

Section 201(h)

How does FDA define a Medical Device?

- ...intended for use in the diagnosis of disease...
- ...intended to affect the structure or any function of the body...
- ...does not achieve its primary intended purposes through chemical action

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Quality System

- 21 CFR PART 820
 - FDA Regulations for medical devices requires that manufacturers establish and maintain a Quality System
- What is a Quality System?
 - Organizational structure, responsibilities, procedures, processes and resources for implementing quality
- Where do we begin?

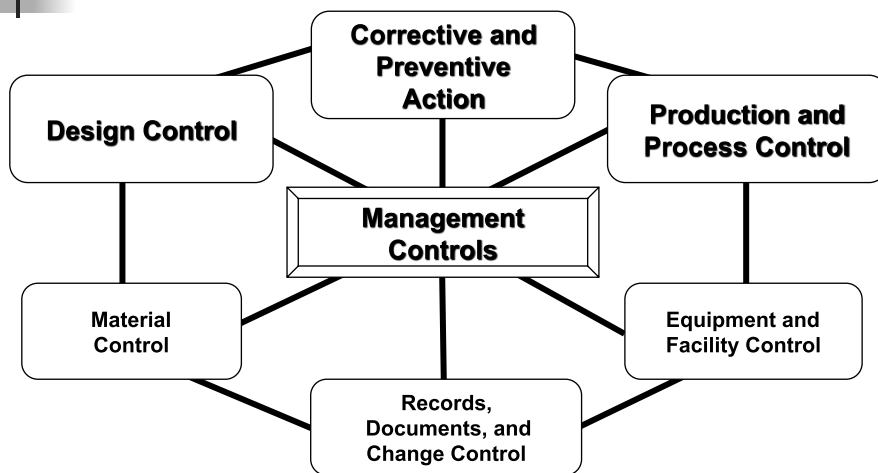
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FDA Quality System Regulation for Medical Devices

21 CFR Part 820

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FDA 21 CFR Part 820



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21 CFR PART 820

- Quality System Regulation
 - Quality assurance program
 - Establish specifications and controls
 - Finished devices meet specifications

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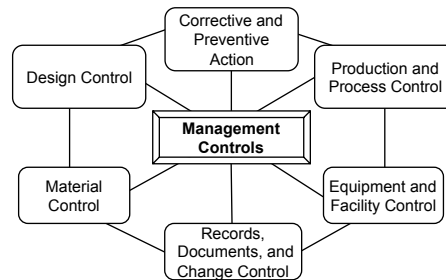
Quality System Foundation

- Management Review
- Audits
- CAPA

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Management Controls

- Scope (820.1)
- Definitions (820.3)
- Quality System (820.5)
- Management Responsibility (820.20)
- Quality Audit (820.22)
- Personnel and Training (820.25)



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Management Controls

- **Quality Policy**
 - Documented
 - Communicated and understood
- **Quality Objectives**
 - Measurable, Monitored
 - Documented
 - Management Review

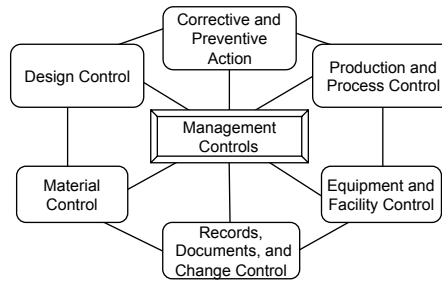


Quality Policy means overall intentions and direction of an organization with respect to quality

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Design Control 820.30

General
Design & Development Planning
Design Input, Design Output
Design Review
Design Verification & Validation
Design Transfer
Design Changes
Design History File (DHF)
Device Packaging 820.130



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SMDA - 1990

Why do we have Design Controls

- 44 % voluntary recalls due to inadequate design controls
 - "Device Recalls: A Study of Quality Problems"
- 90 % of all software-related device failures were due to design-related errors (failure to validate software prior to routine production)
 - "FDA Medical Device Regulation From Pre-market Review to Recall"

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Design Control

- Establish and maintain procedures to control the design of the device
- 820.30 is applicable to
 - All Class II and III products
 - Certain Class I products
 - Automated with software
 - Tracheobronchial suction catheters
 - Surgeon's gloves
 - Protective restraints
 - System, radionuclide applicator, manual
 - Source, radionuclide, teletherapy

