

Overview of the Quality System Regulation and Compliance Interactions

2022 AMDM Annual Submission Workshop

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Administration

Overview

- **Background - Quality System Regulation**
- **Selected Definitions from 21 CFR 820**
- **Inspections**
 - FDA's Seven Major Quality Subsystems
- **21 CFR 820 Regulations**
- **Proposed Rule and Relationship with ISO 13485:2016**
- **References**

FOOD & DRUG
ADMINISTRATION

21 CFR
Part 11

ELECTRONIC RECORDS;
ELECTRONIC SIGNATURES

Parts 210 & 211

cGMP IN MANUFACTURING
PROCESSING, PACKING,
OR HOLDING OF DRUGS AND
FINISHED PHARMACEUTICALS

Part 820

QUALITY SYSTEM REGULATION



*"Helping Companies Meet and Exceed FDA's
Total Quality Management Standards!"*

Background

FDA

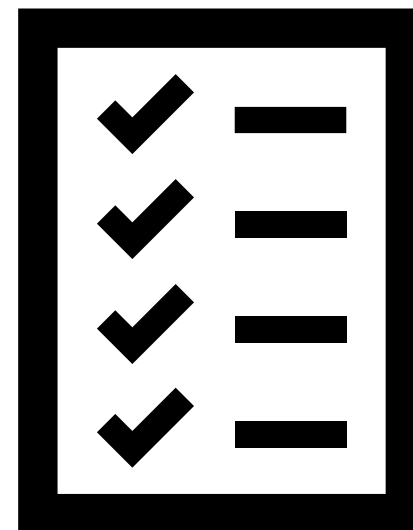
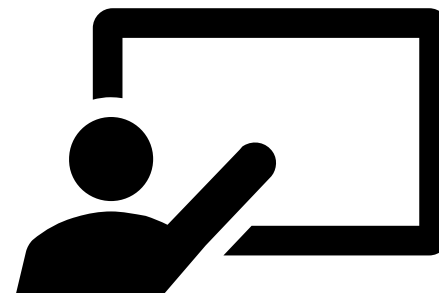
The current Quality System Regulation:

- GMP Regulations promulgated in 1978 for Medical Devices
- Final Rule for a revision of the regulations published in the Federal Register October 7, 1996 and it became effective June 1, 1997
- As part of the 1997 revision, FDA modified it to be consistent with requirements contained in ISO 13485
- Preamble to the 1997 regulation – is an important, often overlooked, part of the regulation.

Background *continued*

The Quality System Regulation:

- The regulation requirements are *not prescriptive*
- It provides a *framework* of basic QS requirements



