# Commissioning Qualification and Validation

*"A journey of a thousand Qualifications starts with a good URS"*

**Oct 2021**

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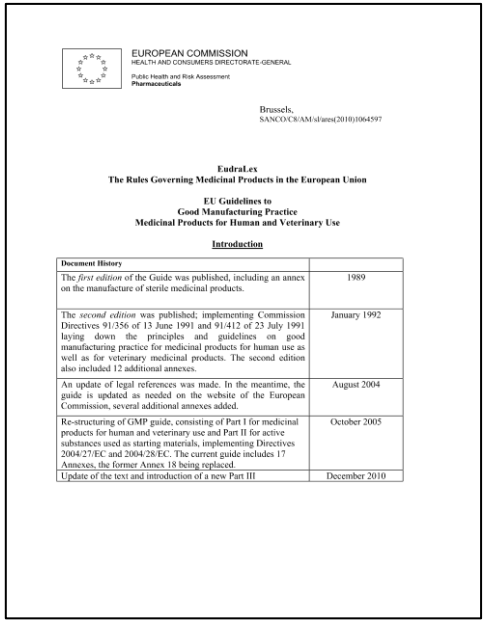
# What is Commissioning, Qualification & Validation?

- Commissioning, Qualification & Validation (CQV) is an integral part of the life sciences and pharmaceutical sector. It is a very detail-oriented process that requires the right mix of knowledge, experience and diligence to correctly place Facilities/Equipment/Utilities into use.
- The main difference between Commissioning and Q&V are the guidelines followed. Commissioning is an exercise made from a Good Engineering Practice (GEP) point of view. Q&V is an exercise made from a Good Manufacturing Practice (GMP) point of view.
- The objective of CQV process is to demonstrate that a system was designed, installed and **performs as per design requirements and/or for its intended use**:
    1. Ensuring the proposed design is **suitable for the intended purpose**;
    2. Verifying that it was **installed correctly** and as agreed with the contractor;
    3. Demonstrate that each parts **works as expected in the anticipated ranges of operation**;
    4. Guarantee that it can **perform as expected**;
    5. And assuring that it remains **under a state of control.**
- The criticality and impact of Facilities/Equipment/Utilities will determine the extent of the CQV activities. Non-critical Facilities/Equipment/Utilities will only require commissioning before being used, as they do not impact on quality.

# Where is it referenced?

**There are several regulatory bodies like European Commission, Food and Drug Administration (FDA) and Therapeutic Good Administration (TGA) that demand that CQV activities take place.**

## European Commission (Eudralex Vol.4)



EUROPEAN COMMISSION
HEALTH AND CONSUMERS DIRECTORATE-GENERAL
Public Health and Risk Assessment
**Pharmaceuticals**

Brussels,
SANCO/C8/AM/sl/ares(2010)1064597

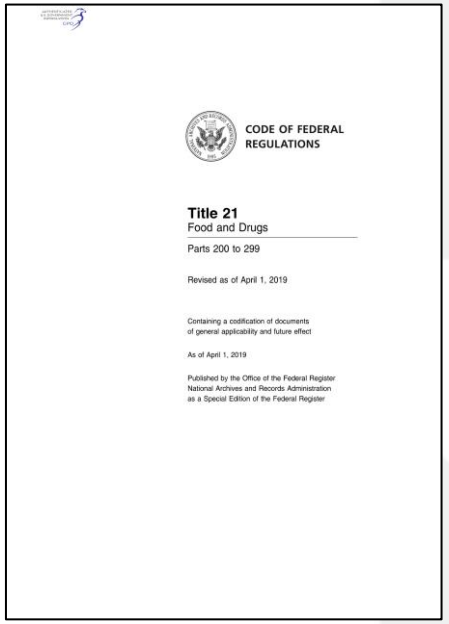
**EudraLex**
**The Rules Governing Medicinal Products in the European Union**

**EU Guidelines to**
**Good Manufacturing Practice**
**Medicinal Products for Human and Veterinary Use**

**Introduction**

| Document History | |
|---|---|
| The *first edition* of the Guide was published, including an annex on the manufacture of sterile medicinal products. | 1989 |
| The *second edition* was published; implementing Commission Directives 91/356 of 13 June 1991 and 91/412 of 23 July 1991 laying down the principles and guidelines on good manufacturing practice for medicinal products for human use as well as for veterinary medicinal products. The second edition also included 12 additional annexes. | January 1992 |
| An update of legal references was made. In the meantime, the guide is updated as needed on the website of the European Commission, several additional annexes added. | August 2004 |
| Re-structuring of GMP guide, consisting of Part I for medicinal products for human and veterinary use and Part II for active substances used as starting materials, implementing Directives 2004/27/EC and 2004/28/EC. The current guide includes 17 Annexes, the former Annex 18 being replaced. | October 2005 |
| Update of the text and introduction of a new Part III | December 2010 |

