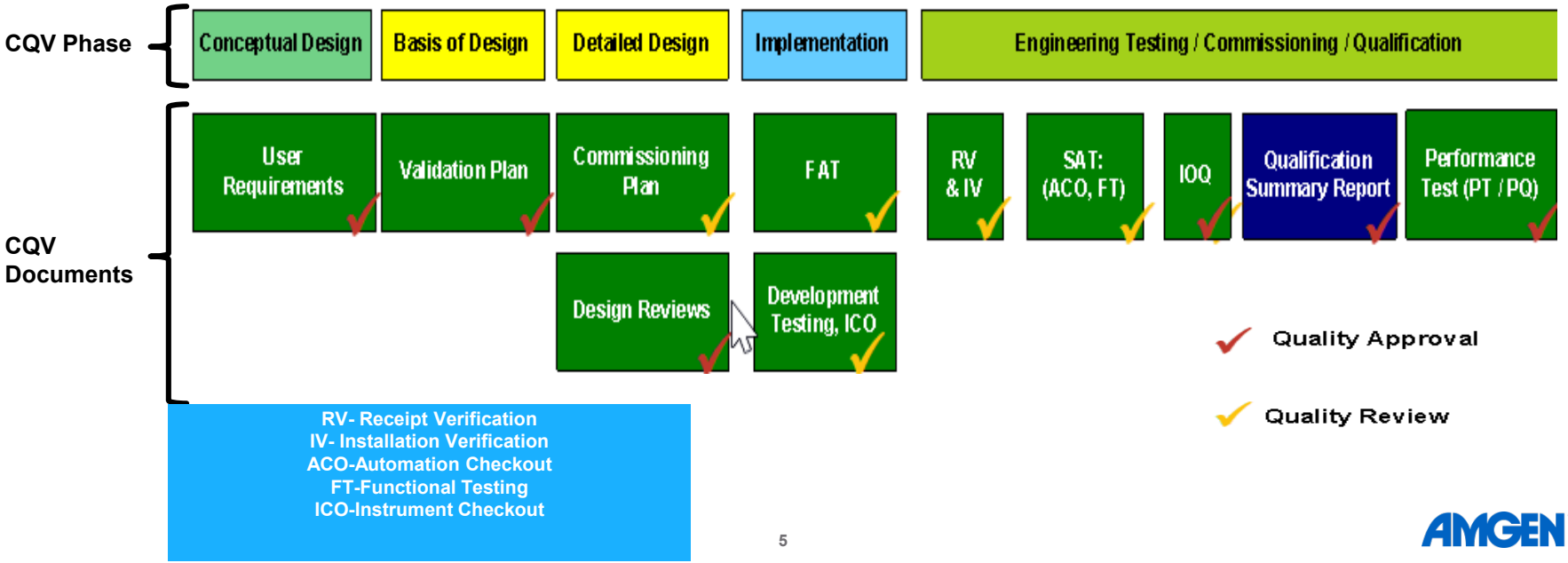
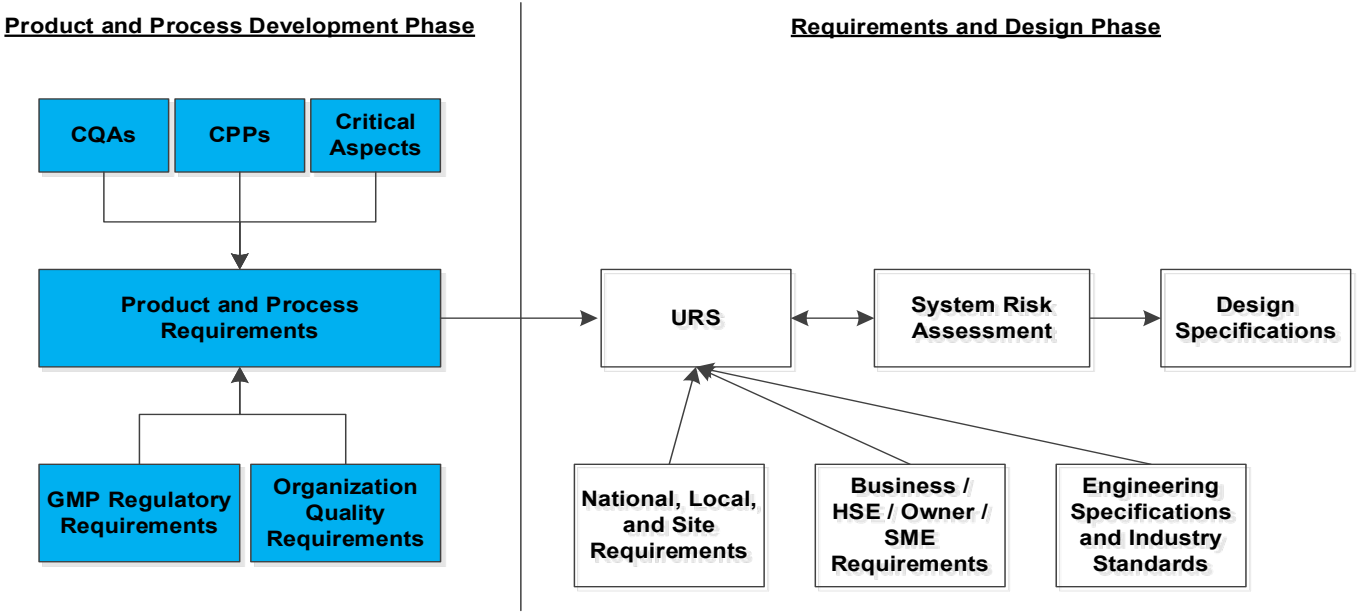
QA CONFIRMS THAT "CRITICAL QUALITY ATTRIBUTE" REQUIREMENTS ARE MET ACROSS THE CQV PROCESS

