Production and Process Controls

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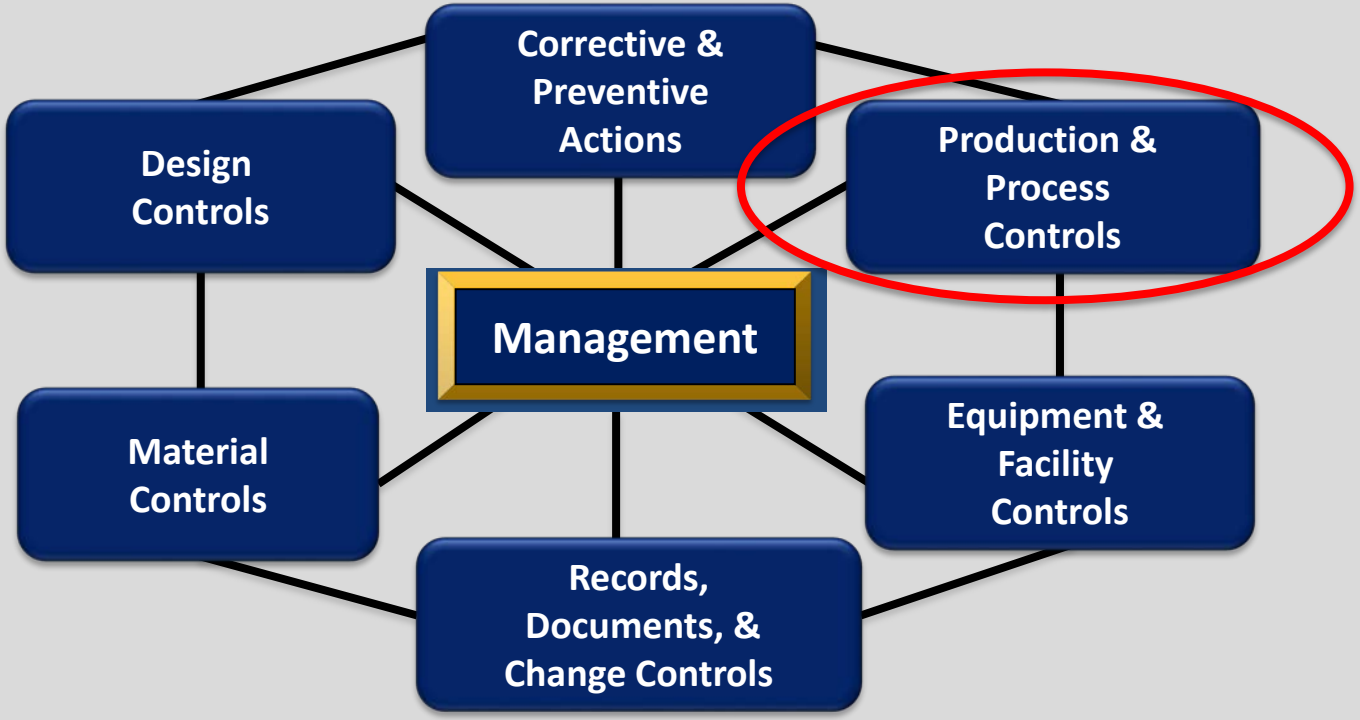
Production and Process Controls: Why Are They Important?

Manufacture products that meet pre-determined specifications

Learning Objectives

1. Explain how Production and Process Controls relate to the overall Quality System
2. Describe the general aspects of Production and Process Controls
3. Describe the aspects of inspection, measuring, and testing equipment
4. Define the concept of Process Validation

The 7 Subsystems of a Quality System



Production and Process Controls: Titles and Regulation Number

Subpart	Title	Regulation Number (21 CFR)
Production and Process Controls	Production and Process Controls	820.70
	Inspection, Measuring and Test Equipment	820.72
	Process Validation	820.75

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General Process Controls
21 CFR 820.70(a)

- Develop, conduct, control and monitor production processes
- To ensure that a device conforms to its specifications

General Process Controls: Example

To ensure proper sealing

- Develop a package sealing process
- Account for temperature, pressure, and time
- Monitor the process over time

