GMP–
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CONGRESS

#sharing challenges
and solutions in practice

Integrated Qualification and Validation

in customer-supplier partnership

Gert Moelgaard, Moelgaard Consulting
Past chairman, ECA Validation Group

GMP/FDA Compliance Conference
Part of PharmaCongress – Düsseldorf/Neuss, 31 May–1 June 2022

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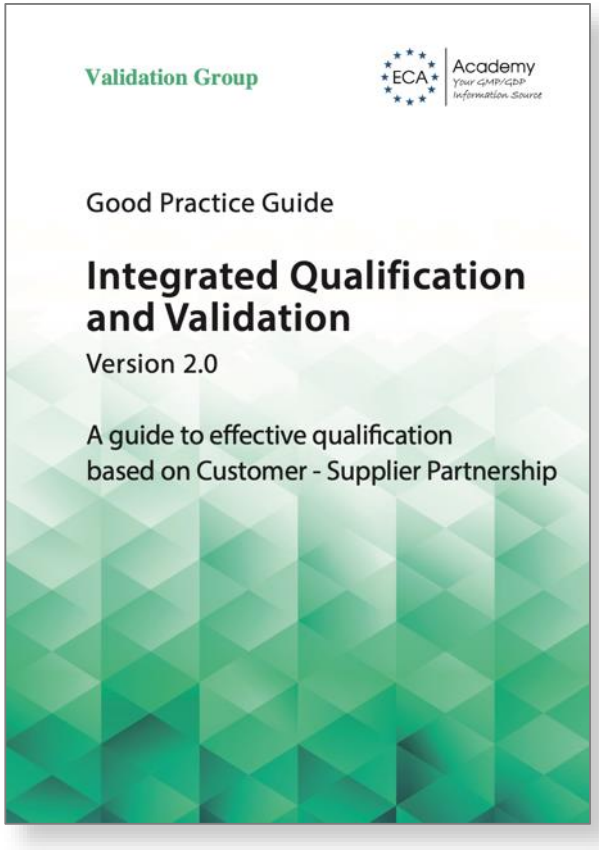
Overview

- Introduction
- Supplier partnership
- Equipment categories
- Remote testing
- Case stories
- Questions



EU GMP Annex 15: Qualification and Validation

EUROPEAN COMMISSION
DIRECTORATE-GENERAL FOR HEALTH AND FOOD SAFETY

Medicinal Products – Quality, Safety and Efficacy

Brussels, 30 March 2015

EudraLex

Volume 4

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

Annex 15: Qualification and Validation

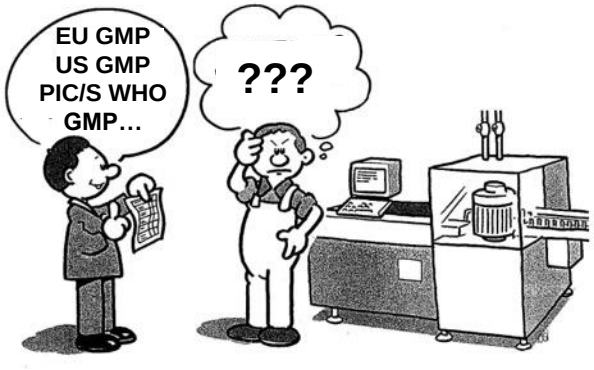
Legal basis for publishing the detailed guidelines: Article 47 of Directive 2001/83/EC on the Community code relating to medicinal products for human use and Article 51 of Directive 2001/82/EC on the Community code relating to veterinary medicinal products. This document provides guidance for the interpretation of the principles and guidelines of good manufacturing practice (GMP) for medicinal products as laid down in Directive 2003/94/EC for medicinal products for human use and Directive 91/412/EEC for veterinary use.

Status of the document: Revision

Reasons for changes: Since Annex 15 was published in 2001 the manufacturing and regulatory environment has changed significantly and an update is required to this Annex to reflect this changed environment. This revision to Annex 15 takes into account changes to other sections of the EudraLex, Volume 4, Part I, relationship to Part II, Annex 11, ICH Q8, Q9, Q10 and Q11, QWP guidance on process validation, and changes in manufacturing technology.