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Design Control

- Design Development and Planning
 - Team members and resources
 - Milestones, timeline, responsibility
 - Interfaces
 - Review, approved, updated

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Design Change

- Design Change
 - Changes must be appropriate (validated or verified), reviewed, and approved
 - Responsibility & authority defined
- Documentation
 - Appropriate to the significance of the change
 - Document verification / validation decisions
 - Include justification / rationale
 - Evaluate the change to determine if a 510(k) or supplement to a PMA is required

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Design Change

- History of changes documented
 - Pre-production and
 - Post design transfer
 - 820.40 (Document) and 820.70 (Process) changes must consider impact to design



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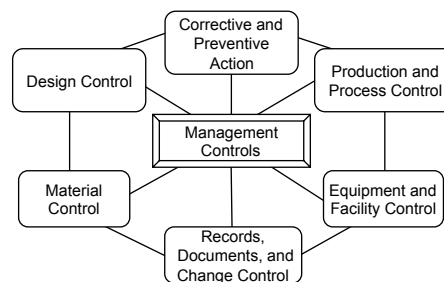
Design Transfer

- Design Transfer
 - Ensure design transfers to manufacturing accurately

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Production and Process Control

Production and process controls (820.70)
Process validation (820.75)
Receiving, in-process, and finished device acceptance (820.80)
Acceptance status (820.86)
Nonconforming product (820.90)
Device labeling (820.120)
Purchasing Controls (820.50)



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Terms & Definitions

- Manufacturing Material *820.3(p)*
- Nonconformity *820.3(q)*
- Rework *820.3(x)*
- Process Validation *820.3(z)(1)*
- Verification *820.3(z)(2)(aa)*

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Production and Process Control

- General *820.70(a)*
 - Documented instructions
 - Monitor/inspect
 - process parameters, component, device characteristics
 - Reference standards
 - Process and equipment approval
 - Workmanship standards

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Production and Process Control

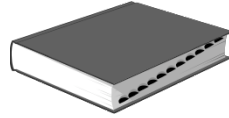
- Personnel *820.70(d)*
 - Requirements for health, cleanliness, personnel practices, and clothing
 - Personnel with temporary exposure to production environment
- Automated processes *820.70(i)*
 - Validate for “intended use”

January 11, 2002
General Principles of Software Validation; Final Guidance for Industry and FDA Staff
<http://www.fda.gov/cdrh/comp/938.pdf>

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Process Validation

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Definition

- 820.3(z)(1) Process validation
 - means establishing by objective evidence that a process consistently produces a result or product meeting its predetermined specifications

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Process Validation

- Process Validation vs. 100% Verification
 - Required when ... process output cannot be confirmed by subsequent inspection and test
- Process Validation Program
 - Master Validation Plan
 - Protocols/reports
 - IQ, OQ, PQ
 - Revalidation

Edition 2, January 2004

GHTF SG3 Quality Management Systems - Process Validation Guidance

<http://www.ghtf.org/sg3/>

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Process Validation

- Control
 - Define methods to monitor and control the validated process
 - Monitor trends in the process to ensure the process remains within the established parameters
 - Ensure that validated processes are performed by qualified individual(s)

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Revalidation

- When changes or process deviations occur, evaluate the process and perform revalidation where appropriate
- Consider design impact

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Revalidation

- Changes should be evaluated to determine the affects of those changes and the extent of revalidation considered
 - Process and /or Product,
 - Raw Materials,
 - Components,
 - Procedures,
 - Methods,
 - Equipment,
 - Personnel

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What about people-dependent processes?

- Qualify any equipment
- Calibration
- Qualify materials and components
- Develop and document manufacturing procedure:
 - Written description
 - Illustrations, photographs, videotapes
 - Samples
- Implement use of fixtures, holders, special equipment to reduce variation
- Challenge manufacturing procedure
 - Have people unfamiliar with process perform it
 - Where they have difficulty, procedure needs refinement
- Identify acceptance criteria; i.e. maximum number of defects
- Train/qualify operators

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Process Change vs. Design Change?

- Change material, component or supplier
 - Re-qualify new material or component
 - Revalidate if not equivalent to old material or component
- Move equipment
 - Re-qualify equipment
 - Revalidate if there is a change in equipment operation
- Change equipment
 - Qualify equipment
 - Revalidate if not equivalent to old equipment
- Change in environment
 - Revalidate if change could affect process
- Seasonal changes
 - Revalidate if change could affect process.

