Process Validation

Compounding Quality Center of Excellence

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Disclaimer

The information in this presentation was obtained from several resources, including but not limited to:

- eCFR :: 21 CFR Part 211 -- Current Good Manufacturing Practice for Finished Pharmaceuticals
- FDA Final Guidance for Industry, Process Validation: General Principles and Practices (January 2011)
- FDA Guidance for Industry PAT – A Framework for Innovative Pharmaceutical Development, Manufacturing, and Quality Assurance
- FDA Guidance for Industry Q8(R2) Pharmaceutical Development*
- FDA Guidance for Industry Q9 Quality Risk Management*
- FDA Guidance for Industry Q10 Pharmaceutical Quality System*
- FDA Guidance for Industry Quality Systems Approach to Pharmaceutical CGMP regulations
- Current Good Manufacturing Practice—Guidance for Human Drug Compounding Outsourcing Facilities Under Section 503B of the FD&C Act Guidance for Industry | FDA (Draft Guidance)
- PDA TR60: Process Validation

* *Note:* The ICH documents have been adopted by FDA and additional information on ICH documents can be found in FDA guidance for industry documents.

Agenda

- Laws, Regulations, and Guidance
- PV Life Cycle Approach
- Stages of Process Validation
  - Stage 1
  - Stage 2
  - Stage 3
- Change Management

Process Validation

PV is defined as the collection and evaluation of data, from the Process Design stage through commercial production, which establishes scientific evidence that a process is capable of consistently delivering quality products.

PV involves a series of activities taking place over the lifecycle of the product and process.

FDA Final Guidance for Industry, Process Validation: General Principles and Practices (January 2011)

Laws, Regulations, Guidance, and Best Practices

Items	Descriptions
Laws (Statutes)	The Federal Food, Drug and Cosmetic (FD&C) Act is a **federal law (statute) enacted by Congress.** Federal laws **establish the legal framework within which FDA operates**. The FD&C Act can be found in the United States Code (U.S.C), which contains all general and permanent U.S. laws, beginning at 21 U.S.C. 301.
Regulations	FDA **develops regulations** (e.g., current good manufacturing practice (CGMP) requirements) **based on the** statutes such as **the FD&C Act** or other laws under which FDA operates. **FDA regulations are also federal laws**, but they are not part of the FD&C Act. FDA regulations can be found in Title 21 of the Code of Federal Regulations (CFR).
Guidance	FDA follows the procedures required by its "Good Guidance Practice" regulation to issue FDA guidance. FDA **guidance describes the agency's current thinking on a regulatory issue**. In general, FDA guidance is not legally binding on the public or FDA.
Standards and Best Practices	Standards are **internationally agreed upon principles by experts**; best practices are **procedures or processes shown by research and experience to produce optimal results** and is established or proposed as a standard suitable for widespread adoption. Best practices are **recommendations and not legally binding**.

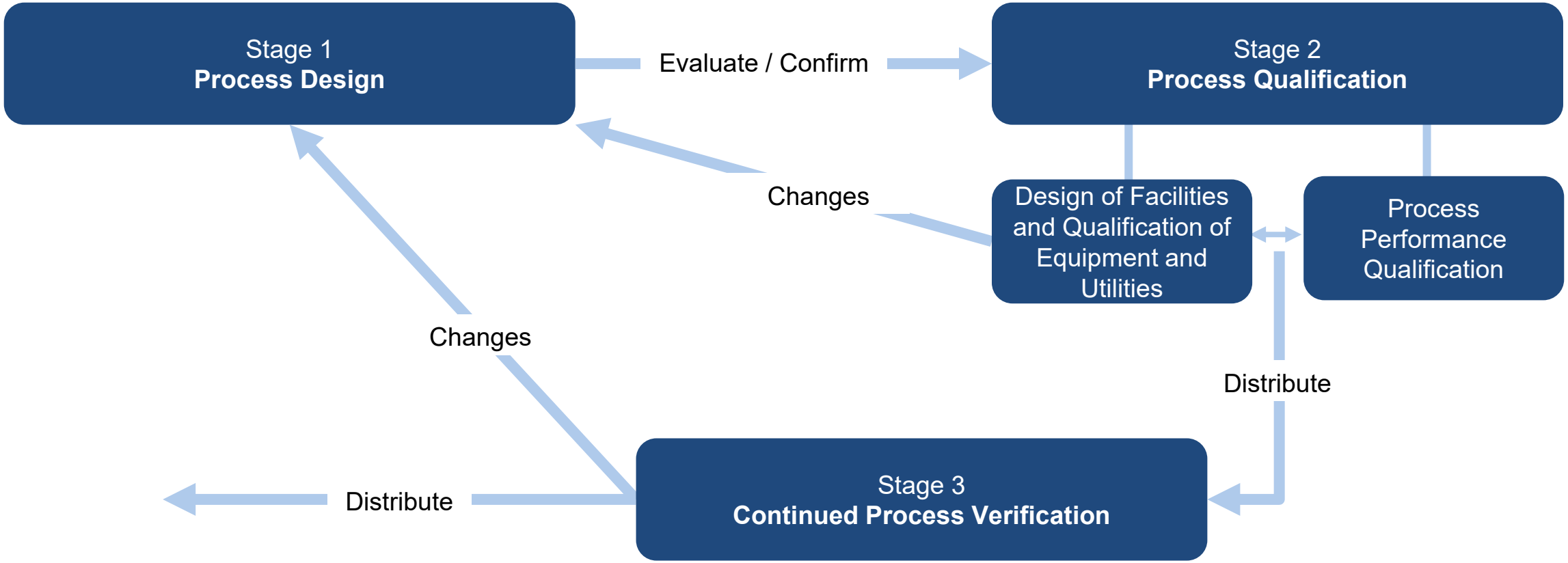
Process Validation in the Regulations

§ 211.100 Written procedures; deviations

a) There **shall** be **written procedures for production and process control** designed to assure that the drug products have the **identity, strength, quality, and purity** they purport or are represented to possess. Such procedures shall include all requirements in this subpart. **These written procedures**, including any **changes**, shall be **drafted, reviewed, and approved** by the **appropriate organizational** units and reviewed and approved by the **quality control unit**.

b) Written production and process control procedures shall be **followed** in the execution of the various production and process control functions and shall be **documented at the time of performance.** Any **deviation** from the written procedures shall be recorded and justified.

Stages of Process Validation



General Elements for Successful PV

1. An **integrated team approach to PV, as appropriate to the size and scale of your organization,** is recommended. Teams are composed of experts from a variety of disciplines.
2. All **studies should be planned and conducted** according to **sound scientific principles,** appropriately documented, and approved in accordance with the **established procedure** appropriate for the stage of the lifecycle.
3. The **degree of control** for **process operations** and **process** parameters should be commensurate with their **risk of impacting** the **desired product quality attributes or in-process specifications.**

Lifecycle Approach to Process Validation

Stages	Parts
Stage 1 Process Design	Part I: Building and Capturing Process Knowledge and Understanding Part II: Establishing a Strategy for Process Control
Stage 2 Process Qualification	Part I: Design of a Facility and Qualification of Utilities and Equipment Part II: Process Performance Qualification
Stage 3 Continued Process Verification (CPV)	Initial CPV Planning Short Term CPV Long Term CPV

Lifecycle Approach to Process Validation: Stage 1, Process Design

- Part I: Building and Capturing Process Knowledge and Understanding
- Part II: Establishing a Strategy for Process Control

Stage 1, Process Design – Overview

The goal of this stage is **to design a process suitable for commercial production** that **consistently** delivers a product that meets **its pre-defined quality attributes.** Process Design defines the commercial production process that will be documented in the master production and control records.

It is important to recognize that ***quality*** cannot be tested into products (i.e., quality is built in by design).

Lifecycle Approach to Process Validation
Stage 1, Process Design

Part I: Building and Capturing Process Knowledge and Understanding

Part I of Stage 1:
Building and Capturing Process Knowledge and Understanding

- **Establish Quality Target Product Profile (QTPP), Critical Quality Attributes (CQA), Critical Process Parameters (CPP), Critical Material Attributes (CMA)**
- Perform Quality Risk Management
- Define the Manufacturing Process
- Perform Process Characterization