Deadline for coming into operation: 1 October 2015

”It is a GMP requirement that manufacturers control the **critical aspects** of their particular operations through **qualification and validation** over the life cycle of the product and process”



EU GMP Annex 15: Pharma Customer Requirements

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Deadline for coming into operation: 1 October 2015

”Decisions on the scope and extent of qualification and validation should be based on a justified and **documented risk assessment of the facilities, equipment, utilities and processes**”

EU GMP Annex 15:
Pharma Customer Standard Guideline

EUROPEAN COMMISSION
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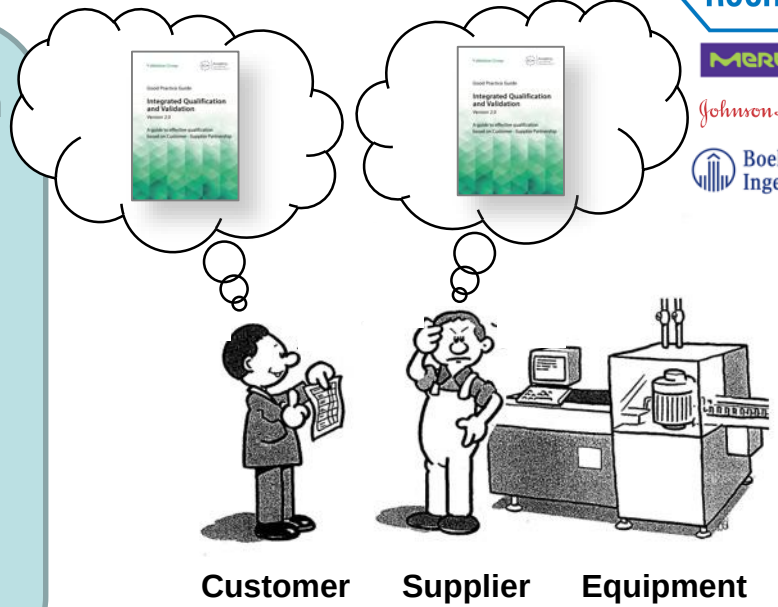
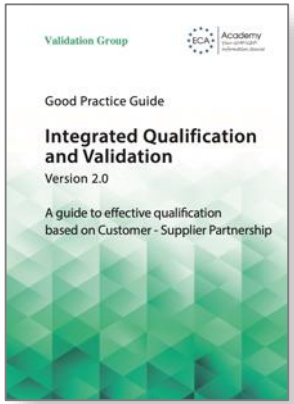
”Data supporting qualification and/or validation studies which were obtained from **sources outside** of the manufacturers own programmes may be used provided that this approach has been justified and that there is adequate assurance that controls were in place throughout the acquisition of such data”



ECA Good Practice Guide on Integrated Q&V

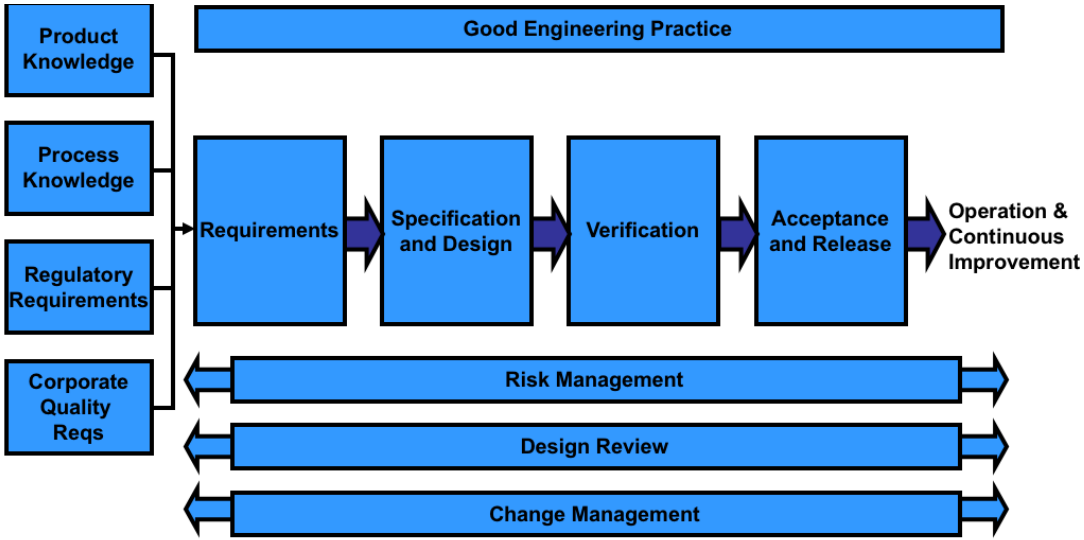
- Subteam of ECA Validation Group
- Pharma companies, suppliers and other industry members
- Practical guideline for pharmaceutical customers and suppliers
- Based on EU GMP Annex 15 Qualification and Validation
- FDA and ISPE compliant
- Improved and enhanced version launched 2021