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

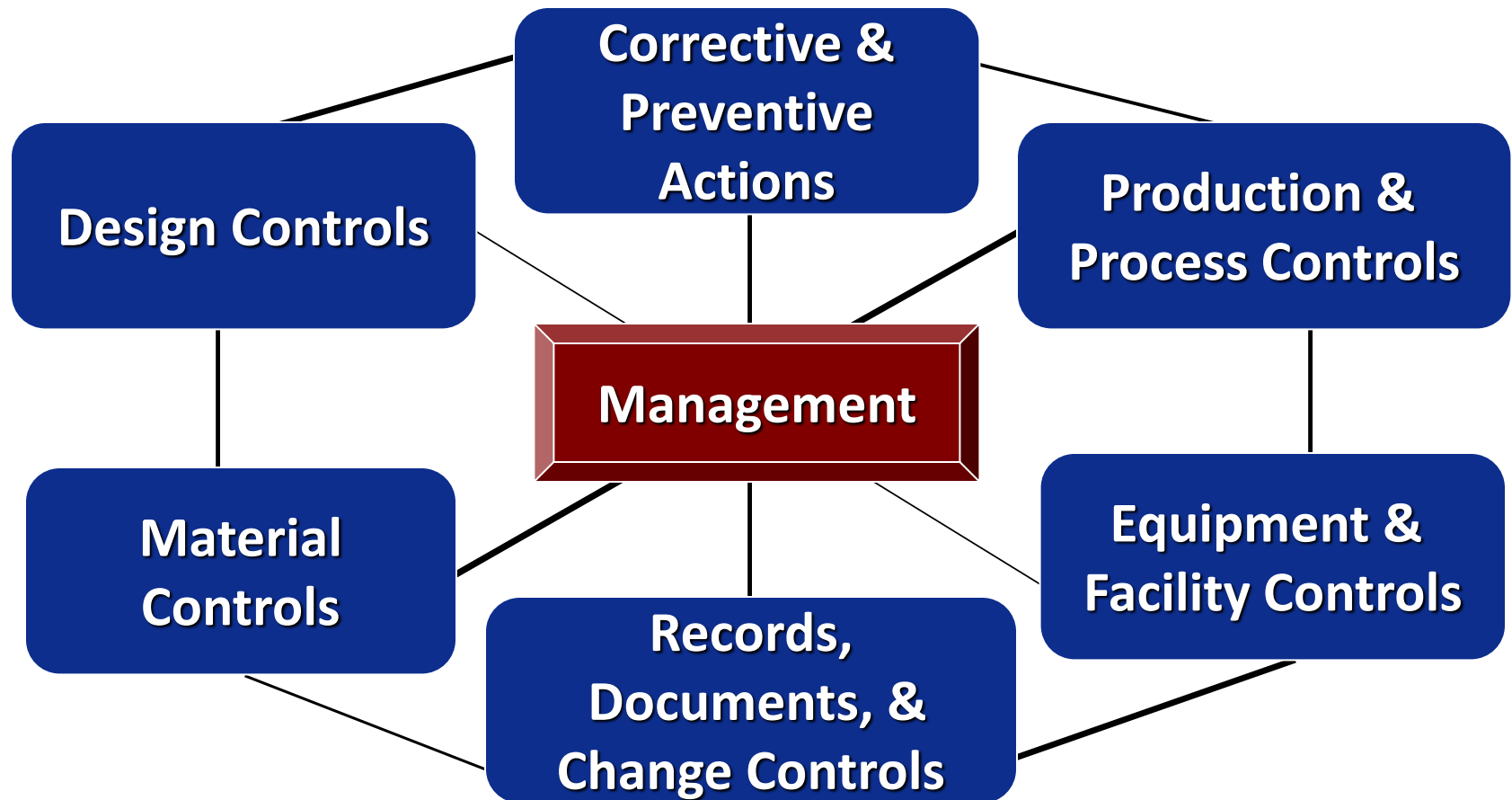


It's Your Quality System....

A manufacturer must develop a QS commensurate with:

- The *complexity and risk* presented by the device
- Complexity of the *manufacturing processes*
- Size and complexity of manufacturing *facility*

7 Subsystems of a Quality System



Types of Inspections

- 1) Pre-Approval Inspections
- 2) Routine Inspections -
Quality System Inspection Technique (QSIT)
 - “*Level 1*” (Abbreviated)
CAPA + P&PC or Design Control
 - “*Level 2*” (Comprehensive)
Surveillance or Initial (baseline)
- 3) Compliance Follow-Up Inspections
 - “*Level 3*”
- 4) “For Cause” Inspections
- 5) Risk Based Work Plan

Management Responsibilities

The Requirements:

- To establish an effective *quality policy* (820.20(a))
- To establish adequate *organizational structure* (820.20(b))
 - (1) Responsibility, Authority, and Independence
 - (2) Resources
 - (3) Management representative

Management Responsibilities *continued*

The Requirements:

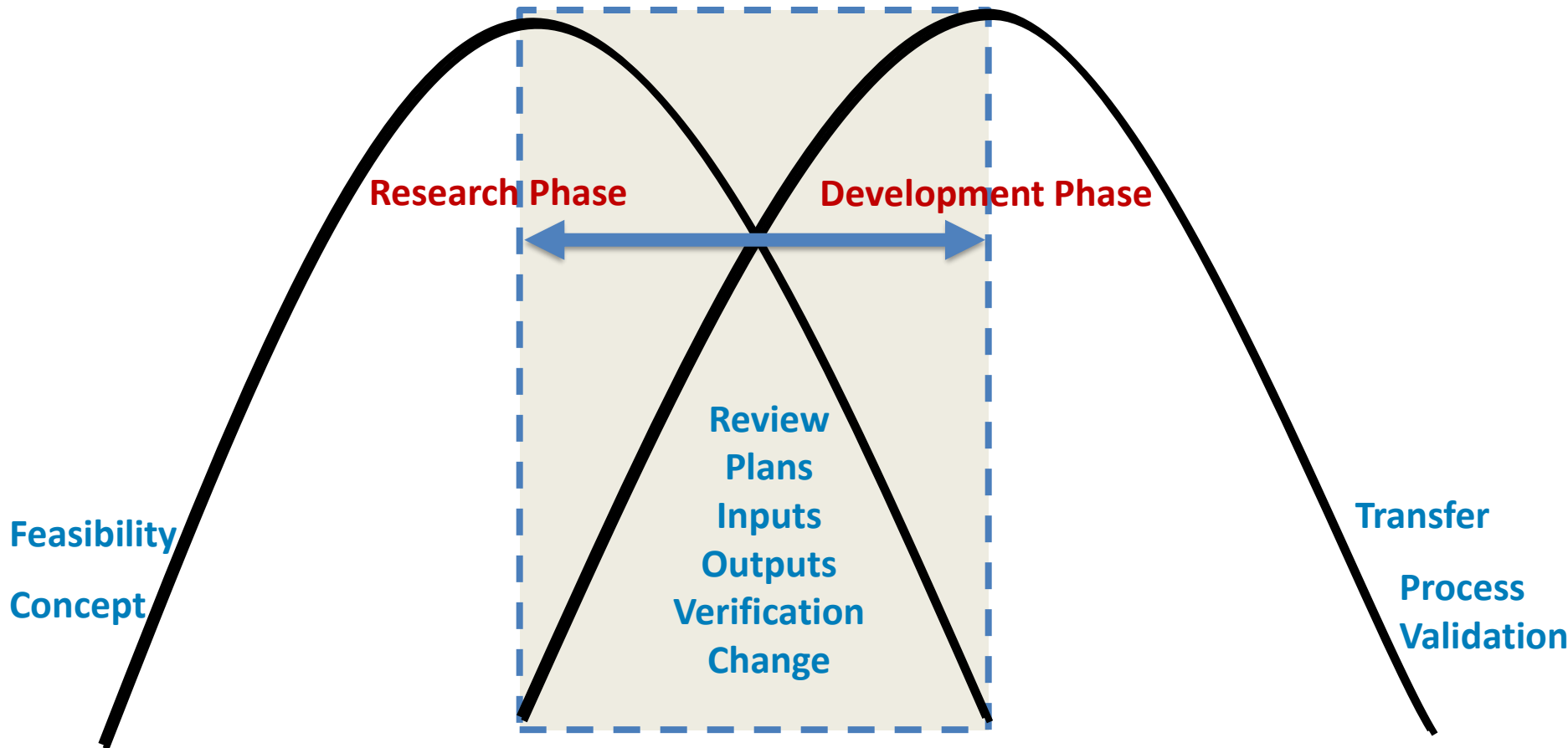
- 1) To monitor the quality system through **management reviews** and make necessary adjustments. **(820.20(c))**
 - 2) To establish QS **procedures and instructions** **(820.20(e))**
-
- 3) To establish procedures for **quality audits** **(820.22)**
 - 4) To ensure having **sufficient personnel** with necessary education, background, **training and experience.** **(820.25)**

Design Controls

Apply To:

- *Class III*
- *Class II*
- Some *Class I* per 21CFR 820.30(a)(2)

Application of Design Controls



820.30(a)

Design Controls

The Requirement:

- Establish procedures to control the device design to

ensure that design requirements are met

820.30(b)

Design and Development Planning

The Requirement:

- Describe or reference the design and development *activities* and define *responsibility* for *implementation*.
- Define interfaces, groups and how they interact

820.30(c)

Design Inputs

The Requirement:

Identify Design Inputs

- Ensure requirements are appropriate and address *intended* use of a device and the *needs of the user*
- Contain the physical and performance *requirements* of a device

820.30(d)

Design Output

The Requirement:

Develop Design Outputs:

- 1) Outputs are results of a design effort at *each phase* and at the end of the *total design* effort
- 2) Outputs consist of the device, its *packaging and labeling*, and the device master record (*DMR*)

820.30(e)

Design Reviews

The Requirement:

Review Design Reviews must:

- Formally *document* design results
- Include representatives from *all functions* concerned as well as “*independent*” individual(s)
- Conducted *at appropriate stages* of design development

820.30 (f)

Design Verification

The Requirement:

- Verify that design outputs meet design inputs
 - Are the product *inputs being met*?
 -and can it be confirmed?