This Diagram shows fit for purpose Quality Engagement across the CQV documents



USER REQUIREMENTS SPECIFICATIONS (URS) ARE DEVELOPED FROM MULTIPLE DATA SOURCES



Use the URS to document Critical Quality Attributes (CQA) and Critical Process Parameters (CPP) and the source of those requirements

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SUPPLIER ASSESSMENTS EVALUATE CAPABILITY AND SUITABILITY

- **Supplier's Technical Capability - What other related project has the vendor performed in the industry?**
- **Engineering procedures - Managing drawings; specifications and engineering change control**
- **Quality Systems - What is the supplier's process for managing procedures and training?**
- **Supplier's Good Documentation Practices – are they sufficient?**
- **Post FAT Controls**

This must be performed when the project intends to use supplier documentation as evidence to support commissioning and qualifications

QUALITY RISK ASSESSMENTS DEFINE THE EQUIPMENT / SYSTEM RISKS AS THEY RELATE TO PRODUCT QUALITY

- Define the risk controls
- Define which instruments / alarms are critical with supporting rational
- Link required product process requirements to quality controls
- QA role is to mitigate identified “High” risks

Know your Risks

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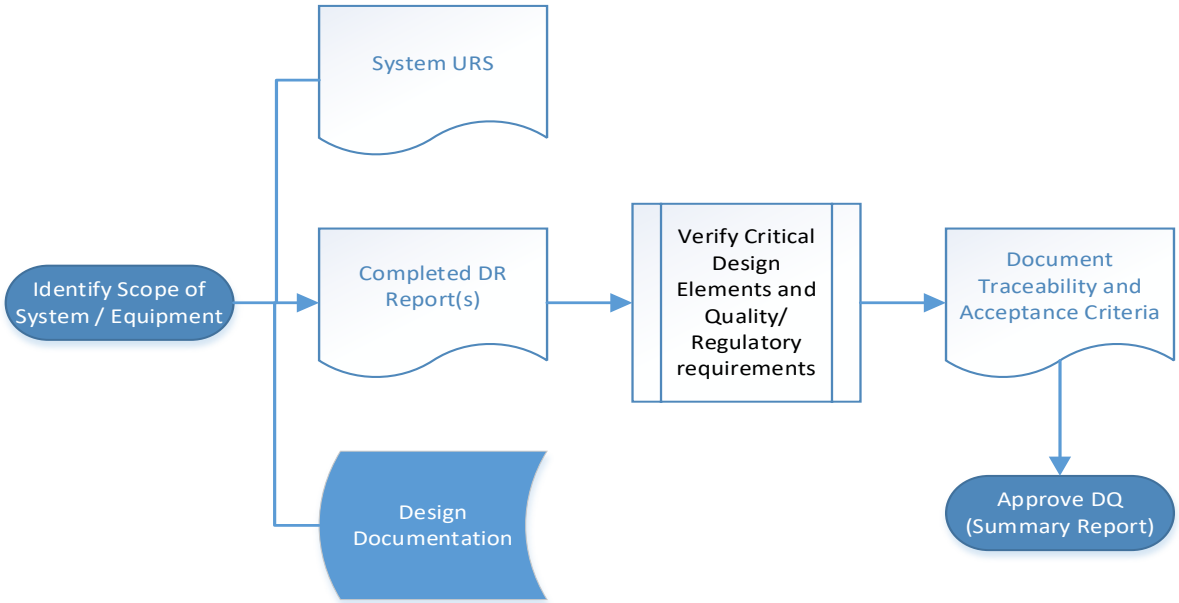
DESIGN REVIEW IS A KEY CROSS FUNCTIONAL REVIEW AND CONFIRMATION THAT REQUIREMENTS ARE INCORPORATED