- Key questions:
  - How to use documents developed by equipment suppliers
  - How to integrate Qualification in Validation activities
  - How to perform a risk-based qualification from URS to PQ



Based on ASTM E2500 Verification Standard

E2500 Verification Life Cycle Approach



Process

Product

Patient

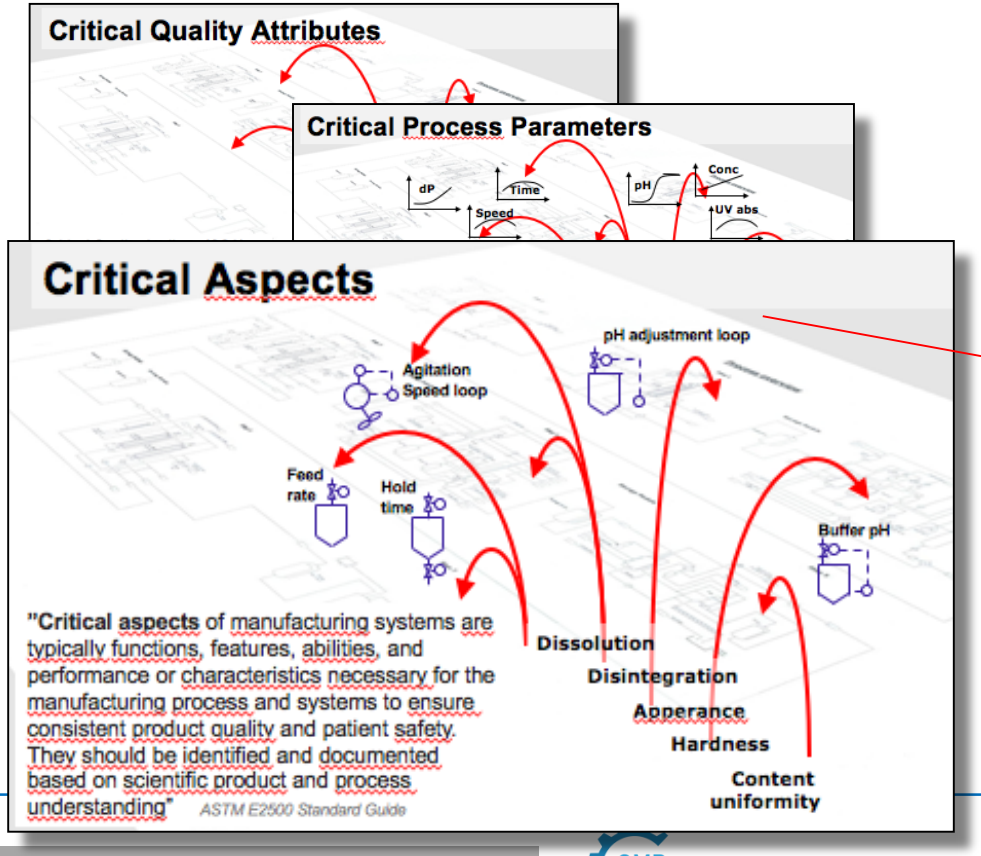
Critical Quality Attributes
Critical Process Parameters
Critical Aspects