General Process Controls
21 CFR 820.70(a)(1) - (5)

- If deviations to specifications could occur as a result of manufacturing

General Process Controls
21 CFR 820.70(a)(1) - (5)

Include

1. Documented instruction, standard operating procedures (SOPs), and methods
2. Monitoring and control of process parameters
3. Compliance to reference standards
4. Approval of process and equipment
5. Criteria for workmanship

Product and Process Changes
21 CFR 820.70(b)

- Establish and maintain procedures for changes
  - to specification, method, process or procedure
- Verify or validate (where appropriate) changes before implementation (per 21 CFR 820.75)
- Approve changes (per 21 CFR 820.40)

Environmental Control
21 CFR 820.70(c)

- If environment conditions could adversely effect product quality
- Establish and maintain procedures to adequately control them

Environmental Control Examples

- Particles
- Humidity
- Air pressure, flow, filtration, ionization
- Temperature
- Lighting
- Sound
- Vibration

Environmental Control Example

Rinsing Process

- Understand water source used for rinsing to prevent residue

Environmental Control
21 CFR 820.70(c)

- Periodically inspect environmental control system(s)
  - to verify that system is adequate and functioning properly
- Document and review environmental control activities

Environmental Control Examples

- Review humidity chart to ensure humidity levels are within operating window
- Check for electrostatic discharge station grounding

Personnel
21 CFR 820.70(d)

- Establish, maintain requirements for personnel:
  - health
  - cleanliness
  - personnel practices
  - clothing

- If contact between personnel and product may have adverse effect on product quality

Personnel
Examples

- Clothing restrictions or required uniforms
  - for cleanrooms or electronic products
  - examples: hair nets or smocks
- Personal hygiene
- Food and drink restricted areas
- Addressing illnesses at work
  - respiratory, skin conditions

Preamble to Quality System Regulation: Importance

- Public Comments received to draft regulation
- FDA response to comments
- FDA clarification of intent of regulation

Preamble: Personnel

"… a manufacturer's requirements must not permit unclean or inappropriately clothed employees, or employees with medical conditions, to work with devices where such conditions could reasonably be expected to have an adverse effect on product quality. The procedures must also address acceptable clothing, hygiene, and personal practices, if contact between personnel and product or environment could reasonably be expected to have an adverse effect on product quality."

Preamble, Comment 129

Personnel
21 CFR 820.70(d)

- For maintenance and other personnel required to work temporarily under special environmental conditions

- Ensure appropriate training or supervision by trained individuals

Personnel: Example

- Janitorial staff or technicians who come to work on machines and need to enter a cleanroom

➢ They need to be trained, or supervised by a trained individual, when entering the cleanroom

Contamination Control
21 CFR 820.70(e)

- Establish, maintain procedures
- To prevent contamination of equipment/product
- By substances that could reasonably be expected to have an adverse effect on product quality

Contamination Control Example

Cardboard Boxes

- If particulate from cardboard boxes may contaminate your product
- Do not store cardboard boxes in clean room

Preamble: Contamination Control

"Contamination control must include establishing and maintaining adequate cleaning procedures and schedules, if such control is necessary to meet manufacturing process specifications. In addition, Sec. 820.25 Personnel, requires that employees have a thorough understanding of their job functions, which would include a requirement that the appropriate employees comprehend the cleanliness and sanitation procedures."

Preamble, Comment 128

Buildings
21 CFR 820.70(f)

Buildings

- shall be of suitable design and contain sufficient space
  - perform necessary operations
  - prevent mix ups
  - assure orderly handling

Equipment
21 CFR 820.70(g)

Ensure that all equipment used in manufacturing process:

- Meets specified requirements
- Is appropriately designed, constructed, placed, and installed

To facilitate maintenance, adjustment, cleaning and use

Equipment Maintenance Schedule 21 CFR 820.70(g)(1)

Establish, maintain schedules

- to adjust, clean and otherwise maintain equipment
- to ensure manufacturing specifications are met

Document maintenance activities

- include date and individual(s) performing maintenance activities

Equipment Inspection
21 CFR 820.70(g)(2)