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Process Change vs. Design Change?

- Change order of operations
 - Re-qualify process
 - Revalidate if change affects device performance and/or conformance to specs.
- Change process control software
 - Change in software
 - Revalidate process if software change affects process

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Warning Letter Example

- The packaging sealing process was not adequately validated for the following reasons:
 - The Installation Qualification was not documented
 - The validation study did not include evaluation of critical parameters such as temperature, time, and pressure; and
 - The validation test sample lacked statistical rationale

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Warning Letter Example

- Failure to establish and maintain procedures for monitoring and control of process parameters for validated processes to ensure that the specified requirements continue to be met, as required by 21 CFR 820.75(b). For example:
 - You have not performed dose audits as required by your sterilization procedure.
 - The packaging sealing process for sterile barrier packaging is not monitored.

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Nonconforming Product

- Control
 - identification, documentation, evaluation, segregation, and disposition
- Review and Disposition
 - responsibility for review,
 - authority for disposition,
 - use as is
- Rework
 - re-evaluation, re-inspection, adverse effects

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Purchasing Controls

- Evaluation of Suppliers
 - Suppliers, Contractors, Consultants
 - Establish quality requirements to be met
 - Evaluate and select based on ability, establish controls based on results
 - Records of Approved Suppliers
- Purchasing Data
 - Establish (via 820.40)
 - PO data/requirements
 - Notification of changes

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Warning Letter Example

- Your firm failed to establish and maintain purchasing control procedures to ensure that all purchased or otherwise received product and services conform to specified requirements as required by 21 CFR 820.50. For example:
 - ... there is no procedure or documentation of any assessment of your contract manufacturer,
 - ... (Contract manufacturer) orders all components and is responsible for qualifying all vendors before the components are shipped
 - ...there is no procedure or documentation of any supplier evaluations or control of purchasing data

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Warning Letter Example

- Your firm failed to adequately establish and maintain procedures or specifications in conjunction with your contract manufacturer, _____ in order for production processes and controls to be established that would ensure that a device conforms to its specifications as required by 21 CFR 820.70.
 - During the FDA inspection, a telephone conference was held between the FDA investigator, Mr. "Smith" and Mr. "Jones" from (contract manufacturer) stating that requirements were made verbally and not placed in writing except the pump test procedure ... No other specifications or process controls were documented.

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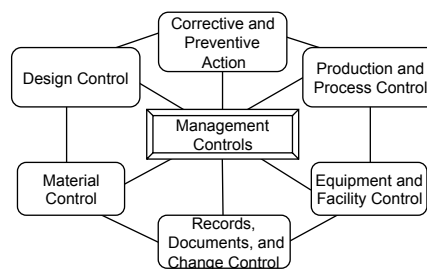
Purchasing Controls

- ***Expect more scrutiny from FDA***
 - Establish clear Quality System Links
 - Design Controls
 - Manufacturing
 - CAPA
 - Supplier Agreements
 - Contract Manufacturers
 - Virtual Manufacturers and Acquisitions

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Corrective and Preventive Action (CAPA)

Corrective and Preventive Action (820.100)
Complaint Handling (820.198)
MDR Reporting (21 CFR Part 803)
Servicing (820.200)
Statistical Techniques (820.250)



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Definitions

Correction

Action taken to eliminate a detected nonconformity

*A disposition decision
repair, rework, scrap*

Corrective Action

Action taken to eliminate the cause of a detected nonconformity or other undesirable situation

*Corrective action is taken to
manage/control
recurrence*

Preventive Action

Action taken to eliminate the cause of a potential nonconformity or other undesirable potential situation

*Preventive action is taken to
prevent
occurrence*

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CAPA program

- Must address both
 - Corrective and Preventive action
- Data sources distinguish CA from PA
 - Corrective actions occur when data analysis detects an actual problem (nonconformity)
 - Preventive actions result when data analysis detects a potential problem (unfavorable trends)

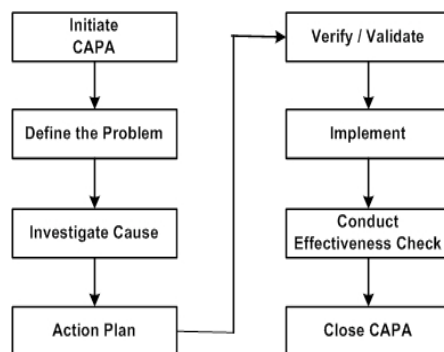
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Corrective and Preventive Action System § 820.100