Establish QTPP, CQA, CPP, CMA

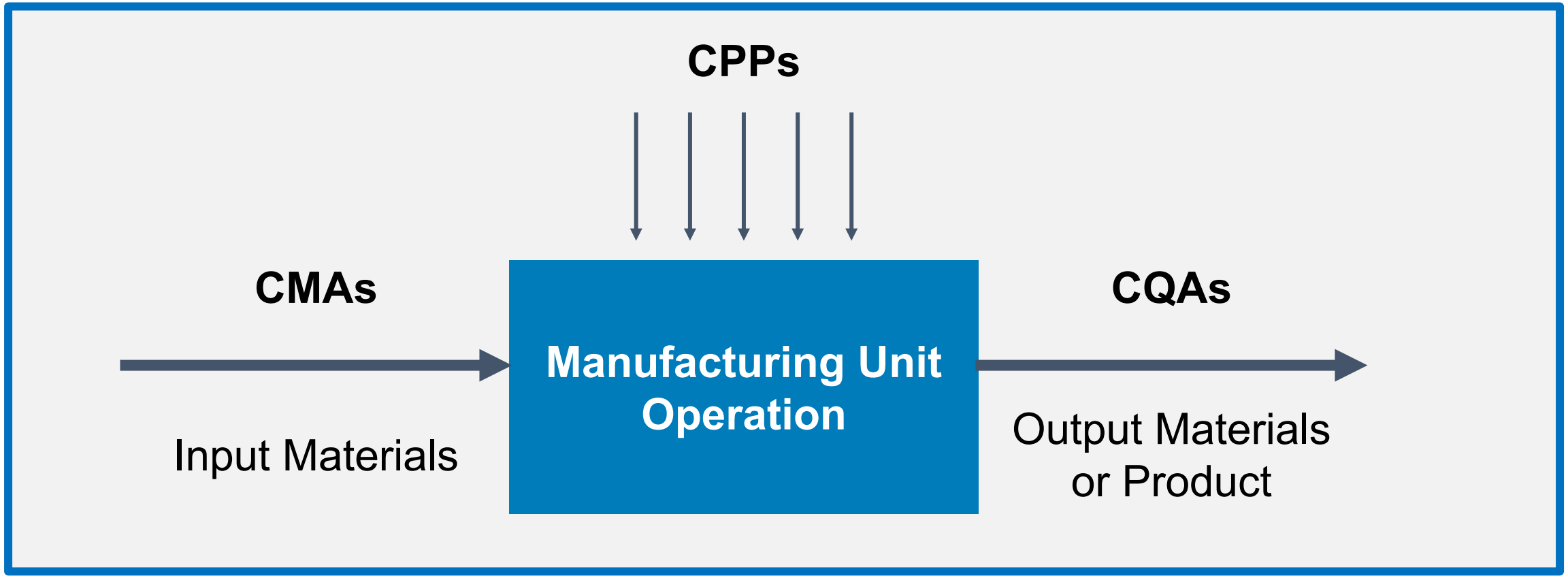
Quality Target Product Profile, QTPP, is a **summary of the quality characteristics** of a finished drug product (like purity, sterility, stability, route of administration, dosage form, and strength) that ideally will be achieved to ensure the desired quality and strength of the drug product.

A Critical Quality Attribute, CQA, is **a physical, chemical, biological, or microbiological property or characteristic** that must be within an **appropriate limit, range, or distribution** to ensure the desired product quality (ICH Guidance for Industry Q8(R2) Pharmaceutical Development).

A Critical Process Parameter, CPP, is a **process parameter whose variability has an impact on a CQA**, and therefore should be monitored or controlled to ensure the process produces the desired quality (ICH Guidance for Industry Q8(R2) Pharmaceutical Development).

Critical Materials: Raw materials (e.g., Bulk Drug Substance (BDS) or excipients), finished product containers, and closures are critical materials. Specifications must be established for critical materials. These specifications are referred to as **Critical Material Attributes (CMAs).**

Relationship Between CMAs, CPPs, and CQAs



Part I of Stage 1:
Building and Capturing Process Knowledge and Understanding (1 of 3)

- Establish QTPP, CQA, CPP, CMA
- **Perform Quality Risk Management**
- Define the Manufacturing Process
- Perform Process Characterization

Quality Risk Management (QRM)

- QRM is a **systematic process** for the **assessment, control, communication, and review of risks** to the quality of the drug product **across the product lifecycle**. The application of risk management principles and approaches is instrumental to effective decision-making in **selecting the correct CQAs and CPPs** (PDA TR60).
- Risk assessment should **occur early in the Design Stage and consciously be assessed, controlled, and communicated throughout the lifecycle** of the finished drug product.
- With a lifecycle approach to PV that employs risk-based decision-making throughout the lifecycle, the perception of criticality as a **continuum** rather than a **binary state** is useful.
- All attributes and parameters should be **evaluated** in terms of their **roles** in the process and **impact** on the product or in-process material and **reevaluated** as new information becomes available.
- The **degree of control** over those attributes or parameters should be **commensurate with their risk** to the process and process output. In other words, a higher degree of control is appropriate for attributes or parameters that pose a higher risk to the process and process output.

Higher Risk	Higher Degree of Control

ICH Q9 Risk Management Framework*

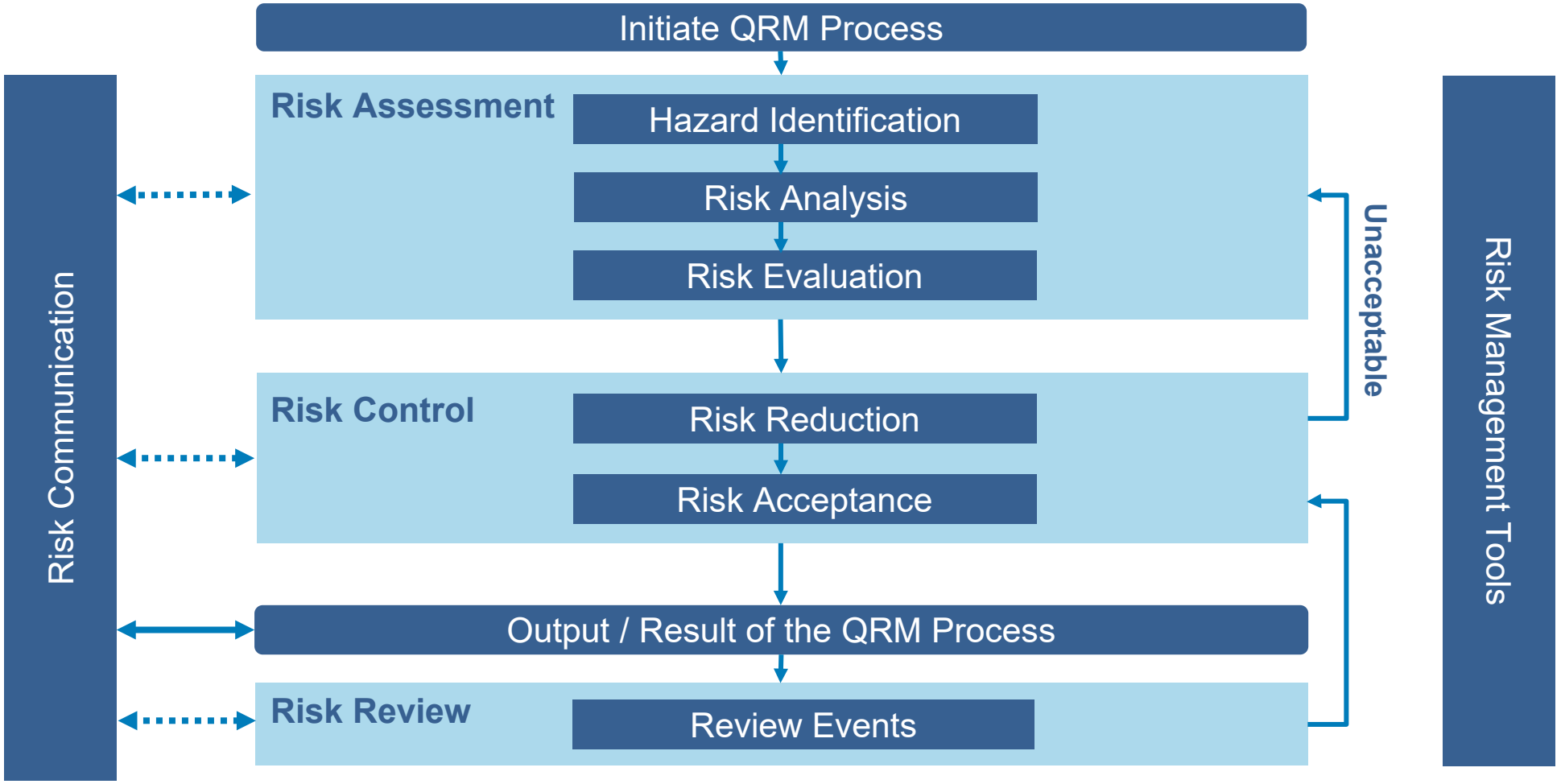


*Figure 1: Overview of a typical quality risk management process from Q9(R1) Guidance

Part I of Stage 1:
Building and Capturing Process Knowledge and Understanding (3 of 3)

- Establish QTPP, CQA, CPP, CMA
- Perform Quality Risk Management
- **Define the Manufacturing Process**
- Perform Process Characterization

Define the Manufacturing Process

Level of Detail

- ✓ Process requirements, including raw materials and order of operations
- ✓ Set points and ranges for the process parameters
- ✓ Identification and quantity of all material flows (e.g., additions, wastes, product streams)
- ✓ Testing, sampling, and in-process controls (IPCs)
- ✓ Hold times and hold conditions for product and additional solutions
- ✓ Materials reconciliation
- ✓ Estimated step yields and durations
- ✓ Sizing for equipment, including such items as mixers or filtration units (e.g., filter surface area, filter volume, and pore size)
- ✓ Specific identification (i.e., manufacturer, part number) for manufacturing (e.g., filters) and packaging components (e.g., vials, stoppers)
- ✓ Other information necessary to successfully reproduce the process
- ✓ Actual and theoretical yields

Part I of Stage 1:
Building and Capturing Process Knowledge and Understanding (2 of 3)

- Establish QTPP, CQA, CPP, CMA
- Perform Quality Risk Management
- Define the Manufacturing Process
- **Perform Process Characterization**

Process Characterization

- Process Characterization is a set of documented studies in which operational parameters are purposely varied to determine their effect on product quality attributes and process performance.
- The output of process design and characterization is a strategy for process control, which is Part II of Stage I of Process Design.
- Process design and characterization should be conducted in accordance with **sound scientific methods and principles, including good documentation practices (GDP)**.
- Process information available from literature sources (e.g., compounding formulations or recipes, United States Pharmacopeia (USP) monographs) or similar production processes already used can be leveraged to design and characterize production processes for new products.

