Process Validation Guidance

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Study Group 3

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Introduction

- Definitions
- How are processes validated?
- What processes must be validated?
- How to maintain state of validation
- Revalidation

1.1 Purpose of Guideline

- To assist manufacturers in understanding quality management system requirements concerning process validation

1.2 Scope of Guideline

- Applicable to manufacturing, servicing and installation processes for medical devices
- Does not cover verification of design output or design validation

What is Process Validation?

Three Elements of Process Validation

1. Verify that equipment is installed and operating properly *(Installation Qualification)*
2. Develop process that can produce product or result that meets all specifications *(Operational Qualification)*
3. Verify that process can produce product or result that meets all specifications consistently over time *(Performance Qualification)*

Steps in Validating a Process

1. Develop validation protocol
2. Conduct installation qualification
3. Conduct operational qualification
4. Conduct performance qualification
5. Analyze results and reach conclusions

2. Definitions

2.4 Process Validation

- Establishing by *objective evidence* that a process *consistently* produces a result or product meeting its *predetermined requirements*.

2.6 Verification

- Confirmation by examination and provision of *objective evidence* that the specified requirements have been fulfilled.

2.5 Process validation protocol

- A document stating how validation will be conducted, including test parameters, product characteristics, manufacturing equipment, and decision points on what constitutes acceptable test results.

2.1 Installation Qualification (IQ)

- Establishing by objective evidence that all key aspects of the process equipment and ancillary system installation adhere to the manufacturer's approved specification and that the recommendations of the supplier of the equipment are suitably considered.

Some IQ Considerations

- Equipment manufacturer's recommendations
- Electricity: supply, reliability
- Water: supply, pressure, quality
- Air: pressure, quality
- Calibration: schedule, documentation
- Maintenance: schedule, procedures, documentation, spare parts

2.2 Operational Qualification (OQ)

- Establishing by *objective evidence* process control limits and *action levels* which result in product that meets *all* predetermined requirements.

Some OQ Considerations

- Establish:
  - Procedure
  - Process control limits
  - Output specifications
  - Alert levels and action levels
  - Specifications for components, manufacturing materials