- Detect problems
- Analyze data
- Investigate cause
- Identify action needed
- Implement and record changes
- Disseminate information
- Submit for management review

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CAPA Simplified



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CAPA Links

- Link CAPA with Design Controls
- Risk Management is an integral part of Corrective and Preventive Action
- Recognize risk control decisions form the basis for identifying CAPA data and establishing action limits
- Identify early detection points
 - Consider both Pre and Post Market data

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Complaint Management

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Complaint Definitions

FDA 820.3(b) **Complaint**

any written, electronic, or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness, or performance of a device after it is released for distribution

ISO 13485:2003 (3.4) **Customer Complaint**

written, electronic or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety or performance of a medical device that has been placed on the market

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What is a complaint?

FDA

- Any report involving the possible failure of a device, labeling, or packaging to meet any of its specifications is subject to the provisions of 820.198 ...includes Use Error

ISO

- Any indication of the failure of a device to meet customer or user expectations for quality or to meet performance specifications

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Medical Device Reporting

Some complaints are more significant than others

- An event where a marketed device may have caused or contributed to
 1. Death
 2. Serious Injury-or-
 3. Malfunction Occurred
- If the malfunction were to recur it may cause death or serious injury if the malfunction recurred

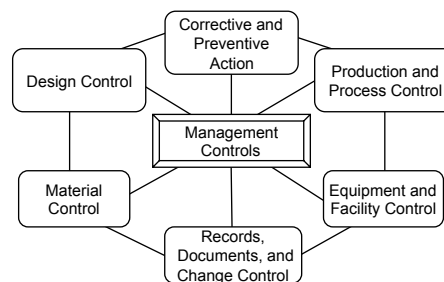


... Same or similar product

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Document Control and Records

Document Controls (820.40)
Production and Process Changes (820.70 (b))
General Requirements (820.180)
Device Master Record (820.181)
Device History Record (820.184)
Quality System Record (820.186)



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Document Control

- Document Approval and Distribution
 - Designated approvers
 - Approval prior to issuance
 - Signature and date of approval
 - Distribution to all points of use
 - Removal of obsolete documents

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Document Control



- **Document Changes**
 - Reviewed and approved by same function that performed the original review and approval
 - Communication of changes
 - appropriate personnel
 - timely manner
 - Maintain records

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Change Records

- Description of change
- Identification of documents affected
- Signature of approving individual(s)
- Approval date
- When the change becomes effective

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Production and Process Changes

- Documented change order
 - In accordance with 820.40
 - Includes process validation decision
 - Rationale when "no" process validation required is indicated
 - Process validation records referenced when "yes" is indicated

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Quality Records

- General Requirements
 - Accessibility
 - Legibility
 - Storage to prevent damage, loss, etc.
 - Back-up of automated storage
 - Record Retention Period
 - Confidentiality
 - Exceptions

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Device Master Record - DMR

- Reviewed and approved per 820.40
 - Device specifications
 - Production process specifications
 - Quality assurance procedures and specifications
 - Packaging and labeling specifications
 - Installation, maintenance, and service procedures and methods
- ...DHF is the basis for the DMR*



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Device History Record (DHR)

- DHR proves that device produced meets DMR
 - Dates of manufacture, quantity manufactured, quantity released for distribution, acceptance records, primary identification label, device identification and control number



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Quality System Record (QSR)

- Quality System Record (QSR)
 - Non-device specific records (Quality Manual, SOPs, Quality Policy, etc.)

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Record Keeping



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Good Record Keeping Practices

- How To Make A Correction
 - Draw a single line through the incorrect information
 - Record the correct information
 - Initial and date the new information

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Good Record Keeping Practices

- Use only permanent Ink
 - **No** pencil
- Repetitive data entries
 - Such as signatures, dates, accept or reject, check marks, etc.
 - All entries must be individually recorded
 - Arrows, connecting lines and "dittos" acceptable



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Good Record Keeping Practices



- Blank Spaces
 - All space on a data entry form must be completed
 - If not the entry space is considered "not applicable" write **n/a** in the space and initial and date the entry

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Good Record Keeping Practices