- Ensure product, process, client requirements, design criteria, design standards and specs are incorporated into design documents
- Incorporate lessons learned from other projects
- Ensure all stakeholders review the design

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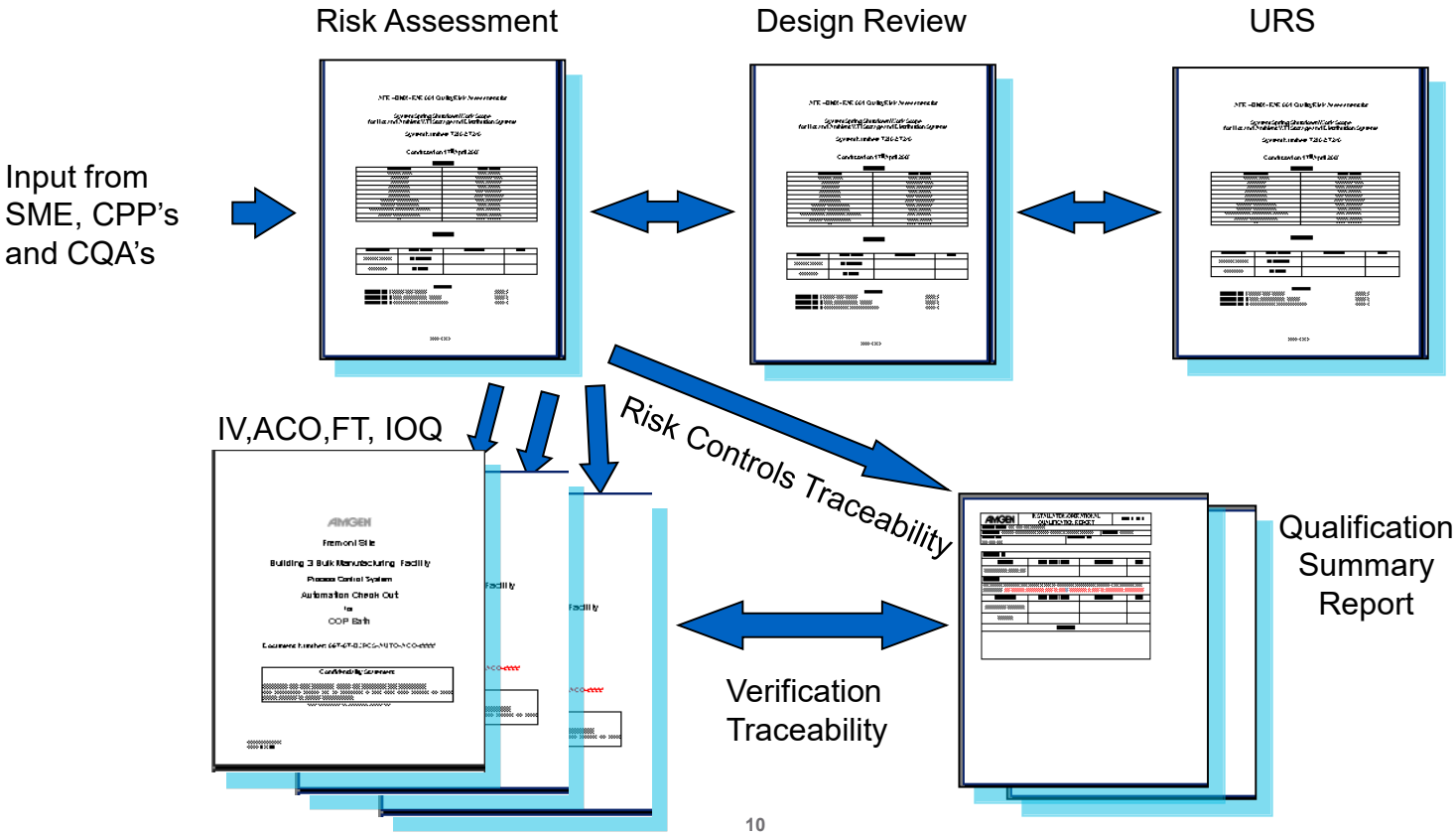
TRACEABILITY OF INFORMATION IS KEY ACROSS COMMISSIONING DOCUMENTATION