Lifecycle Approach to Process Validation (1 of 3)

Part II: Establishing a Strategy for Process Control

Stage 1 Part II: Establishing a Strategy for Process Control

- **Categorization of Parameters and Establishment of Control Strategy**
- System Classifications / Boundaries (Direct vs. Indirect Impact Systems Based on CQAs and CPPs)

Process Control Strategy

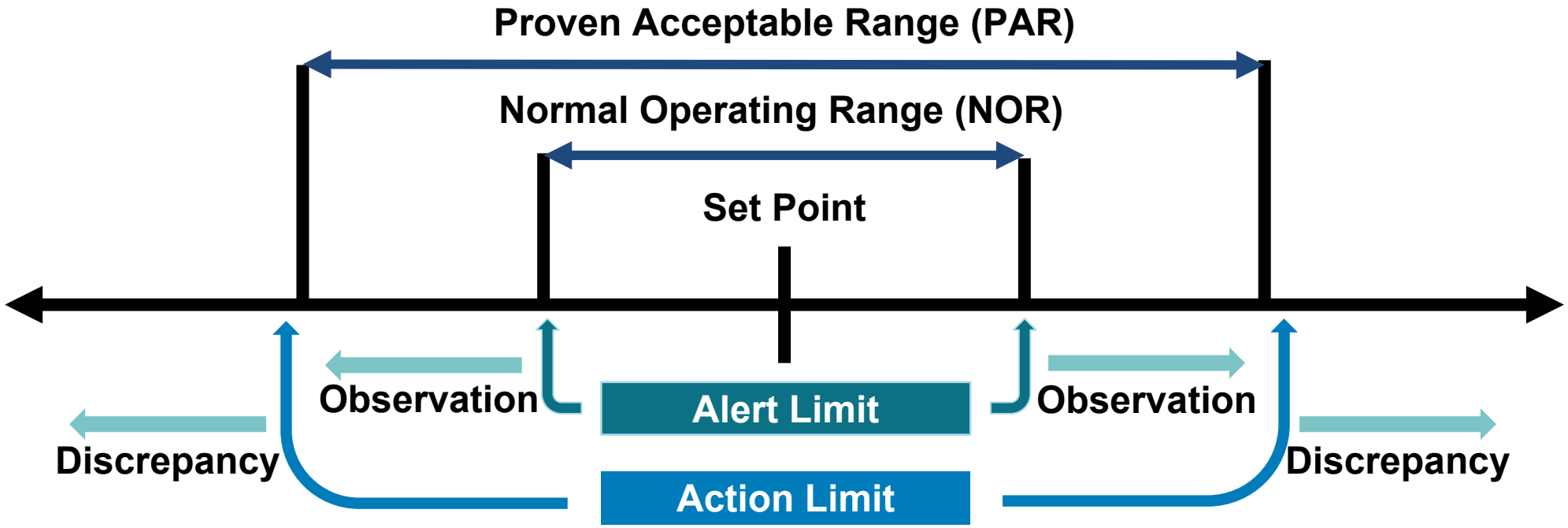
A process control strategy is **a planned set of controls**, derived from product and process understanding, which **ensures process performance and product quality**.

Elements of a Process Control Strategy

A robust process control strategy encompasses all unit operations in the process. All product quality attributes and process parameters, regardless of whether they are classified as critical, are included in a comprehensive process control strategy, which includes the elements detailed below:

- ✓ Facility
- ✓ Personnel
- ✓ Raw Material Controls
- ✓ Process Parameters (Set Points and Ranges)
- ✓ Process Monitoring (Data Review, Sampling, Testing)
- ✓ In-Process and Release Specifications
- ✓ Processing Times
- ✓ Hold Times
- ✓ Containers and Closures Control

Process Parameters (Set Points and Ranges)



Stage 1, Part II: Establishing a Strategy for Process Control

- Categorization of Parameters and Establishment of Control Strategy
- **System Classifications / Boundaries (Direct vs. Indirect Impact Systems Based on CQAs and CPPs)**

System Classification: Direct and Indirect Impact Systems

Direct Impact Systems

- Directly impact CQAs and / or CPPs, and therefore have direct impact on process and product quality.
- **Should be commissioned and qualified.**

Direct Impact System operations are often recorded in batch records such as filling equipment and sterilization equipment (e.g., blenders, mixers, filters, autoclaves, depyrogenation ovens).

Indirect Impact Systems

- May be referred to as indirect impact, no impact, process non-critical, etc.
- Systems that do not directly impact any CPPs and CQAs and, therefore, have no direct relationship to process and product quality, and
- Require less scrutiny.
- **Will only be commissioned.**

Based on need, some processes may be commissioned, but not qualified. For example, heating, ventilation, and air conditioning (HVAC) for the office space.

Their data will not be recorded in the batch / production record; however, a catastrophic failure on their part could impact the Direct Impact Systems they support.

System Boundaries *define at which point the indirect systems end and the direct systems begin.*

Computer and Electronic Systems

Computerized and electronic systems used for production applications are qualified per 21 CFR part 11 and Data Integrity and Compliance with Drug CGMP Questions and Answers Final Guidance for Industry and EU Annex 11.

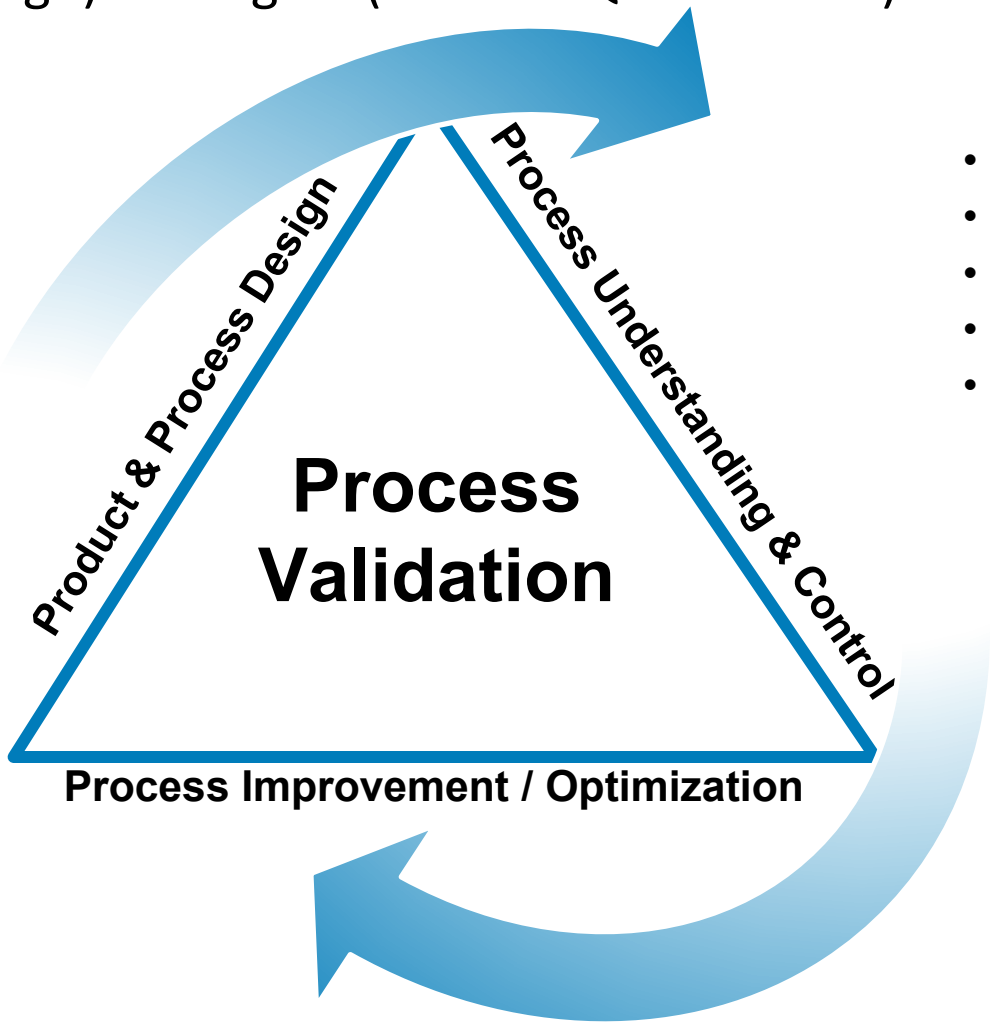
Qualification criteria include, but are not limited to:

- Specificity
- Accuracy
- Data management
- Sensitivity
- Communication
- Electronic integration requirements of information technology compatibility

Summary of Stage 1 Process Design

The representative list below summarizes the information needed to transition from Stage 1 (Process Design) to Stage 2 (Process Qualification) in the PV lifecycle.