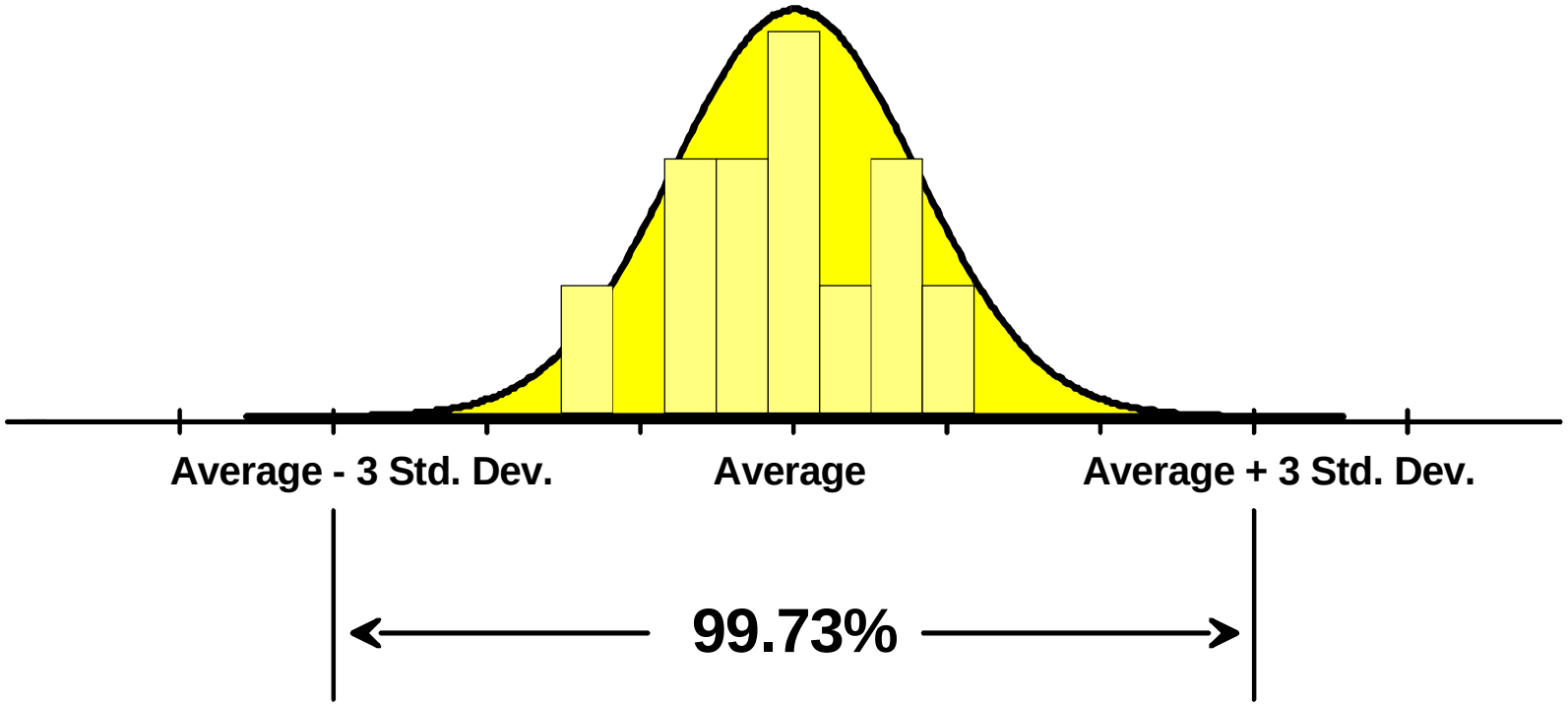
Some OQ Considerations

- Some environmental conditions that may affect process stability
  - Temperature
  - Humidity
  - Light
  - Particle count, contamination
  - Other

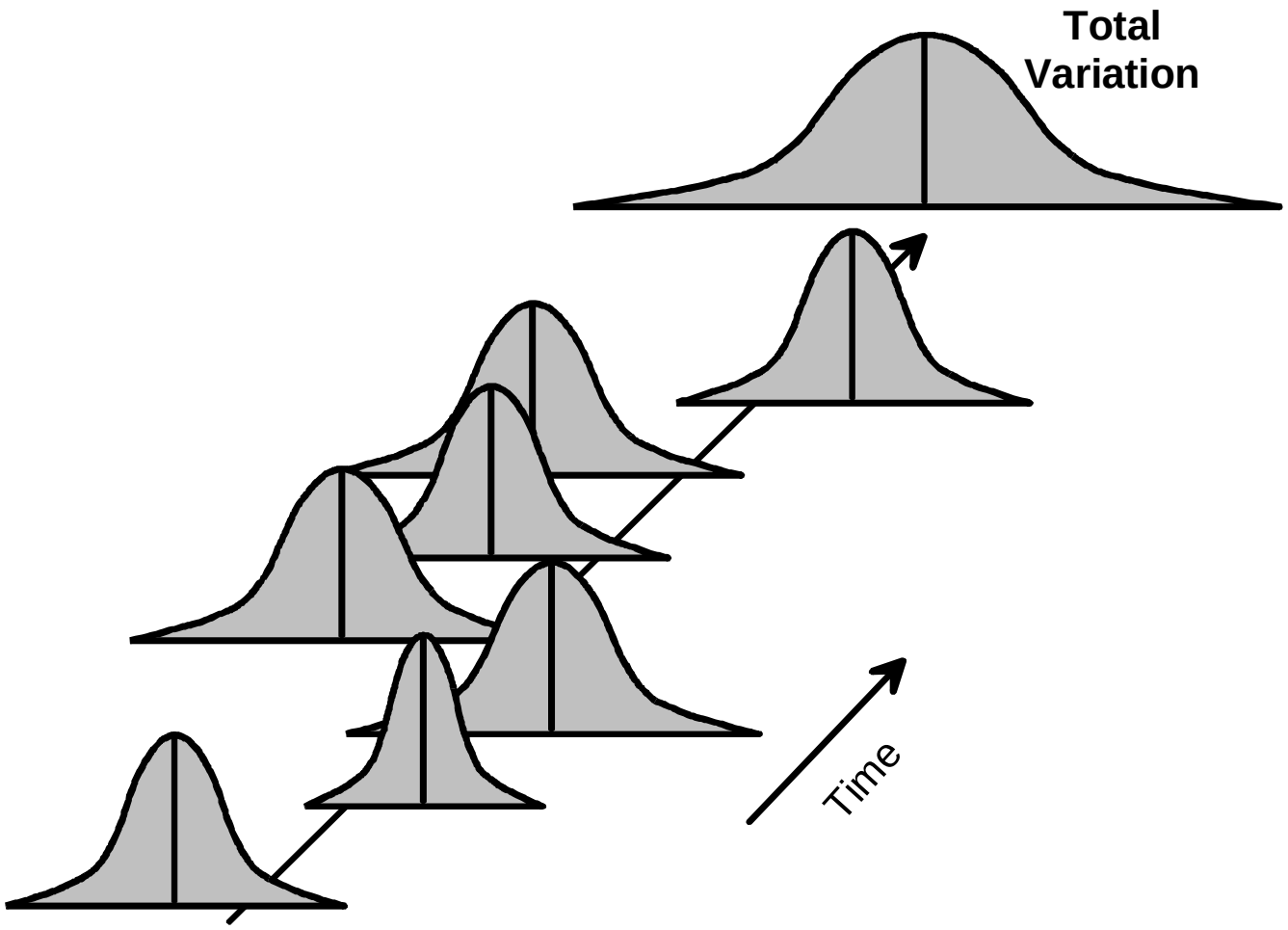
2.3 Performance Qualification (PQ)