## Food and Drug Administration (FDA)



CODE OF FEDERAL REGULATIONS

**Title 21**
Food and Drugs

Parts 200 to 299

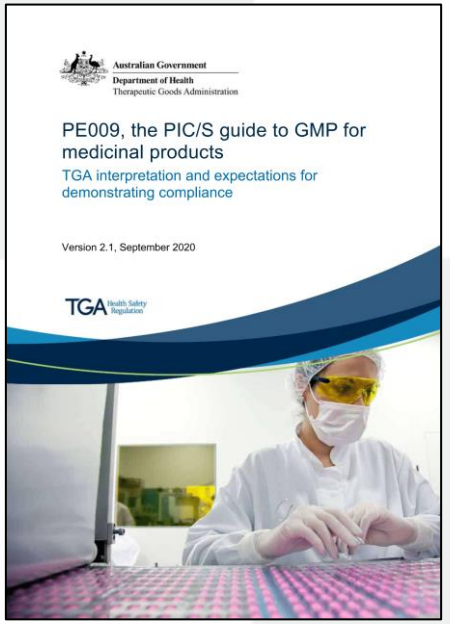
Revised as of April 1, 2019

Containing a codification of documents of general applicability and future effect

As of April 1, 2019

Published by the Office of the Federal Register National Archives and Records Administration as a Special Edition of the Federal Register

## Therapeutic Good Administration (TGA)



Australian Government
Department of Health
Therapeutic Goods Administration

PE009, the PIC/S guide to GMP for medicinal products

TGA interpretation and expectations for demonstrating compliance

Version 2.1, September 2020

TGA Health Safety Regulation

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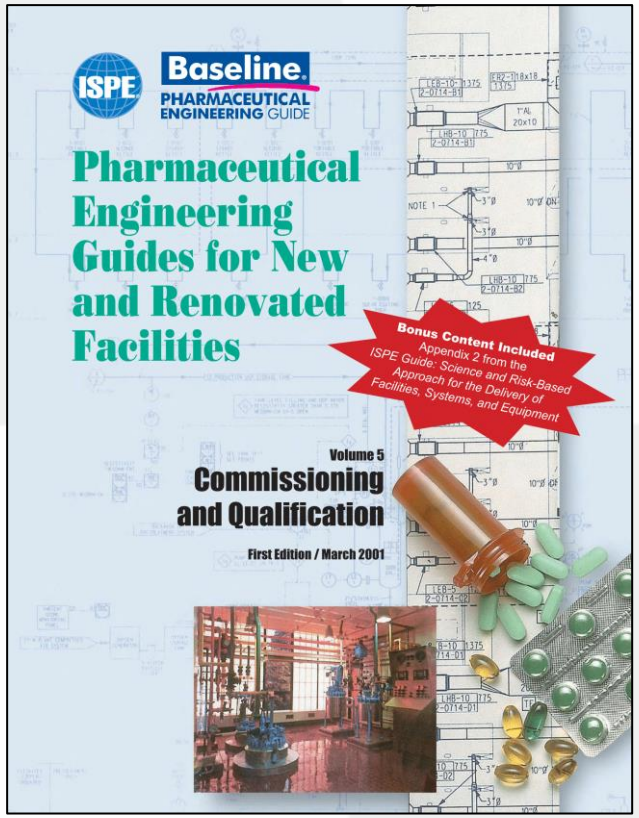
# Where can you find guidance?

