



# Quality System Regulation Overview

**FDA Small Business  
Regulatory Education for Industry (REdI)**  
Burlingame, CA  
June 17, 2014



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# Outline

- Background and Definitions
- QS Subsystems Covered
  - Management Responsibility
  - Quality Audit and Personnel
  - Corrective and Preventive Action
  - Complaint Handling
  - Production and Process Controls
  - Process Validation
  - Equipment and Facility Controls
  - Document, Records & Change Controls
- Warning Letter Data and Resources



# Background

- The Quality System Regulation
  - Effective June 1, 1997
  - Replaces 1978 GMP for medical devices
- Preamble to QS Regulation
- Requirements are not prescriptive
  - Provides framework of basic requirements for manufacturers to follow



# **Harmonization of Quality System Requirements**

- ISO 13485: revised & reissued 2003 as a stand alone quality system standard for medical device manufacturers
- ISO 13485: 2003 and 21 CFR Part 820 are harmonized; Each may have additional requirements but they do not conflict with one another.



# How can the QS Regulation cover so many types of devices?

- Flexible regulation
- Requirements are stated in general terms...

Each manufacturer shall establish and maintain a quality system that:

1. Is appropriate for the specific medical device(s) designed and/or manufactured
2. Meets the requirements of this part (part 820)

*21 CFR 820.5 (Quality System)*



# **Bottom line ... It's your Quality System!**

A manufacturer must develop a Quality System (QS) commensurate with the:

- Risk presented by the device
- Complexity of the device and the manufacturing processes
- Extent of the activities to be carried out
- Size and complexity of the manufacturer



# Quality System Regulation

## Definitions 21 CFR 820.3 (I)

***Finished device*** means any device or accessory to any device that is suitable for use or capable of functioning, whether or not it is packaged, labeled, or sterilized.



# Quality System Regulation

## Definitions 21 CFR 820.3 (o)

**Manufacturer** means any person who designs, manufactures, fabricates, assembles, or processes a finished device. Manufacturer *includes* but is not limited to those who perform the functions of contract sterilization, installation, relabeling, remanufacturing, repacking, or specification development, and initial distributors of foreign entities performing these functions.



# Quality System Regulation

Definitions 21 CFR 820.3 (v)

***Quality system*** means the organizational structure, responsibilities, procedures, processes, and resources for implementing quality management

# Evolution of Quality

- ***Quality Control:*** Test/inspect components/finished products vs. approved specifications
- ***Quality Assurance:*** Manufacture quality into product
- ***Quality System:*** Design and manufacture quality into products



## The 7 Subsystems of a Quality System



# Purpose of the Management Subsystem

- To establish responsibility and authority
- To provide adequate resources for device design, manufacturing, quality assurance, distribution, installation, and servicing
- To ensure the establishment and effective functioning of the quality system

# Quality Policy

*Management with executive responsibility shall:*

- Establish its policy and objectives for, and commitment to quality
- Ensure that the ***quality policy*** is understood, implemented, and maintained at all levels of the organization

*21 CFR 820.20(a)*



# Organization

Establish and maintain an adequate organization structure to ensure that devices are designed and produced in accordance with the requirements of this part.

*21 CFR 820.20(b)*

# The Preamble on Organization

The organizational structure should ensure that the technical, administrative and human factors functions affecting the quality of the device will be controlled, whether these functions involved hardware, software, processed materials, or services. All such control should be oriented towards the reduction, elimination, or ideally, prevention of quality nonconformities.

*Preamble, Comment 46*



# Appointment of Management Representative

Management with executive responsibility shall

- Appoint a member of management as ***management representative***
- Document such appointment

*21 CFR 820.20(b)(3)*



# Management Representative's Responsibilities

- Ensure that quality system requirements are effectively established and effectively maintained in accordance with this part
- Report on the performance of the quality system to ***management with executive responsibility*** for review

21 CFR 820.20(b)(3)



# Management Review

- *Management with executive responsibility* shall review the effectiveness of the quality system:
  - At defined intervals
  - With sufficient frequency
  - According to established procedures
- to ensure that the quality system satisfies the requirements of this part and the manufacturer's established quality policy and objectives  
*21 CFR 820.20(c)*



# Management Review (continued)

- Document dates and results of quality system reviews
- Manufacturers are not required to make management review minutes or quality audit reports available to FDA during inspections
- Manufacturers must make procedures for management reviews available to FDA employees for review during inspections  
*21 CFR 820.20(c) & 820.180(c)*



# Quality Audits

- Establish procedures for quality audits.
- Conduct audits to assure compliance by individuals not having direct responsibility for areas audited.
- Perform corrective action(s), including re-audit of deficiencies.
- Generate a written report of audit results for management review.