Subject Matter Experts

Use of Vendor Documentation

Continuous Process Improvement

Critical Aspects and ASTM E2500



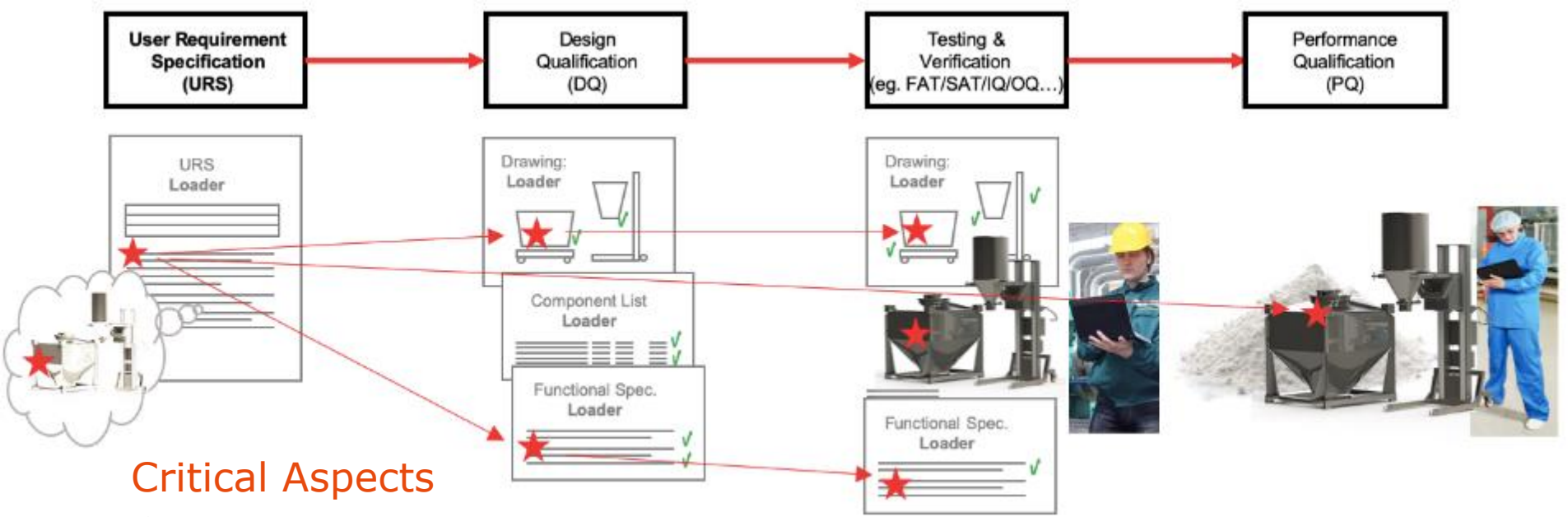
"**Critical aspects** of manufacturing systems are typically functions, features, abilities, and performance or characteristics necessary for the manufacturing process and systems to **ensure consistent product quality and patient safety.**

They should be **identified and documented based on scientific product and process understanding** (...)

Verification activities should focus on these aspects of manufacturing systems and should be documented (...)"

ASTM E2500 Standard Guide for Specification, Design, and Verification of Pharmaceutical and Biopharmaceutical Manufacturing Systems and Equipment (2013)

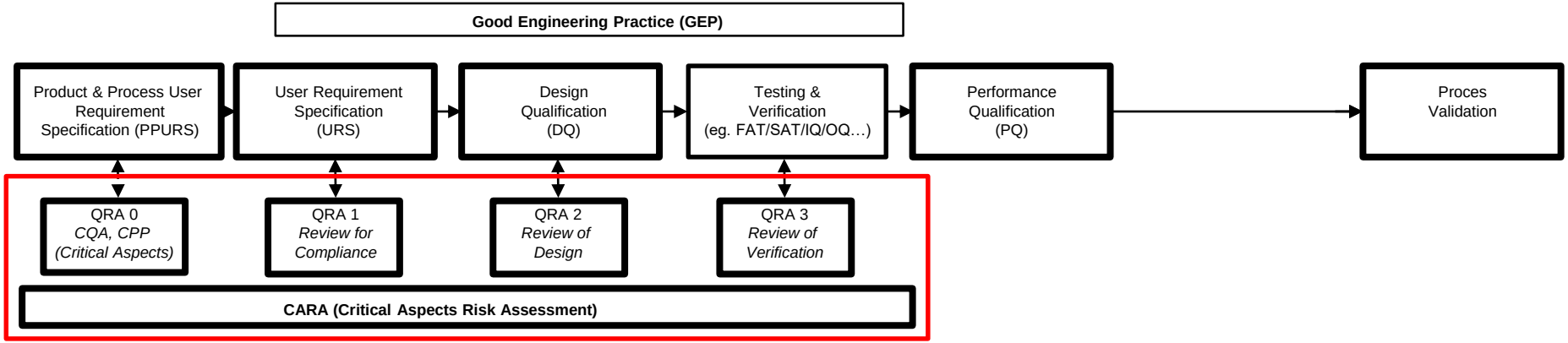
Critical Aspects and Good Engineering Practice