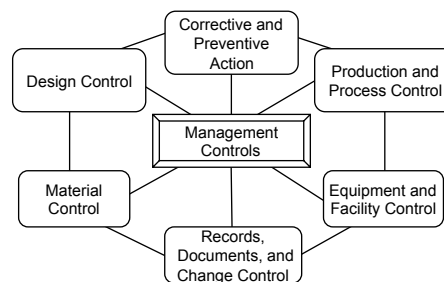
- **No** Write over's
- **No** Cross outs
- **No** Erasures
- **No** Correction fluid or correction tape



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Material Control

Identification (820.60)
Traceability (820.65)
Purchasing Controls (820.50)
Handling (820.140)
Storage (820.150)
Distribution (820.160)
Installation (820.170)



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Identification and Traceability

- Establish procedure for Identification
 - prevent mix-ups, during all stages
- Establish procedure for Traceability “where appropriate”
 - Surgical implant, support or sustain life
 - Document lot or serial number in DHR
 - System needs to facilitate corrective action (e.g., recall)

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Handling and Storage



- Handling
 - Prevent mix-ups, damage, deterioration, contamination, etc., applies to all stages where manufacturing handles product
- Storage
 - Control of storage area, including authorized access and dispatch to/from
 - Prevent mix-ups, damage, deterioration, contamination, use of expired product, etc.

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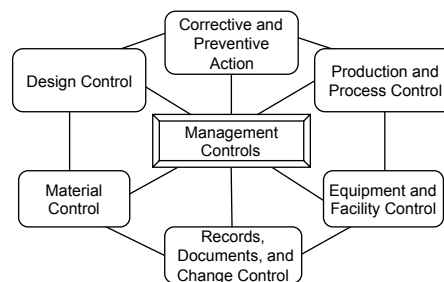
Distribution and Installation

- Distribution
 - Distribution release approval
 - Only approved devices, devices that have not expired and devices meeting customer purchase orders
 - Distribution records
- Installation
 - Instructions documented and distributed
 - Installation records, inspection and testing results

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Facility and Equipment Control

Environmental control 820.70(c)
Contamination control 820.70(e)
Buildings 820.70(f)
Equipment 820.70(g)
Inspection, measuring, and
test equipment 820.72



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Environmental Controls

- Environmental Control Procedures
"where appropriate"
 - Periodic inspection - review system, including equipment
 - Document and review, typically a management review subject
- Contamination Control Procedures
"where appropriate"
 - Prevent contamination of product and equipment

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Buildings and Equipment

- Building(s)
 - Adequate space and organization/design
 - Prevent mix-ups, provide for orderly handling and appropriate operations
- Equipment
 - Meets requirements and suitable design
 - Maintenance schedule, inspection and adjustment

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Inspection, Measuring, and Test Equipment

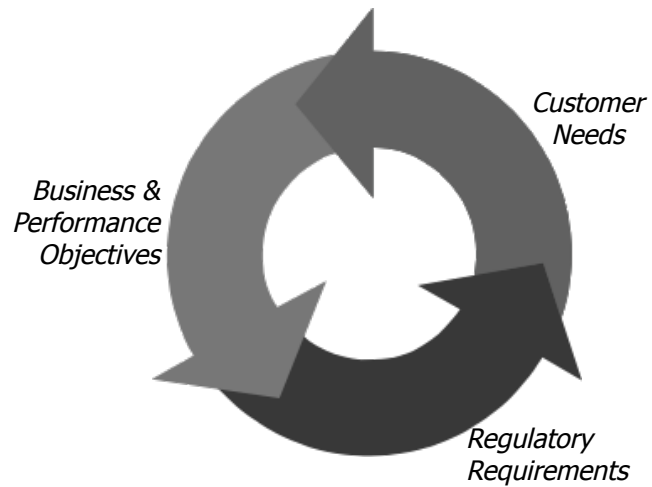
- **General Requirements**
 - Establish procedure, Ensure equipment is suitable for use, Handling, Calibration and Inspection schedule, Records
 - **Adequate instructions**
 - Limits and accuracy requirements
 - Remedial action requirements
 - Calibration standards
-
- **Calibration record requirements**
 - Equipment I.D.
 - Individual performing calibration
 - Calibration date and next date due
 - Records on or near equipment

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Why is the Quality System Important?

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It makes good business sense!



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Thank You!



Adding Value...Period

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