AIR VISUALIZATION STUDIES (AVS) DURING PERFORMANCE QUALIFICATION

Water vapor fog is used to visualize airflow

- When “In operation” operations shall match actual operations, important to film interventions
- Areas demonstrating slight turbulence should have increased routine environmental sampling
- Lessons learned:
  - QA and Operations are present during filming and review footage real time
  - Ensure staff are proficient in the operation and trained before AVS
  - Watch the background, gowning, and overall clean room conduct
  - Assess AVS when making changes to the design, operation or planned interventions

PERFORMANCE QUALIFICATION OF ISOLATOR DECONTAMINATION DEMONSTRATES ASEPTIC CAPABILITY

- Cycles are developed to confirm decontamination capability prior to qualification runs
  - Temperature mapping
  - AVS results
  - Chemical Indicator mapping
  - Biological Indicator (BI) location
  - Network Experiences

BI Location Selection Technical Report

- Three consecutive successful runs are required
- 6 log reduction is required, thus termed “Decontamination”

PROCESS PERFORMANCE QUALIFICATION USES MEDIA AS A PRODUCT SURROGATE TO DEMONSTRATE ASEPSIS

- **Process Simulation (Media Fill) are performed in triplicate**
- **Bracketing of fill container sizes can be used, however rationale shall be provided when doing so**
- **All planned interventions should be performed**

Vials filled with media used to simulate an aseptic fill

THE PERIODIC MONITORING PROGRAM MAKES CERTAIN THAT REQUIREMENTS CONTINUE TO BE MET

- **A single yearly decontamination run shall demonstrate that the system shall continue to meet pre-established acceptance criteria**
- **Ensure Air Visualization Study videos are reviewed on a periodic bases and are reflective of current operations**
- **When making changes, make sure to assess all commissioning documents as well as any performance qualification documents**

Sustaining the validated state

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LESSONS LEARNED AND SHARED - WHAT DOES NOT WORK

- Lack of source requirements in URS's
- Being overly administrative, remember all requirements are traced back to source documentation
- Not having enough components to test during commissioning
- Not being clear as to when there are protocol exceptions versus protocol generation errors with the various client groups
- Commissioning Plans not having sufficient detail causing different interpretations

LESSONS LEARNED AND SHARED – WHAT DOES WORK

"Quality is Everyone's Responsibility"

- W. E. Deming

- QA staff involvement early in a project to learn technical details and system understanding
- There will be multiple hand offs of the system from vendors, process development staff, commissioning agents to eventual system owners, QA is a role that remains with the system from design to implementation
- During commissioning focus on technical issues and not on administrative issues, QA contributes to issue resolution
- Well developed cycles lead to qualification success
- Requirements traceability reports linking CQA's and CPP's are vital

SUCCESS HAPPENS THROUGH TEAMWORK WHEN QUALITY IS VALUED AND INTEGRATED FROM START TO FINISH

Thank you!

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