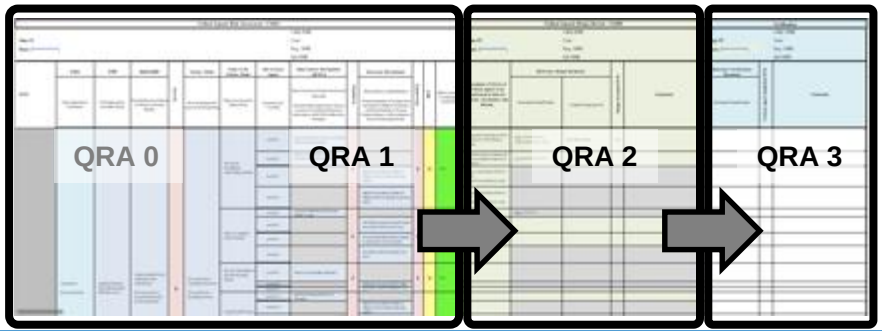
Critical Aspects

GEP

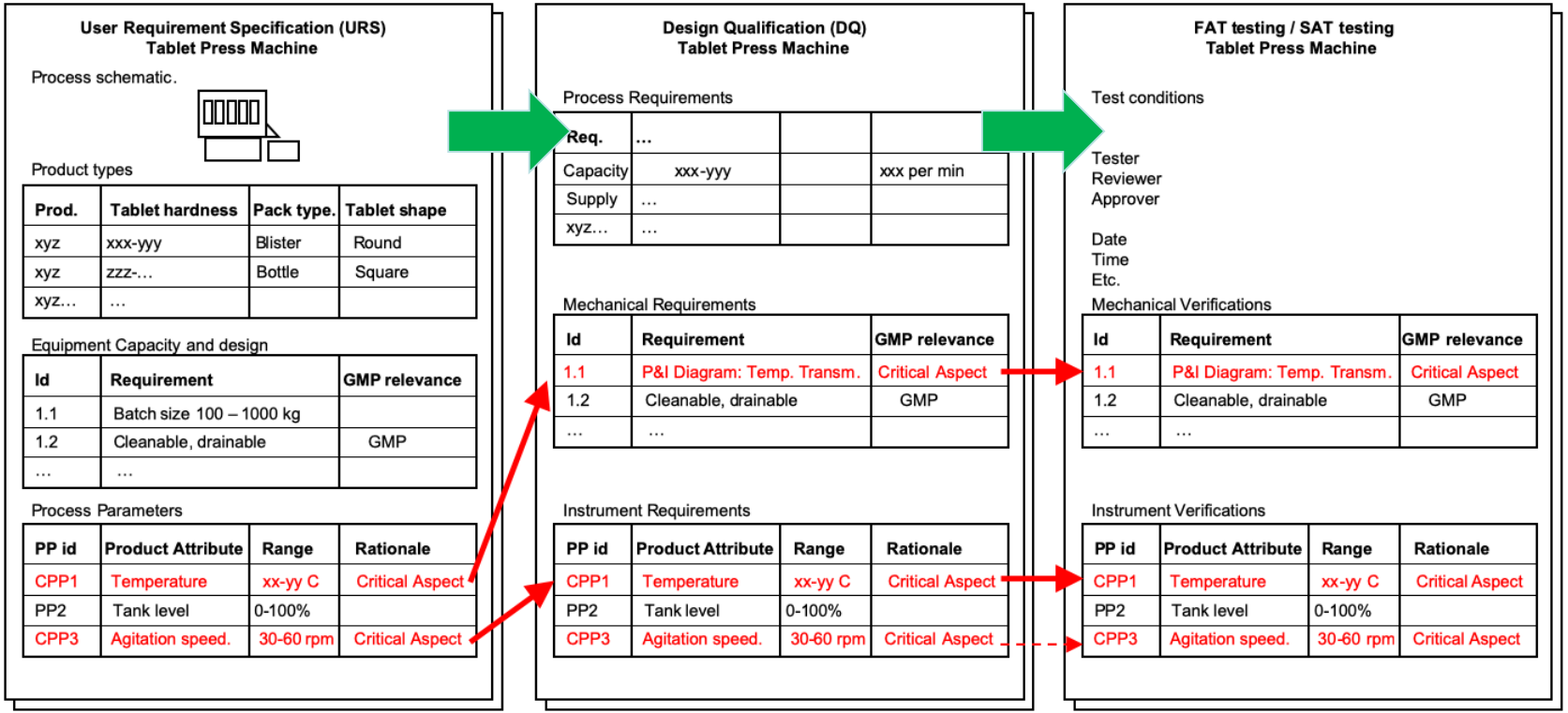
ECA Risk-based Qualification Project Life Cycle