**The International Society for Pharmaceutical Engineering (ISPE) has provided over the years several guidelines on how Qualification & Validation activities should be implemented.**

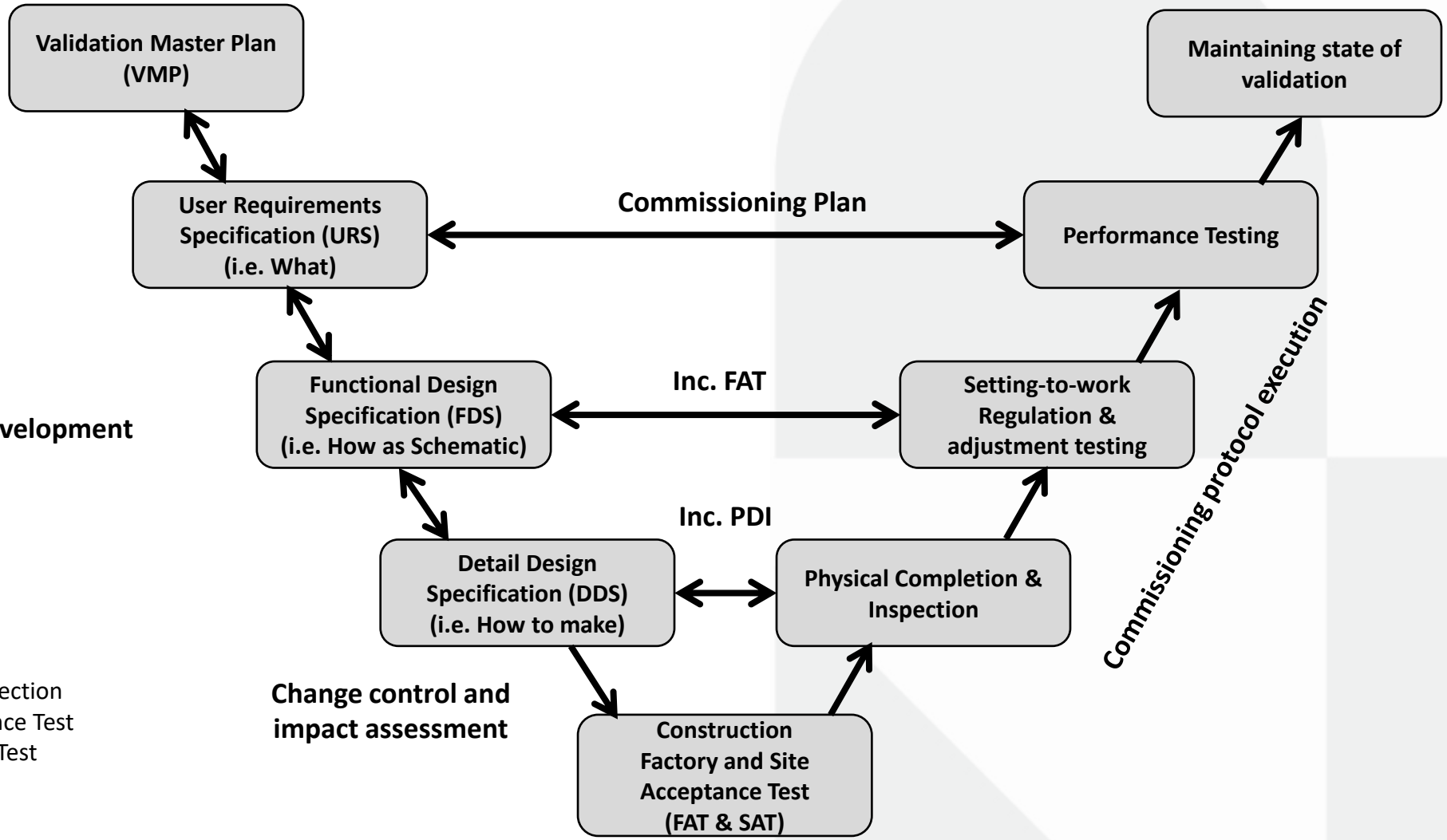
**International Society for Pharmaceutical Engineering (ISPE)**




- Within their guidelines, one of the most widely used Lifecycle Development models is the **"V" Model**, which is a framework or structure for undertaking the design, execution, commissioning and qualification of a design project. It was first promoted by the International Society of Pharmaceutical Engineers (ISPE) back in 1994 in the first edition of their Good Automated Manufacturing Practices guideline (**GAMP**).
- The **"V" Model** creates a solid basis for testing the functionality of the system against the original design specifications and proving that the delivered technical solution achieves the desired outcome.