- Quality Target Product Profile (QTPP)
- Critical Quality Attributes (CQAs)
- Quality Risk Assessment
- Critical Process Parameters (CPPs)
- Manufacturing Process Design
- Analytical Methods



- Process Characterization
- Process Validation Master Plan
- Process Control Strategy
- Manufacturing Technology
- Documentation Development

Updated Master Batch Record

Master Batch Record

Change Control

Lifecycle Approach to Process Validation

Stage 2: Process Qualification

- Part I: Design of a Facility and Qualification of Utilities and Equipment
- Part II: Process Performance Qualification

Stage 2, Part I
Design of a Facility and Qualification of Utilities and Equipment

- **Commissioning, Factory Acceptance Test (FAT), and Site Acceptance Test (SAT)**
- Qualification
  - Installation Qualification (IQ), Operation Qualification (OQ), and Performance Qualification (PQ)

Understanding and Leveraging Commissioning, FAT, and SAT

Commissioning

Commissioning verifies the facility, utility, and equipment (the "system") are installed properly, function properly, have the proper utilities connected correctly, (e.g., are the fans blowing in the right direction?), are accessible (e.g., can I get to sampling points, or can I get the HEPA filter changed if it is installed too close to the wall?), and thus was successfully turned over to the end user. Commissioning, when executed properly, is important to support the success of the subsequent qualification activities.

FAT

FAT provides documented evidence a piece of equipment or system has been adequately tested at the manufacturer's facility and performs to the end user's expectations prior to delivery to the end user. FAT is not mentioned or discussed in the FDA PV guidance, but ~~it~~ **provides an opportunity** to head off problems by finding any issues while it is still in the factory where it can be corrected more easily.

SAT

SAT provides documented evidence a piece of equipment or system has not been affected in the transportation and has been adequately tested at the end user's facility and performs to the end user's expectations. SAT is not mentioned or discussed in the FDA PV guidance, but it **provides an opportunity** to arrange for either factory representatives or supplier service personnel to participate in the first start-up and tests, and for the receiving site's personnel to ask them questions.

Stage 2, Part I : Design of a Facility and Qualification of Utilities and Equipment

- Commissioning, Factory Acceptance Test (FAT), and Site Acceptance Test (SAT)
- **Qualification**
  - **Installation Qualification (IQ), Operation Qualification (OQ), and Performance Qualification (PQ)**

Qualification (IQ / OQ / PQ) of Equipment and Systems

Installation Qualification (IQ)

IQ provides documented verification all aspects of a facility, utility, or equipment that can affect product quality (i.e., critical) adhere to approved specifications as defined in the URS (e.g., materials of construction) and are correctly installed.

Operational Qualification (OQ)

OQ is the documented verification the facilities, systems, and equipment, as installed or modified, operate as intended throughout the anticipated operating ranges.

Performance Qualification (PQ)

PQ is the documented evidence that provides a high degree of assurance the equipment and systems function accurately and consistently according to predetermined specifications within the operating ranges defined in Stage 1 in its operating environment.

Qualification Throughout the Lifecycle

After the successful qualification of the equipment and systems in the manufacturing facility, it is important to ensure the equipment and systems are maintained in a state of control and operate in a manner consistent with their qualified state throughout the product lifecycle.

This is done by:

Preventive Maintenance

Maintenance is performed routinely according to a defined schedule (e.g., the certification of HEPA filters every six months).

Predictive Maintenance

Individual(s) assigned the responsibility to maintain equipment take advantage of available information, forecast possible failures, and take maintenance action before a failure occurs.

Calibration

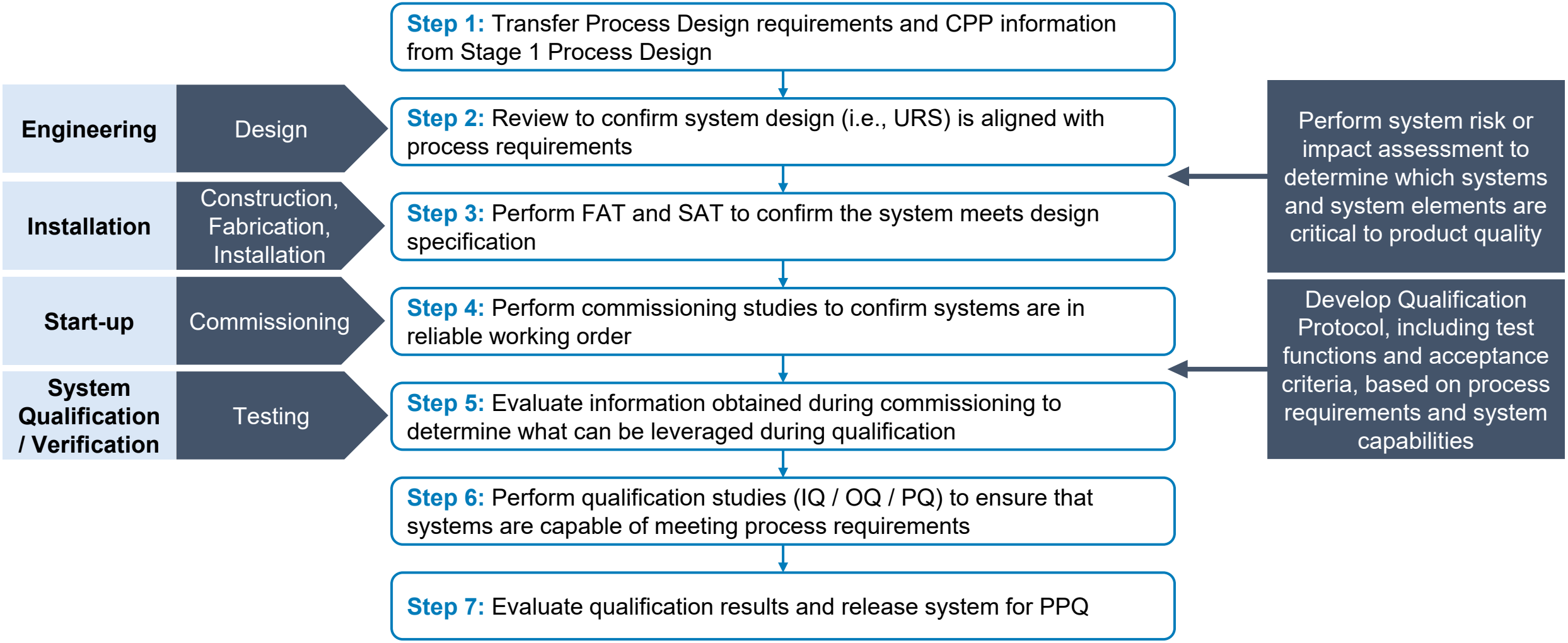
A calibration program assures data collected from instruments and devices are both precise and accurate within the acceptable range. Periodic and annual calibration should be incorporated into the calibration program (may also be part of a preventive maintenance program).

Requalification

Requalification may be required whenever qualified systems have been changed or modified. The extent and impact of the change must be evaluated for their impact on the original qualification. Requalification is also routinely performed on a periodic basis to ensure that systems continue to operate in their qualified state throughout the lifecycle of the product. How often a system will need to be requalified will depend on the criticality of that system.

Summary of PV Stage 2: Part I

The typical system qualification sequence is displayed in the figure below.



Lifecycle Approach to Process Validation (2 of 3)

Stage 2: Process Qualification

Part II: Process Performance Qualification

Process Performance Qualification, PPQ

PPQ combines the qualified facility, utilities, and equipment and trained personnel with the commercial manufacturing process, control procedures, and components to produce the PPQ batches. The goal of PPQ is to establish scientific evidence that the commercial production process is reproducible and will consistently deliver quality products.

PV Stage 2, Part II: Process Performance Qualification, PPQ

Prepare for PPQ	Readiness Assessment	Prepare for PPQ by reviewing the status of activities required to be completed prior to commencement of the PPQ batches.
Design of PPQ	Develop Strategy and Approach	Design PPQ based on multiple considerations specific to the manufacturing process and determine the number of manufacturing runs and sample plan.
	Compile PPQ Protocol	Document all of the necessary elements in the PPQ protocol, including pre-determined acceptance criteria.
Execute the Process	Execute PPQ Protocol	Perform the procedures as outlined in the PPQ protocol, including manufacturing steps and testing of analytical samples.
Analyze PPQ Results Against Acceptance Criteria	Analyze Results and Compile PPQ Report	Analyze the data obtained during PPQ following statistical methodology and acceptance criteria from the PPQ protocol and address deviations and failures.