*21 CFR 820.22*



# Personnel

- Hire sufficient personnel with necessary education, background, training, and experience.
- Establish procedures for identifying training needs and to ensure personnel are adequately trained.
- Document training.

*21 CFR 820.25*



# Personnel (cont.)

- Make personnel aware of device defects that could occur from improper job performance.
- Make personnel who perform verification & validation activities aware of defects and errors that could be encountered as part of their job.

*21 CFR 820.25*



# Purpose of the Corrective and Preventive Action Subsystem

- To collect and analyze information to identify actual and potential product and quality problems
- To investigate product and quality problems and take appropriate and effective corrective or preventive action
- To verify or validate the effectiveness of corrective and preventive actions



# Purpose of the Corrective and Preventive Action Subsystem

- To communicate corrective and preventive actions to the appropriate people
- To provide information for management review
- To document activities

# Definition: Correction

**“Correction”** action to **eliminate** a detected nonconformity.

1. A correction can be made in conjunction with a corrective action.
  
2. A correction can be, for example, rework or regrade

ISO 9000:2005(E)



# Definition: Corrective Action

**“Corrective action”** action to **eliminate the cause** of a detected non-conformity or other undesirable situation.

1. There can be more than one cause for a nonconformity.
2. Corrective action is taken to prevent recurrence.
3. There is a difference between correction and corrective action.

ISO 9000:2005(E)



# Definition: Preventive Action

**“Preventive action”** action to **eliminate** the cause of a ***potential*** non-conformity or other undesirable situation

1. There can be more than one cause for a potential nonconformity.
2. Preventive action is taken to prevent occurrence.

ISO 9000:2005(E)



# Where to Start? Planning

Plans should include...

- I. Establishing Data Sources and Criteria
- II. Measuring and Analysis of Data Sources
- III. Improvement Plans
- IV. Input to Management

# Data Sources

## Internal Sources

- Process Control data
- Test/Inspection data
- Device History Records
- Internal Audits
- Training Records

## External Sources

- Complaints
- Supplier Controls
- Adverse Event Reports (MDR)
- FDA
- Similar devices on the market



# Data Analysis

Analyze processes, work operations, concessions, quality audit reports, quality records, service records, complaints, returned product, and other sources of quality data to identify existing and potential causes of nonconforming product, or other quality problems.

*21 CFR 820.100(a)(1)*



# Approaches to Data Analysis Non-statistical & Statistical Techniques

- Use a risk-based approach to rank areas
  - Select items with major impact, i.e. Product related or Process related
  - Proceed with items from high to low impact and eventually assure all areas are addressed
- Use of Statistical Methodology
  - CFR 820.100(a)(1) Appropriate statistical methodology shall be employed where necessary to detect recurring quality problems



# Investigate to Determine Root Cause

Investigate the cause of nonconformities relating to product, processes, and the quality system

*21 CFR 820.100(a)(2)*



# The Preamble on Investigations

The requirement in this section is broader than the requirement for investigations under Sec. 820.198, because it requires that nonconforming product discovered before or after distribution be investigated to the degree commensurate with the significance and risk of the nonconformity.



# Identify Action(s) to be taken

- No further action necessary
- Correction
- Corrective Action
- Preventative Action



# Verify/Validate Corrective and Preventive Actions

Verify or validate the corrective and preventive action to ensure that such action is effective and does not adversely affect the finished device

*21 CFR 820.100(a)(4)*



# Implement Corrective and Preventive Actions

Implement and record changes in methods and procedures needed to correct and prevent identified quality problems

*21 CFR 820.100(a)(5)*



# Communicating and Documenting CAPA Information

- Disseminate information related to quality problems or nonconforming products to those directly responsible for assuring the quality of such product or the prevention of such problems.
- Submit relevant information on identified quality problems, as well as corrective and preventive actions, for management review.
- Document all activities required under this section, and their results



# The Preamble on CAPA and Internal Audits and Mgmt Reviews

Two comments stated that the records required under Sec 820.100(b) should be treated as part of the internal audit. FDA disagrees with these comments...FDA has the authority to review such records and the obligation to do so to protect the public health. . . Manufacturers will be required to make this information readily available to an FDA investigator

*Preamble, comments 166*



# Guidance Available

- GHTF: Quality Management System Medical Devices – Guidance on corrective action and preventive action and related QMS processes; SG3; 2010
- GHTF: Quality Management System Medical devices - Nonconformity Grading System for Regulatory Purposes and Information Exchange; SG3; 2012



# Complaint Files

- **Definition: 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.

- **All manufacturers must:**

- Maintain complaint files.
- Designate a formal complaint handling unit.
- Establish and maintain procedures for receiving, reviewing, and evaluating complaints.