Conduct periodic inspections per established procedures

- to ensure adherence to applicable equipment maintenance schedules

Document inspections

- including date and individual(s) conducting inspections

Equipment Adjustment
21 CFR 820.70(g)(3)

- Post any inherent limitations or allowable tolerances
  - visibly or near equipment requiring periodic adjustments
- Or make information readily available to persons performing adjustments

Manufacturing Material: Definition

Any material or substance used in or used to facilitate the manufacturing process, a concomitant constituent, or a byproduct constituent produced during the manufacturing process, which is present in or on the finished device as a residue or impurity not by design or intent of the manufacturer

21 CFR 820.3(p)

Preamble: Manufacturing Material

"FDA amended the definition of manufacturing material to help clarify this definition. Concomitant material refer to those material or substances that naturally occur as part of the material or during the manufacturing process which are intended to be removed or reduced in the finished device…"

Preamble, Comment 26

Manufacturing Material
21 CFR 820.70(h)

- Establish, maintain procedures for use and removal of manufacturing material where it could reasonably be expected to have an **adverse effect** on product quality

Manufacturing Material Example

- Concomitant constituents
  - The allergenic or adverse proteins that occur naturally in the natural rubber latex components

Manufacturing Material Example

- Use and removal may be part of another procedure
- Procedures should have an associated data form for recording values
- SOPs, data forms, and purchasing requirements are part of the Device Master Record

Automated Processes
21 CFR 820.70(i)

- Validate computer software used as part of production or Quality System for its intended use
- Validate according to established protocol
- Validate all software changes before approval and issuance
- Document validation activities and results

Automated Processes Examples

- Injection molding process
- Statistical process control software
- Complaint tracking software
- Inventory tracking
- Document control

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Control of Inspection, Measuring and Test Equipment 21 CFR 820.72(a)

- Ensure that all inspection, measuring, and test equipment is suitable for intended purposes and capable of producing valid results

Why Control Equipment?

- Used to evaluate whether product does or does not conform design, process validation and routinely in production

- Must provide valid results for evaluation to be meaningful

Control of Inspection, Measuring and Test Equipment 21 CFR 820.72(a)

- Establish procedures to ensure equipment is routinely inspected, checked, maintained and calibrated
  - Address equipment handling, preservation, storage
- Document activities

Calibration
21 CFR 820.72(b)

- Establish procedures
  - including specific directions/limits for accuracy and precision
- For valid results, equipment should be:
  - Accurate
    - how close the measured value is to actual value
  - Precise
    - proximity of multiple measurements to each other (that is, how close they are to each other)

Calibration
21 CFR 820.72(b)

- Include provisions for remedial action to
  - reestablish limits
  - evaluate for adverse effect on device quality
    - Consider all usage since last known good condition
    - Include “as found condition to recognize the need for remedial action”

Calibration Standards
21 CFR 820.72(b)(1)

Calibration standards must be traceable to:

- National standards
- International standards
- Independent reproducible standards

Calibration Records
21 CFR 820.72(b)(2)

- Must include:
  - equipment identification
  - calibration dates
  - individual performing each calibration
  - next calibration date
- Readily available and posted on/near equipment

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Process Validation: Definition

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

21 CFR 820.3(z)(1)

Process Validation:
For More Information

CDRH Learn Module: Process Validation

fda.yorkcast.com/webcast/Play/090c4052bc2b4f90ba94245204e745061d

QS Regulation and Guidance

- **Quality System Regulation and Preamble**

  www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=820&showFR=1

  www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/PostmarketRequirements/QualitySystemsRegulations/ucm230127.htm

- **Inspection Guide**

  https://www.fda.gov/ICECI/Inspections/InspectionGuides/ucm074899.htm

- **Guide to Inspections of Quality Systems [Quality System Inspection Technique (QSIT)]**

  www.fda.gov/iceci/inspections/inspectionguides/ucm074883.htm

Summary

1. We showed how Production and Process Controls relate to the overall Quality System
2. We discussed the general aspects of Production and Process Controls
3. We described the aspects of inspection, measuring, and testing equipment
4. We introduced the concept of Process Validation

Your Call to Action

Establish your Production and Process Controls, so you manufacture products that meet your specifications

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