Analyze PPQ Results Against Acceptance Criteria
Sections of the PPQ Report

The PPQ report will typically include the following sections:

- Summary
- Deviations
- Methods and Materials
- Conclusions
- PPQ Results
- Approvals

Aseptic Process Simulation (Media Fills) Where Does It Fit?

- An aseptic process simulation (APS) is designed to evaluate whether processes may pose a risk to product sterility are adequately controlled.
- The terms “aseptic process simulation” and “media fills” are often used interchangeably.
- APS does not equal process validation; it is a component of process validation.
- APS is narrower in focus than PV in that the goal is primarily microbiological. qualification – can product be made that is free from microbial contamination.
- APS can be done before or after PPQ. There are pros and cons to both.
- **A media fill has to be completed before a firm releases any aseptically filled products.**
- The FDA Compounding Quality Center of Excellence offers a free, self-guided on-line course available here: Aseptic Process Simulations.

Lifecycle Approach to Process Validation (3 of 3)

Stage 3: Continued Process Verification

- Initial CPV Planning
- Short Term CPV
- Long Term CPV

Stage 3: Continued Process Verification (CPV)

CPV provides ongoing assurance that during routine production the process remains in a state of control.

Source: FDA Final Guidance for Industry, Process Validation: General Principles and Practices (January 2011)

Key Elements of CPV

- Collect data (e.g., process parameters, test results)
- Analyze and review data
- Review trends and evaluate process performance
- Identify problems and determine whether action must be taken to correct undesirable variation in the production, process, deviations, or failures
- Ensure process remains in a state of control throughout the life cycle
- Incorporate process improvements

CPV Overview

Overview of CPV (Stage 3)

Initial CPV Planning

Establishes:

- Data to include for review and analysis (e.g., process parameters, testing results, batch yields)
- Elements to measure (e.g., critical process parameters (CPPs), in-process controls (IPCs), Critical Quality Attributes (CQAs), yields)
- Sampling plans
- Data collection and reporting
- Reporting frequency
- Data analysis methods (e.g., statistical tools, trending methods)
- Action plan to respond to out-of-trend results or observed variation

Short-term CPV 6

Includes:

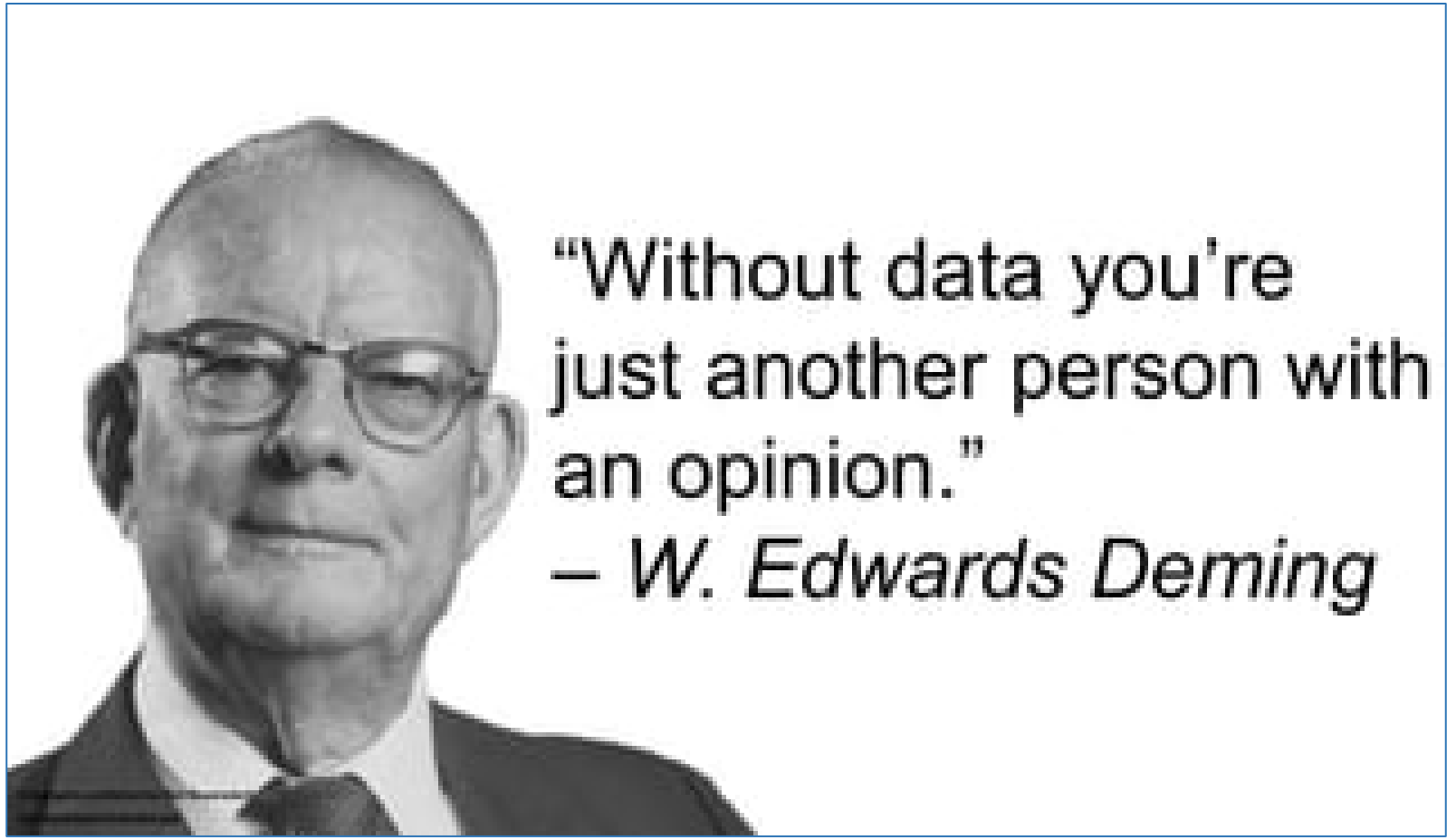
- Data are collected and reported per the plan.
- Control limits, for any of the parameters or elements defined in the CPV plan, are created and summarized in a short-term CPV report.
- A report and long-term CPV planning are outputs.

Long-term CPV 7

Includes:

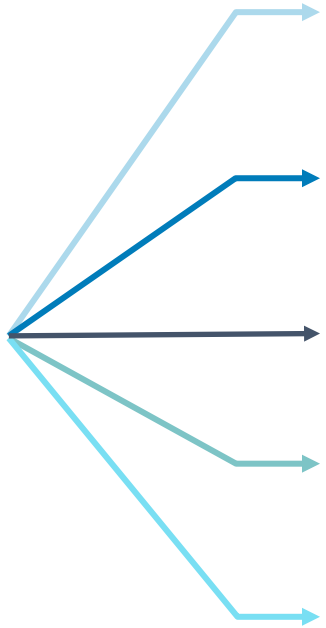
- Parameters and product attributes (e.g., CQAs, CPPs) are monitored and trended.
- Reactions to trends are commensurate with the risk established throughout the PV process.
- Periodic reporting based upon frequency of manufacturing

Quote


"Without data you're just another person with an opinion."
– W. Edwards Deming

Data Collection Plans and Statistical Procedures in the PV Lifecyle

A **statistician** (or person with adequate training in statistical process control (SPC)) techniques) is recommended to **develop the data collection plan and statistical methods / procedures** used in measuring and evaluating process stability and process capability.

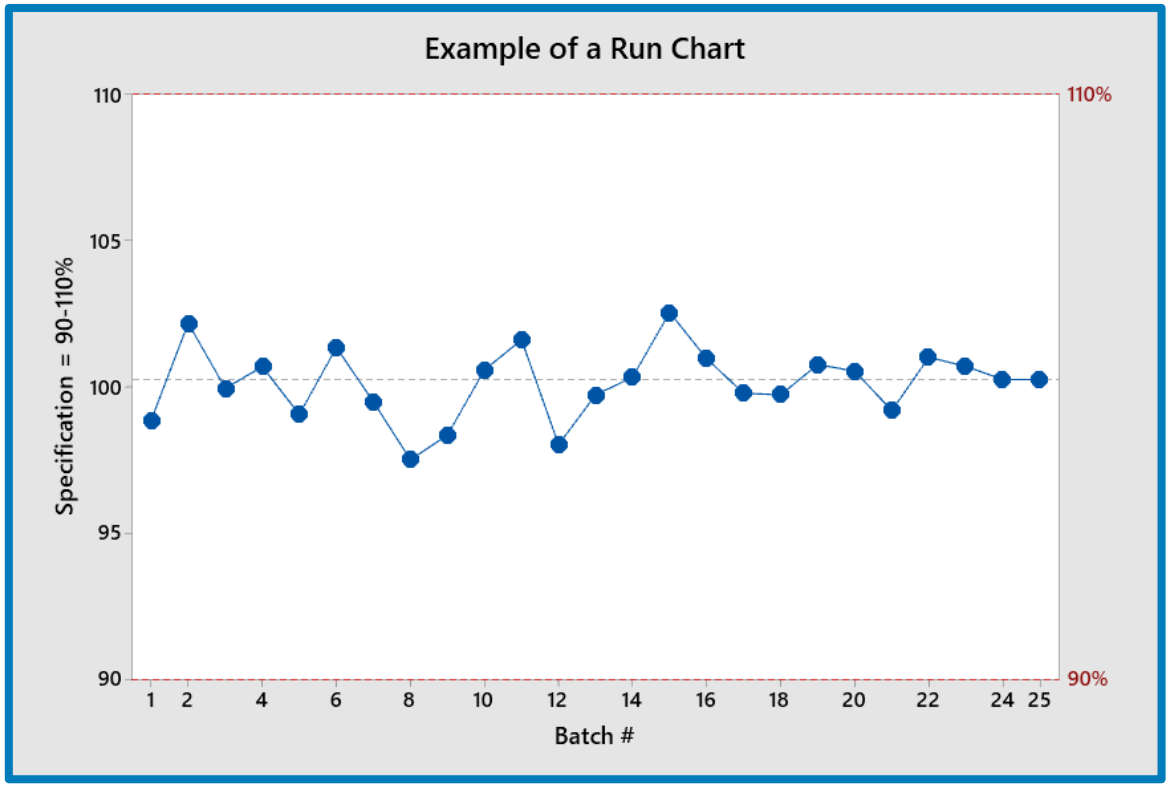


Commonly Used Statistical Procedures Include:

- Run Charts
- Individual Value Plots
- Tolerance Intervals (TIs)
- Variance Components
- SPC Charts (I Charts) and Capability Analysis

Examples of Data Collection Tools: Run Charts

A run chart is used to study collected data for trends or patterns over a specific time period.



X-axis: Units of time by which measurements are made

Y-axis: Attribute being measured

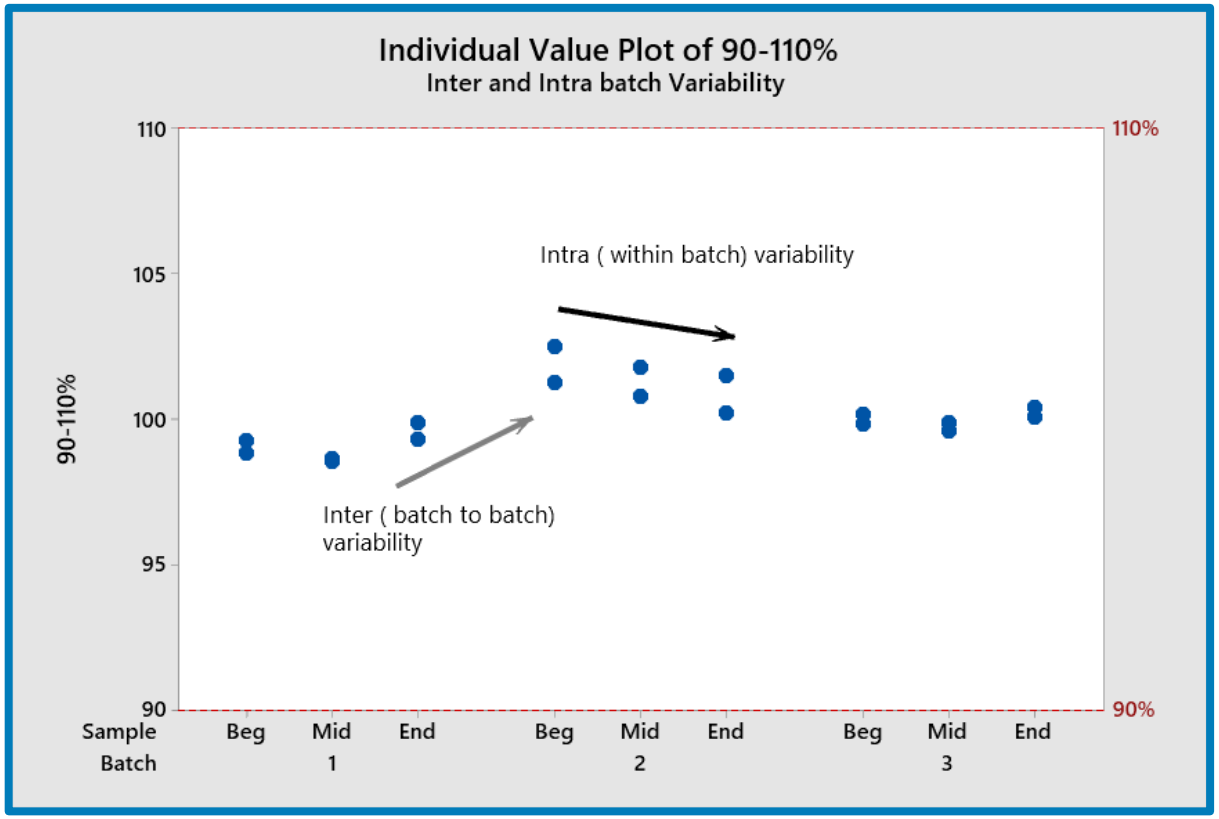
Centerline: Mean (or average)

A run chart will help you:

- Monitor data over time to detect trends, shifts, or cycles
- Compare / measure data before and after the implementation of a change or corrective action to measure impact
- Focus attention on important changes (i.e., not normal variation)
- Track useful information for predicting trends.

Examples of Data Collection Tools: Individual Value Plot

An individual value plot displays the individual values in each sample to assess and compare sample data distributions.



Each circle represents **one reported value**, making it easy to spot **outliers** and see **distribution spread**.

For example: Batch to batch and sample positions within batch.

X-axis: Inter and intra batches being measured

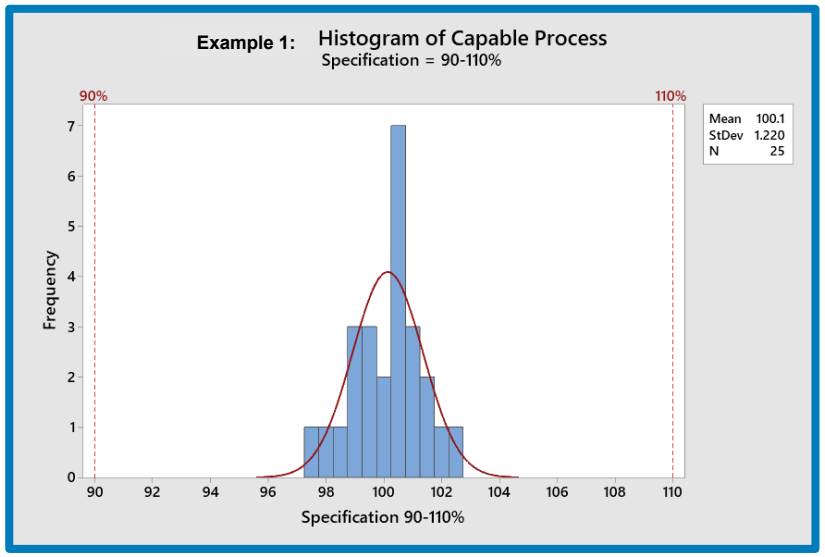
Y-axis: Attribute being measured

Process Capability

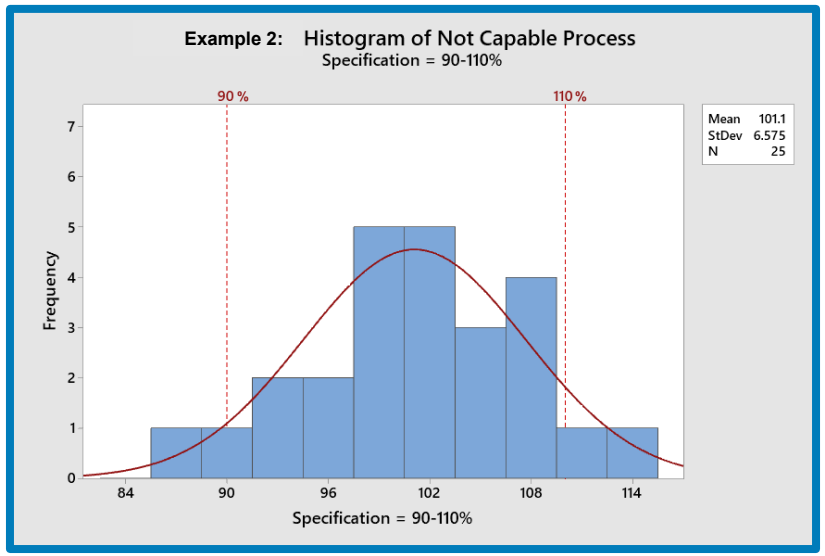
Ability of a process to produce a product that will fulfill the requirements of that product. A capability study is used to determine whether a process is capable, which involves collecting samples over a period of time and analyzing the samples. There are both complex and simple methods to assess capability.