# Complaint Files Continued

## Procedures must ensure:

- All complaints are processed in a uniform and timely manner.
- Oral complaints are documented when received.
- Complaints are reviewed and evaluated to determine if an investigation is needed. When no investigation is made, document why and who made the decision.
- Complaints are evaluated to determine whether the complaint represents a reportable event, Medical Device Report (MDR), according to 21 CFR 803.
- Promptly review, evaluation and investigation of complaints representing an MDR.
  - Such complaints should be maintained in a separate portion of the complaint file or otherwise clearly identified.

# Complaint Files Continued

- **Records of investigation** will include determination of:
  - Identifiers related to the device and reported event
  - If MDR reportable:
    - Whether the device failed to meet specifications
    - Whether the device was being used for treatment or diagnosis
    - If applicable, the relationship of the device to the reported event
- Complaint files need to be reasonably accessible to the manufacturer



# Purpose of the Production & Process Control Subsystem

- To develop, conduct, control and monitor production processes to ensure that a device conforms to its specifications
- Where deviations from device specifications could occur due to manufacturing process, establish and maintain process controls to ensure conformance to specifications.



# Production and Process: Changes

- Establish and maintain procedures for changes to a specification, method, process or procedure.
- Verify or **where appropriate** validate changes according to 21 CFR 820.75 before implementation
- Approve changes in accordance with *21 CFR 820.40*



# Personnel Practices - Production

Establish and maintain requirements for the health, cleanliness, personnel practices, and clothing of personnel if contact between such personnel and product or environment could reasonably be expected to have an adverse effect on product quality

*21 CFR 820.70(d)*



# Process Validation

*Process Validation Definition:* Establish by objective evidence that a process consistently produces a result or product meeting its intended and predetermined specifications.

21 CFR 820.3 (z)(1)

Where the results of a **process cannot be fully verified** by subsequent inspection and test, the process shall be validated with a high degree of assurance and approved according to established procedures.

21 CFR 820.75



# Guidance Available

GHTF: Quality Management System  
Medical Devices – Process Validation  
Guidance; SG3; 2004



# Process Validation continued

- Monitor and control process parameters for validated processes so the specified requirements continue to be met
  - Ensure validated processes are performed by qualified individuals
- Perform revalidation where appropriate
- Document all validation activities



# Purpose of the Facility & Equipment Controls Subsystem

- To assure devices are not adversely affected by the manufacturing environment, buildings or equipment
- To design facilities that work, control the environment and implement contamination controls.
- To qualify equipment installation, maintain equipment and calibrate equipment



# Buildings

Buildings should be of suitable design and contain sufficient space to perform necessary operations, prevent mix-ups, and assure orderly handling

*21 CFR 820.70(f)*



# Environmental and Contamination Control

- Where environmental conditions could be expected to have adverse effects on product quality, establish procedures to control those conditions, and periodically inspect environmental control systems.
- Establish and maintain procedures to prevent contamination of equipment or product by substances that could be expected to have an adverse effect on product quality

*21 CFR 820.70(c) and (e)*



# Equipment: Installation

Ensure that all equipment used in the manufacturing process meets specified requirements and is appropriately designed, constructed, placed and installed to facilitate maintenance, adjustment, cleaning and use.

21 CFR 820.70(g)



# Equipment Requirements

- Establish and maintain equipment maintenance schedules and procedures.
- Conduct and document periodic inspections in accordance with procedures
- Post any limitations or allowable tolerances visibly close to equipment or make it readily available to persons performing periodic adjustment

*21 CFR 820.70(g)(1),(2) and (3)*



# **Purpose of Documents, Records and Change Control Subsystem**

- To assure only current documents are used and all records are maintained.
- To make sure changes are reviewed, approved and incorporated into documents.
- Documents are maintained for the required length of time



# Document Controls

- Establish and maintain procedures to control all documents required by Part 820 (approval/distribution/changes)
- Documents required by Part 820 shall be available at all locations for which they are designated, used, or otherwise necessary. Remove all obsolete documents promptly or otherwise prevent their unintended use

21 CFR 820.40



# Documents, Records and Change Control continued

Document Retention- assure records are maintained for the required length of time

Retain all records required by Part 820 for the **expected life of the device or at least 2 years** from the date of release for commercial distribution -- if the device is short-lived

21 CFR 820.180



# Device Master Record

Definitions 21 CFR 820(j)

***Device master record (DMR)*** means a compilation of records containing the procedures and specifications for a finished device.