# Lifecycle Development "V" Model

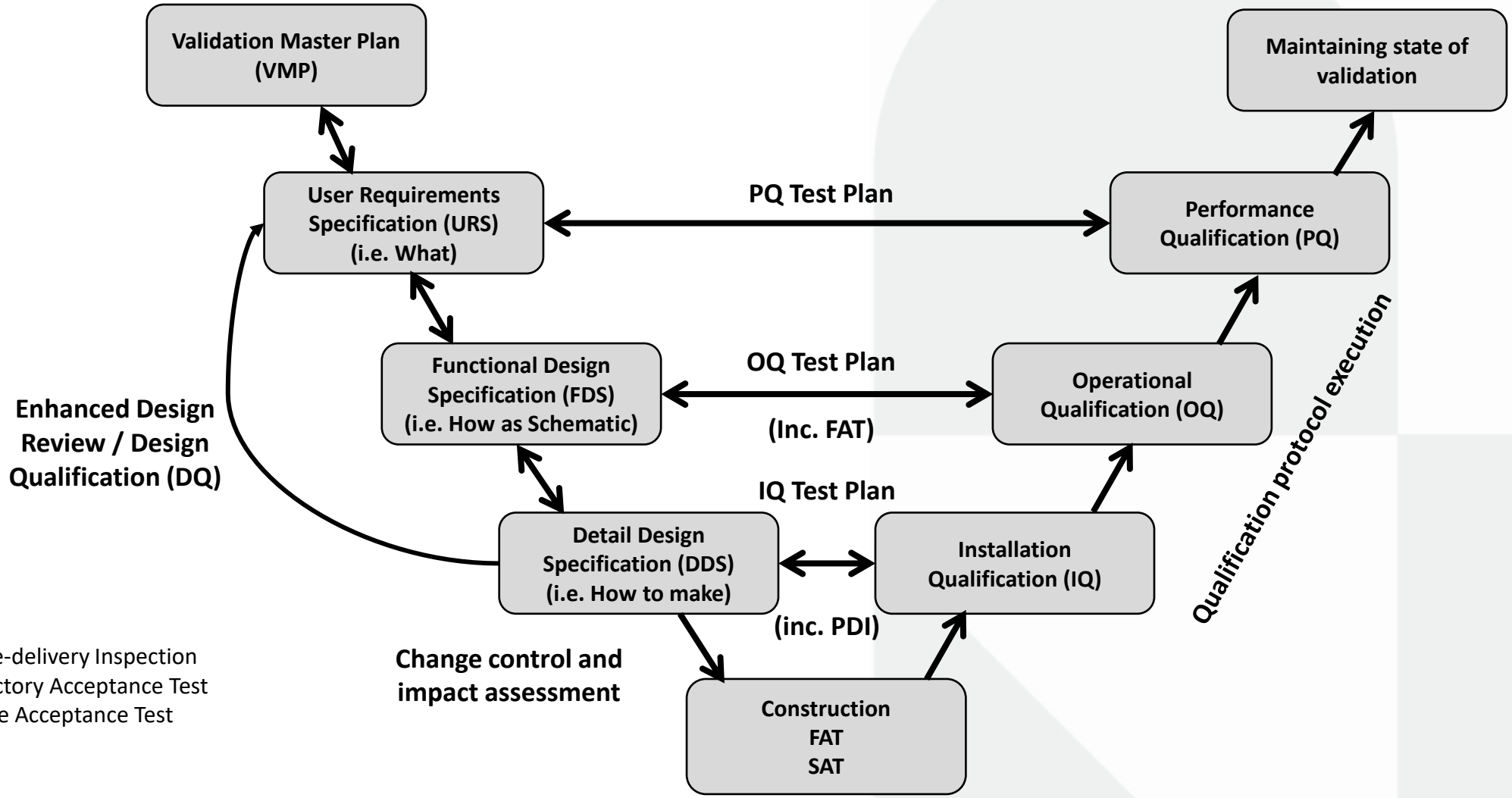
For Indirect Impact Systems - **Commissioning**




PDI – Pre-delivery Inspection
FAT – Factory Acceptance Test
SAT – Site Acceptance Test