CARA Tool Example



Critical Aspects and Good Engineering Practices for Integrated Qualification and Validation



User Requirement Specification (URS)
Tablet Press Machine

Process schematic.

Product types

Prod.	Tablet hardness	Pack type.	Tablet shape
xyz	xxx-yyy	Blister	Round
xyz	zzz-…	Bottle	Square
xyz…	…		

Equipment Capacity and design

Id	Requirement	GMP relevance
1.1	Batch size 100 – 1000 kg	
1.2	Cleanable, drainable	GMP
…	…	

Process Parameters

PP id	Product Attribute	Range	Rationale
CPP1	Temperature	xx-yy C	Critical Aspect
PP2	Tank level	0-100%	
CPP3	Agitation speed.	30-60 rpm	Critical Aspect

Design Qualification (DQ)
Tablet Press Machine

Process Requirements

Req.	…		
Capacity	xxx-yyy		xxx per min
Supply	…		
xyz…	…		

Mechanical Requirements

Id	Requirement	GMP relevance
1.1	P&I Diagram: Temp. Transm.	Critical Aspect
1.2	Cleanable, drainable	GMP
…	…	

Instrument Requirements

PP id	Product Attribute	Range	Rationale
CPP1	Temperature	xx-yy C	Critical Aspect
PP2	Tank level	0-100%	
CPP3	Agitation speed.	30-60 rpm	Critical Aspect

FAT testing / SAT testing
Tablet Press Machine

Test conditions

Tester
Reviewer
Approver

Date
Time
Etc.

Mechanical Verifications

Id	Requirement	GMP relevance
1.1	P&I Diagram: Temp. Transm.	Critical Aspect
1.2	Cleanable, drainable	GMP
…	…	

Instrument Verifications

PP id	Product Attribute	Range	Rationale
CPP1	Temperature	xx-yy C	Critical Aspect
PP2	Tank level	0-100%	
CPP3	Agitation speed.	30-60 rpm	Critical Aspect

Equipment Categories

- System categorisation should be based on a risk assessment
- Equipment Categories in other guidelines:
  - US Pharmacopeia: analytical equipment (USP 1058)
  - GAMP Guide categories of software (GAMP 5).
- Equipment Categories in ECA GPG for Integrated Q&V:
  - A. **Standard** (Commercial off-the-shelf systems (COTS))
  - B. **Configured** (COTS with specific configuration of, e.g., sequence, setpoints, timers, etc.)
  - C. **Customised** (designed for the specific customer with specific requirements, that is not available commercially, due to a special application, technology innovation etc.)