Assessing Process Capability in the PV Lifecycle

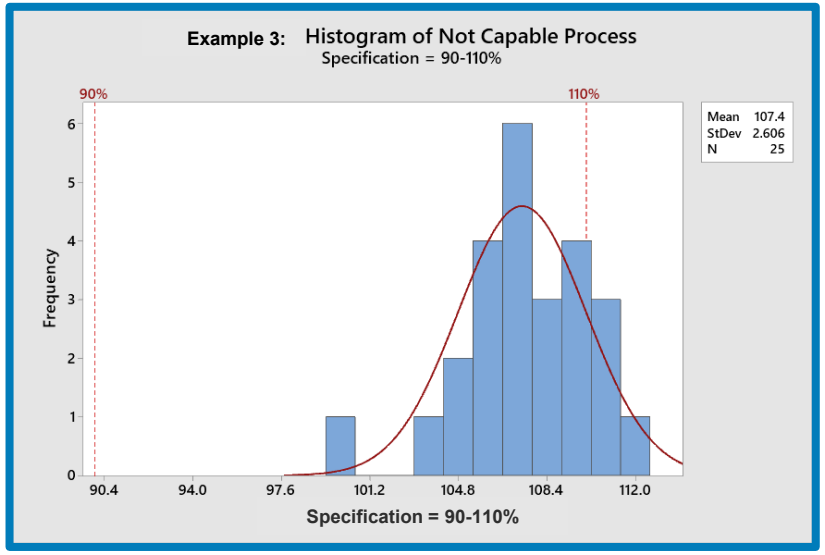
Example 1



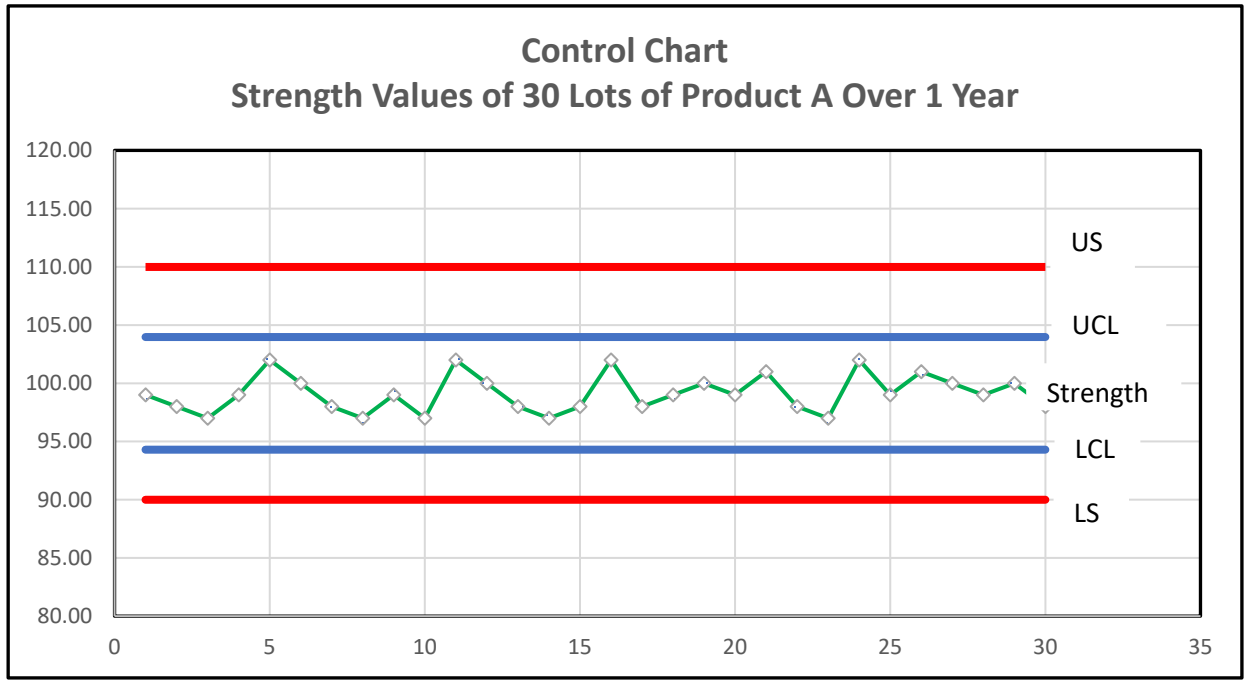
Example 2

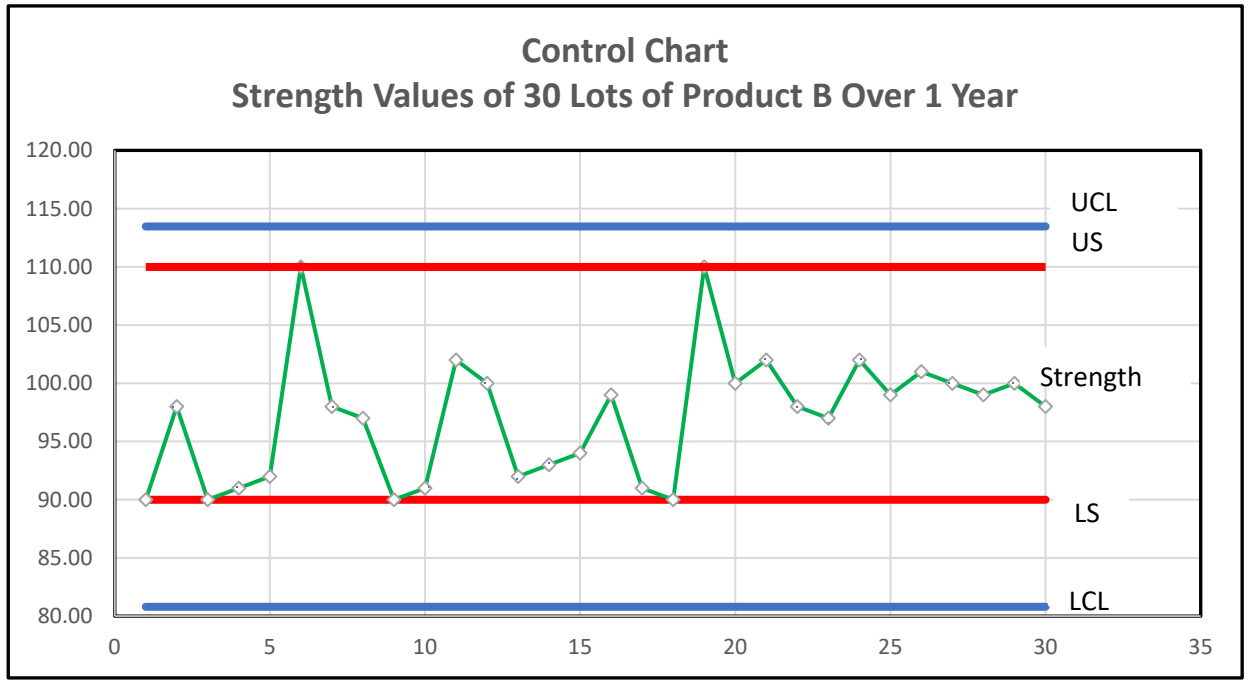


Example 3

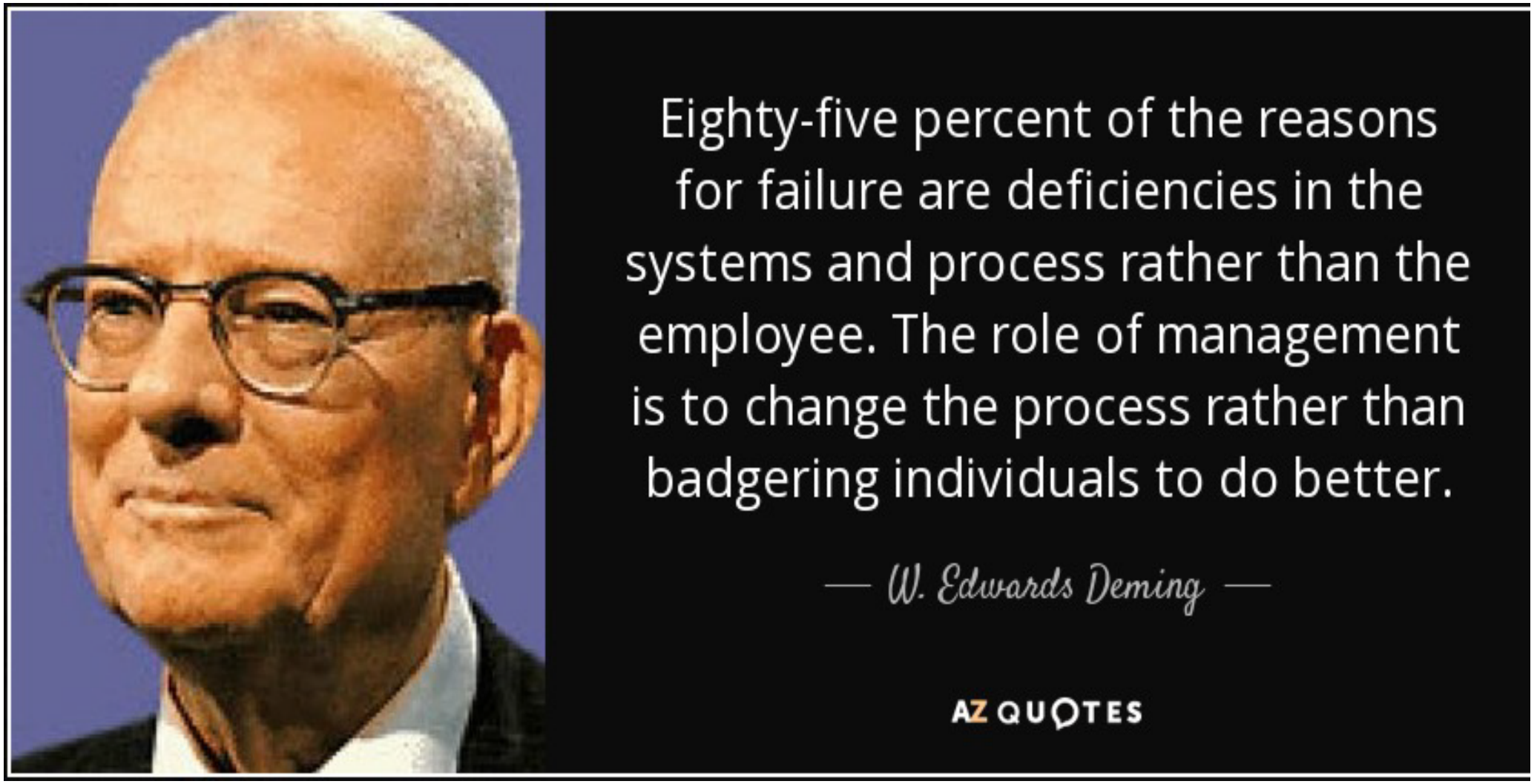


Control Charts - Examples





PV and Change Management

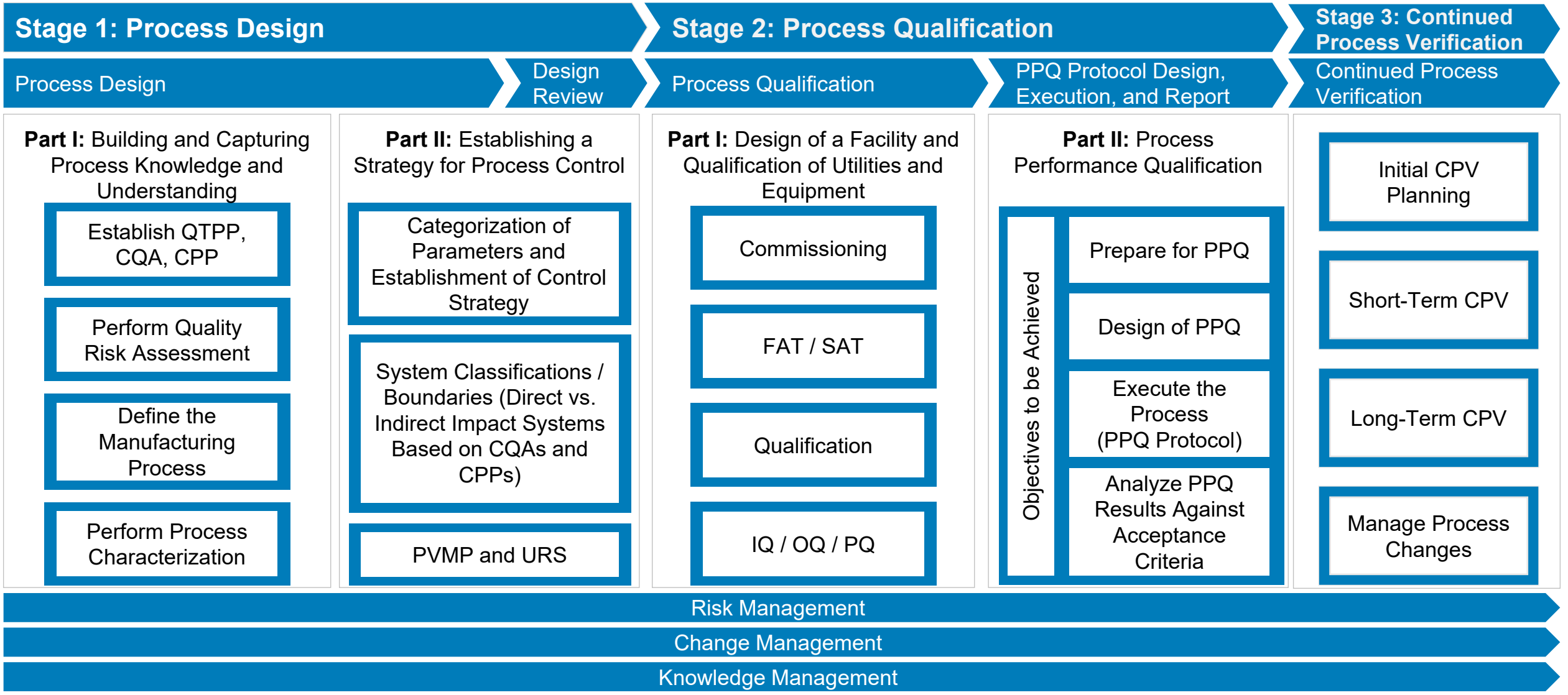


PV and Change Management (cont.)

- Change management is a systematic approach to proposing, evaluating, approving, implementing, and reviewing changes.*
- Before changes are implemented, proposed changes should be evaluated by teams composed of people with a diverse background, including ones familiar with the change at issue (e.g., manufacturing, quality) using pre-established criteria.
- A description of the planned change, a well-justified rationale for the change, an implementation plan, and QU approval must be documented before implementation.
- Depending on how the proposed change might affect product quality and safety, additional process design and process qualification activities may be warranted.
- Quality risk management (QRM) should be utilized to evaluate proposed changes.

*Source: ICH Guidance for Industry Q10 Pharmaceutical Quality System

PV Diagram


Stage 1: Process Design
Stage 2: Process Qualification
Stage 3: Continued Process Verification
Process Design
Design Review
Process Qualification
PPQ Protocol Design, Execution, and Report
Continued Process Verification
Part I: Building and Capturing Process Knowledge and Understanding
Establish QTPP, CQA, CPP
Perform Quality Risk Assessment
Define the Manufacturing Process
Perform Process Characterization
Part II: Establishing a Strategy for Process Control
Categorization of Parameters and Establishment of Control Strategy
System Classifications / Boundaries (Direct vs. Indirect Impact Systems Based on CQAs and CPPs)
PVMP and URS
Part I: Design of a Facility and Qualification of Utilities and Equipment
Commissioning
FAT / SAT
Qualification
IQ / OQ / PQ
Part II: Process Performance Qualification
Objectives to be Achieved
Prepare for PPQ
Design of PPQ
Execute the Process (PPQ Protocol)
Analyze PPQ Results Against Acceptance Criteria
Initial CPV Planning
Short-Term CPV
Long-Term CPV
Manage Process Changes
Risk Management
Change Management
Knowledge Management

Regulatory Requirements

Regulatory requirements contained in the CFR include:

Regulatory Requirements	CFR
Written Procedures; Deviations	21 CFR 211.100, and 211.192
Sampling and Testing of In-process Materials and Drug Products	21 CFR 211.110
Adequate Facilities, Maintenance, and Calibration	21 CFR 211.42(a), 211.63, and 211.68(a)
Control of Microbial Contamination	21 CFR 211.113
Annual Product Review	21 CFR 211.180(e)