# Lifecycle Development "V" Model

For Direct Impact Systems - **Qualification**




PDI – Pre-delivery Inspection
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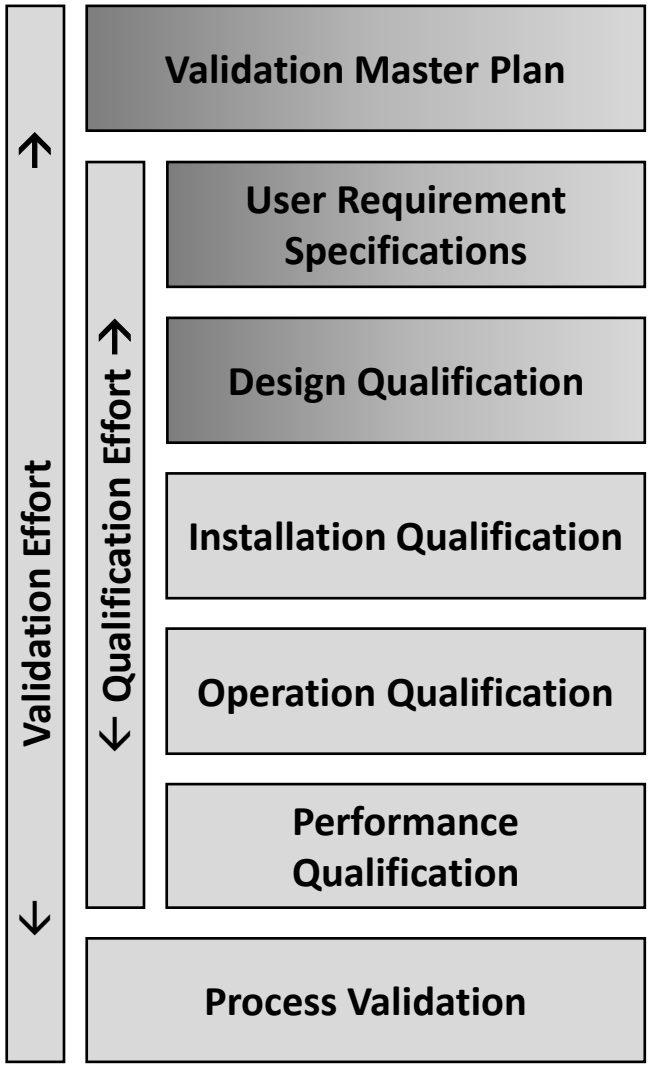
# Qualification & Validation Stages




**Validation Master Plan:**

The Validation Master Plan is a summary of the validation strategy and outlines, according to their criticality, which Facilities/Equipment/Utilities are to be qualified with the objective of validating the processes.

**User Requirement Specifications:**

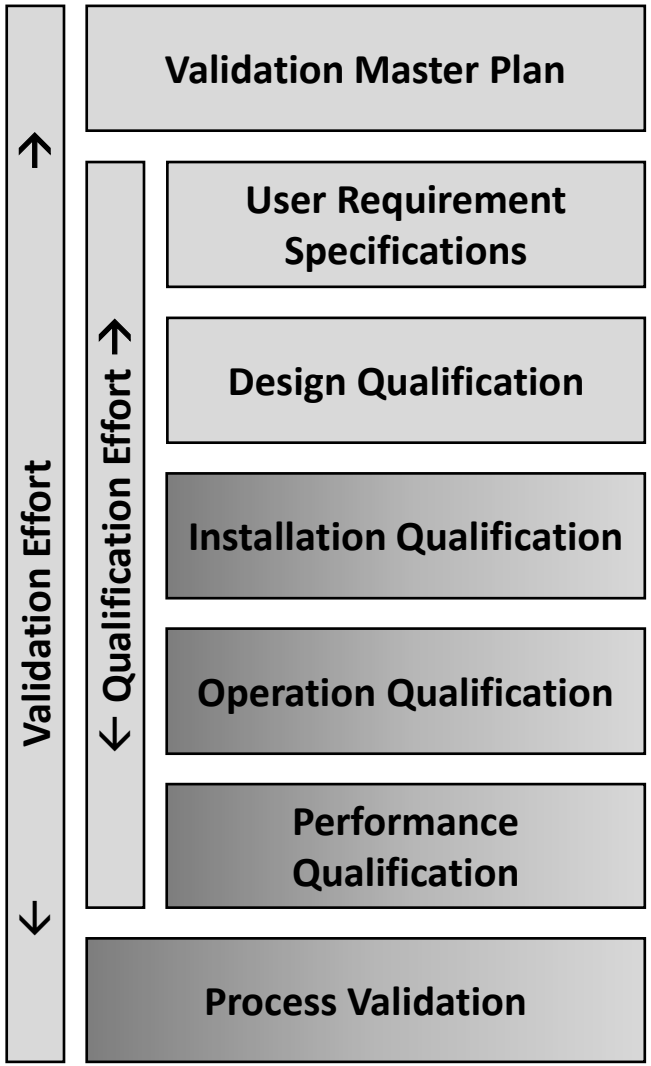
The User Requirement Specifications (URS) is a high-level document where a multidisciplinary team (e.g.: User, Owner, Engineering, Quality, etc.) defines the essential requirements to assure the system achieves its intended purpose.