Equipment Categories Examples

A. **Standard**

Mobile tanks
Stand-alone transfer pump
Safety working bench

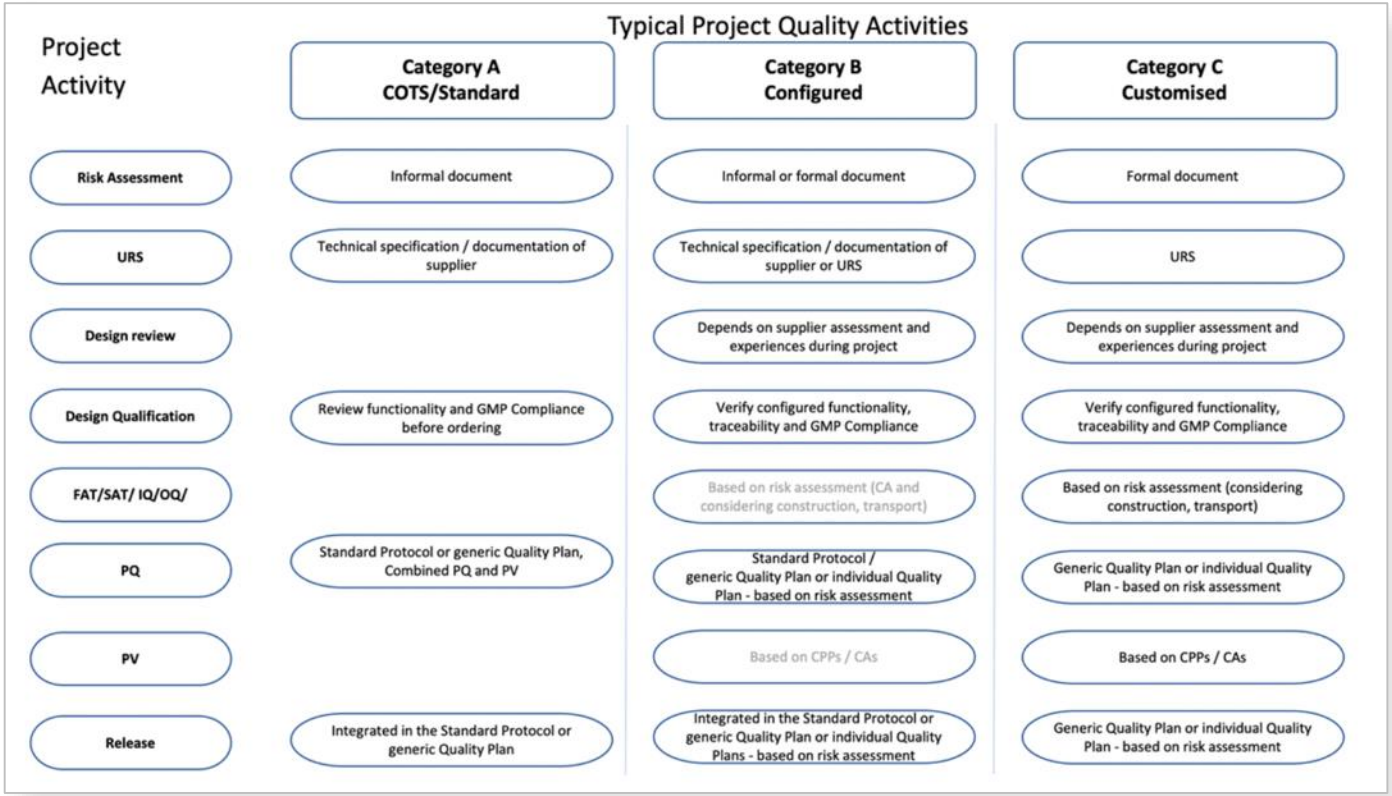
B. **Configured**

Blender
Purified water generator
Stand-alone CIP System

C. **Customised**

Bioreactor
WFI distribution systems
Purification Column
Integrated CIP system

Typical Project Quality Activities for Categories



ECA Good Practice Guide Integrated Q&V 2021

Remote Testing

Appendix 8: Remote Testing of GMP Manufacturing Systems

8.1 General

Different constraints can impact on efficient customer's follow up of tests in manufacturing systems at supplier's facility: project budget restrictions, geographical distance between facilities, customer personnel availability for traveling, amongst others.

Remote testing can reduce these constraints by a trustful relation between supplier and customer allied to supplier's flexibility and the breakthrough of telecommunication technologies.

The herewith proposed concept is due to different types of acceptance tests, beginning from large equipment FAT, documentation test, software FAT skid FAT, skid SAT as well as any individual tests for IQ or OQ.