ICH Guidance

ICH is the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use. ICH is a joint effort to align regulations in what has become a global environment. The following ICH documents have been adopted in published FDA guidance documents.

- **ICH Q8(R2) Pharmaceutical Development**

This guidance document on pharmaceutical development defines procedures for linking product and process development planning to the final commercial process control strategy and quality system.

- **ICH Q9 Quality Risk Management**

This guidance document describes the use of a risk-based approach to pharmaceutical development and manufacturing quality. These approaches identify and prioritize those process parameters and product quality attributes with the greatest potential to affect product quality.

- **ICH Q10 Pharmaceutical Quality System**

This guidance document is intended to assist pharmaceutical manufacturers by describing a model for an effective quality management system for the pharmaceutical industry, referred to as the Pharmaceutical Quality System (PQS). To achieve the goals outlined in this guidance document, it is essential to integrate the Process Design into the quality system.

Knowledge Management

Knowledge management is a “systematic approach to acquiring, analyzing, storing, and disseminating information related to products, manufacturing processes, and components.”

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Why Is It Important?

Knowledge management supports how knowledge is acquired, analyzed, stored, disseminated, and applied across the PV lifecycle. Information should be consistently maintained, either manually or automatically, depending on the system used by each firm.

Introduction to Legacy Products

Legacy products are existing products currently on the market for which some current PV lifecycle concepts may not have been formally established and/or implemented.

Manufacturers of legacy products can take advantage of the knowledge gained from the original process development and qualification work to develop a pathway for validation.

Pathway for Validating Legacy Products

Gap Analysis

A gap analysis helps to reveal what elements are missing (e.g., CQAs, CPPs, control strategy, qualification of a piece of equipment) and needed to complete PV.

Data Analysis and Risk Assessment

Data analysis should show the production process was robust and reliably operating in a state of control.

The extent of the validation activities to perform will be commensurate with the overall risk as determined based on the gap analysis and risk assessment.

Stage 3: CPV

Questions?


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