# Device Master Record

Include in the DMR:

1. Device specifications
2. Production process specifications
3. Quality assurance procedures and specifications
4. Packaging and labeling specifications
5. Installation, maintenance and servicing procedures and methods

*21 CFR 820.181*



# Device History Record

Definitions 21 CFR 820.3(i)

***Device history record (DHR)*** means a compilation of records containing the production history of a finished device.



# Device History Record

DHR shall include:

1. *Dates of manufacture*
2. *Quantity manufactured*
3. *Quantity released for distribution*
4. *Acceptance records which demonstrate the device is manufactured in accordance with DMR*

21 CFR 820.184



# **Additional Quality System requirements not discussed**

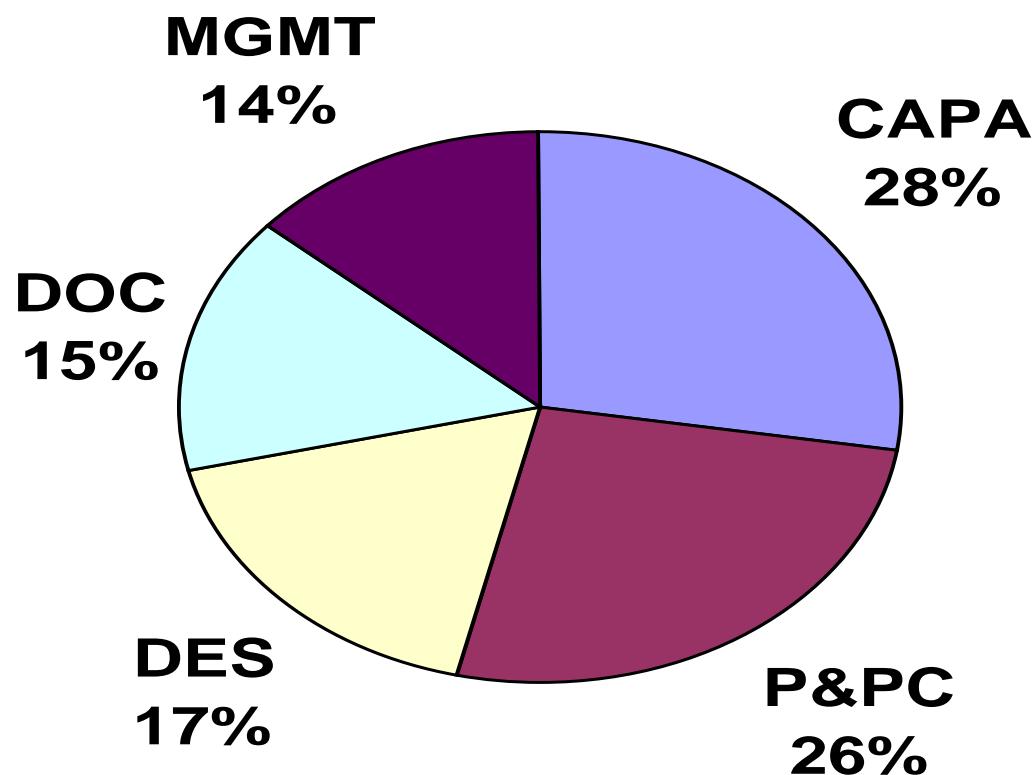
- Design Controls - 820.30
- Purchasing Controls – 820.50
- Identification and Traceability - 820.60 & 820.65
- Acceptance Activities - 820.80 & 820.86
- Labeling & Packaging - 820.120 & 820.130
- Handling, Storage, Distribution & Installation - 820.140, 820.150, 820.160 and 820.170
- Servicing - 820.200
- Statistical Techniques - 820.250



# Warning Letters with QS Citations

Year	# WL's	# Inspections	% Resulting in WL
2012	164	2087	8%
2011	122	2121	6%
2010	89	1900	5%
2009	77	1593	5%
2008	98	1423	7%
2007	74	1474	5%
2006	79	1643	5%

# Warning Letter Cites by QS Subsystem





# Top Ten Most Frequent 2012 QS Warning Letter Cites

Citation	QS Subsystem	Number of WL Cites
21 CFR 820.198(a)	CAPA	82
21 CFR 820.100(a)	CAPA	78
21 CFR 820.184	DOC	51
21 CFR 820.75(a)	P&PC	49
21 CFR 820.22	MGMT	43
21 CFR 820.30(g)	DES	43
21 CFR 820.50	P&PC	36
21 CFR 820.90(a)	CAPA	31
21 CFR 820.181	DOC	31
21 CFR 820.30(i)	DES	30



# For more information

- Device Advice website at  
<http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/PostmarketRequirements/QualitySystemsRegulations/default.htm>
- CDRH Learn QS Module Training  
<http://www.fda.gov/Training/CDRHLearn/ucm162015.htm>
- Contact DICE  
[DICE@fda.hhs.gov](mailto:DICE@fda.hhs.gov)  
301 796-7100, 9am to 4:30pm EST