8.2 Basics for remote testing execution

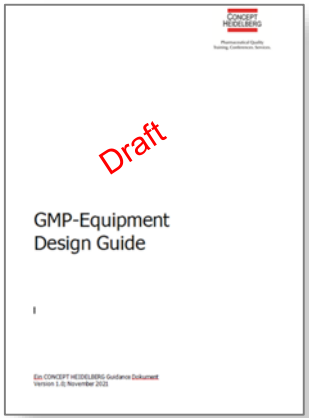
No process for remote testing sessions of GMP manufacturing systems has been described in GMP regulations or guidelines so far. The following points have been included to help customers and suppliers finding the most suitable way to perform successful remote testing.

ECA Good Practice Guide
Integrated Q&V
2021

ECA Q&V and GMP Equipment Design Guides

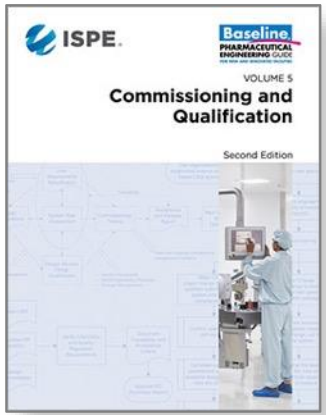
- ECA Integrated Qualification and Validation Guide
- 2nd version available from ECA

- ECA GMP Equipment Design Guide
- 1st version available later in 2022

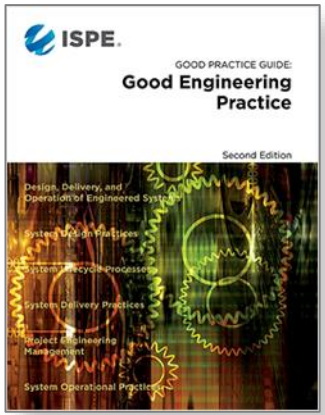


ISPE C&Q and GEP Guides

- ISPE Commissioning and Qualification Baseline Guide
- Second Edition, 2019



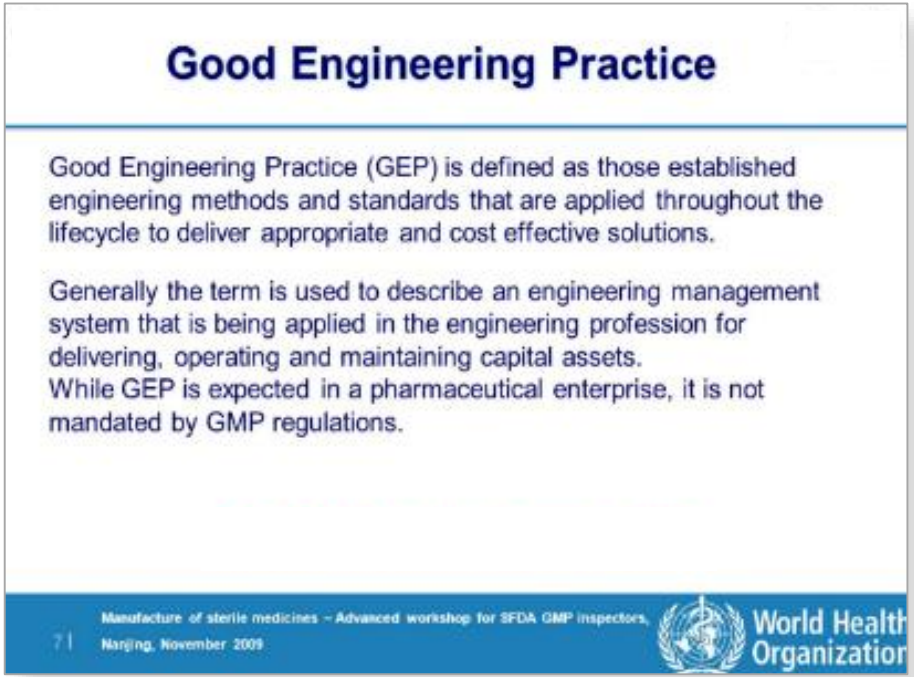
- ISPE Good Engineering Practice Guide
- Second Edition, 2021



A final word on Qualification, Validation and GEP

- GMP regulations are **legally binding** and must be followed by pharmaceutical companies
- GEP Standards and Guidelines are normally non-binding but are state-of-the art

- *gtm@moelgaardconsulting.com*



Thank you for your attention

QUESTIONS ?