At the specification stage, the URS preparation involves a risk assessment exercise focused on GMP risks specific to the equipment or system undergoing specification.

**Design Qualification:**

The documented verification that the proposed design of the facilities/equipment/system is “suitable for the intended purpose”.

# Qualification & Validation Stages




**Installation Qualification:**
The documented verification that the Facilities/Equipment/Utilities as installed or modified, comply with the approved design and the manufacturer's recommendations.
Typical tests include instrument criticality assessment, the verification of electrical drawings, piping and instrumentation (P&ID) diagrams, materials (direct contact parts), etc.

**Operation Qualification:**
The documented verification that the Facilities/Equipment/Utilities, as installed or modified, perform as intended throughout the anticipated operating ranges.
Typical tests include temperature and pressure control, charging and discharging operations, etc.

**Performance Qualification:**
The documented verification that Facilities/Equipment/Utilities can perform effectively and reproducibly based on the approved process method and product specification.
Typical tests may include an engineering batch.

**Process Validation:**
The documented evidence that the process, operated within established parameters, can perform effectively and reproducibly to produce a medicinal product meeting its predetermined specifications and quality attributes throughout the product lifecycle.
Operational control activities may include Maintenance, Calibration, Temperature Mapping, Load Qualification, Annual Clean Room Testing, etc.

# Key Takeaways

- **Qualification** and **Validation** activities are mandatory to comply with **GMP, Commissioning** activities are not. However, a robust commissioning strategy will ensure your facilities, equipment and utilities were installed adequately and are operating according to the specified conditions.
- The **User Requirements Specification** is a document that can be and should be used to its' full potential by procurement, engineering, quality, operations (i.e., lean improvements) and validation departments instead of "just another document to complete and file away".
- **A GMP Impact Assessment** is a crucial step for the **CQV** activities because it distinguishes between **Direct**, **Indirect** and **No Impact Systems**, as well as **Critical** and **Non-critical Components** optimizing the **Commissioning** and **Qualification & Validation** effort.
- **CQV activities** are not a one time only activity. **Periodic review / requalification routines** must be implemented to revise the system status, associated change controls and deviations or operational control results with the objective of detecting any trends and implement preventive measures avoiding future deviations.

# References


1. EudraLex, Volume 4, EU Guidelines for Good Manufacturing Practice, Annex 15: Qualification and Validation
2. 21 CFR Part 210 - Current Good Manufacturing Practice in Manufacturing. Processing, Packing, or Holding of Drug
3. 21 CFR Part 211 - Current Good Manufacturing Practice for Finished Pharmaceuticals
4. TGA - PE009, the PIC/S guide to GMP for medicinal products
5. ICH Q9: Quality Risk Management, Step 5 version
6. ISPE Baseline Guide Volume 5: Commissioning and Qualification
7. ISPE GAMP 5: A Risk-Based Approach to Compliant GxP Computerized Systems

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The entire pharmaceutical and life science industries manufacturing lifecycle is supported by us helping to set direction, assessing benefits of strategic investments and optimizing manufacturing and business processes.

We assist our customers from Research and Development (R&D) to Commercial manufacturing.

Our goal is to help our customers to achieve and maintain GMP manufacturing excellence and assist them in the route to market.

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Junior Pharma Consultant

### About João:

- Chemical and Biochemical Engineer by nature with a strong problem-solving capacity and flexibility.
- Has been part of one of the fastest growing tech companies in Europe as an Operation Specialist developing tools for market analysis and leading and implementing new products on the Portuguese market.
- Postgraduate in Medicinal cannabis GxPs, and an industry enthusiast.
- Highly Motivated hands-on person passionate for innovation and new challenges.

**Sérgio Guerreiro**
CQV Manager

### About Sérgio:

- Chemical Engineer with over 9 years' experience in the pharmaceutical industry, from parenteral to oral dosage forms.
- Quality Assurance professional with wide experience in Metrology, Validation & Qualification, Risk Assessment & Process Mapping, Auditing.
- International experience in QMS system implementation.
- Leader committed to the creation of motivated and highly devoted teams.

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