- Establishing by objective evidence that the process, under *anticipated conditions*, *consistently* produces a product which meets *all* predetermined requirements

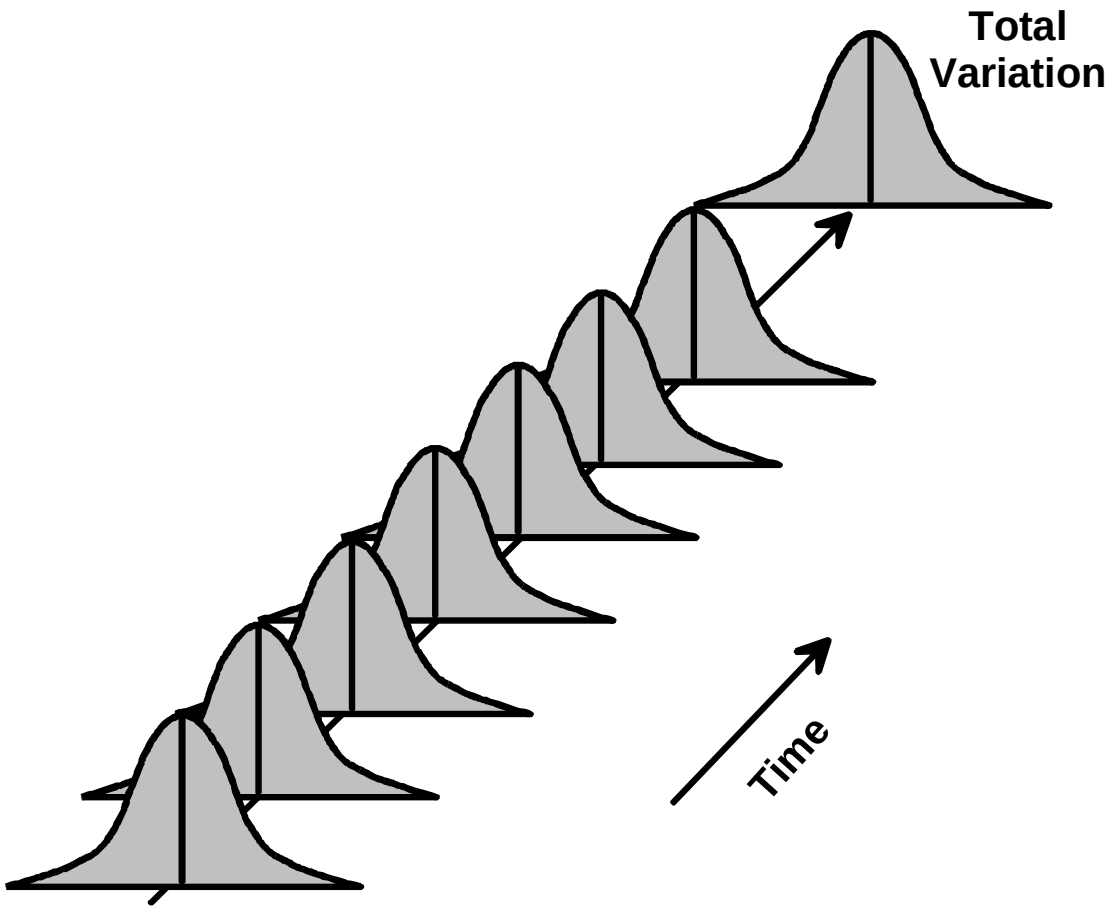
Normal curve applied to histogram



UNSTABLE PROCESS



STABLE PROCESS



Maintaining a State of Validation

6.1 Monitor and control process

- Purpose: to ensure process remains within established parameters under anticipated conditions
- Investigate deviations from established parameters
- Take corrective action
- Consider whether revalidation is necessary

6.2 Changes in process or product

- Evaluate changes in process, product, procedures, equipment, personnel, environment, etc. to determine effect of change
- Is revalidation necessary?
- How much revalidation is necessary to assure process is capable and stable?

Periodic revalidation

- Consider periodic revalidation where *cumulative* minor changes to process and raw materials may eventually affect process
- Sterilization processes typically are revalidated periodically (once a year) as specified in voluntary standards

Some reasons for revalidation

- Change in process that may affect quality or validation status
- Negative trend in quality indicators
- Change in the product design that affects the process
- Process is moved within facility or transferred from one facility to another
- Change in the application of the process

Using historical data for validation

- Validation can be partially based on accumulated historical manufacturing, testing, control and other data
- Sources of historical data:
  - batch or lot records
  - manufacturing log books
  - test and inspection results
  - control charts
  - customer feedback
  - field failure reports
  - service reports
  - audit reports
  - generic feedback

Using historical data for validation

- All appropriate data must have been collected AND collected in a manner that allows adequate analysis
- Historical pass/fail manufacturing data usually is not adequate

Summary

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