820.30(g)

Design Validation

- **Requirement:**
Validate the design (*include software validation and risk analysis*)
 - Is the product meeting user needs and intended uses for all specifications, even after remanufacturing and can I prove it?

Design Validation vs. Process Validation

Process Validation...(820.75)

....establishing, by objective evidence, that a process consistently produces a result or product *meeting* its predetermined *specifications*.

820.30(h)

Design Transfer

The Requirement:

Transfer the design to production

- Ensure the device design is correctly translated into *production specifications*

820.30(i)

Design Changes

The Requirement:

- Establish procedures for identification, documentation, *validation* or where appropriate *verification*, *review*, and *approval* of design changes before implementation

820.30(j)

Design History File

Requirement:

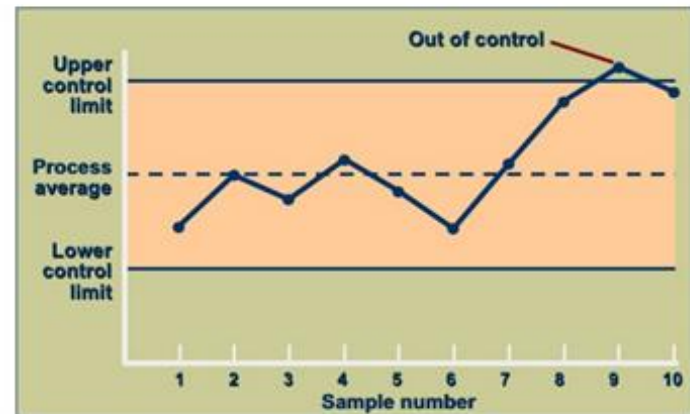
- The DHF shall *contain or reference* the records necessary to demonstrate that the design was *developed* in accordance with the *approved* design plan...
- Each DHF should be *specific* for each type of device.

Production and Process Controls Subsystem

The Requirements:

- *Develop, conduct, control, and monitor production processes* to ensure device conforms to its specifications

Process Control Chart



4-12

Production and Process Controls Subsystem *continued*

- 1) Production and Process Changes 820.70(b)
- 2) Environmental control 820.70(c)
- 3) Personnel 820.70(d)
- 4) Contamination Control 820.70(e)
- 5) Buildings 820.70(f)
- 6) Equipment 820.70(g)
- 7) Manufacturing Material 820.70(h)
- 8) Automated Processes (Software Validation) 820.70(i)

820.50

Purchasing Controls

The Requirement

- 1) Establish and maintain purchasing control procedures
- 2) *Evaluate* supplier, contractors, and consultants
- 3) Establish, maintain, and approve *purchasing data*/documents

820.72

Inspection, measuring, and test equipment

The Requirements:

- Ensure all inspection, measuring, and test equipment is suitable for *intended purposes* and able to produce *valid results*.



The Requirements:

820.250

Statistical techniques

- Identify *valid statistical techniques* required for the acceptability of *processes capability and product characteristics*
- Write and base **sampling plans** on a valid statistical rationale
- Ensure *sampling* methods are *adequate*

820.100

Corrective and Preventive Action Subsystem

The Requirement:

- 1) Collect and analyze information/data from *various sources*
- 2) Identify and *investigate* product and quality problems
- 3) Identify and implement effective *actions to correct and prevent recurrence*
- 4) *Verify or validate* corrective and preventive actions
 - a) *Effective*
 - b) *No adverse effects*

Corrective and Preventive Action Subsystem *continued*

The Requirement:

- 5) *Update methods* and procedures with changes need to correct and prevent problems
- 6) *Communicate* corrective and preventive actions *to appropriate personnel*
- 7) Provide information for *management review*
- 8) *Document* all results and related activities

21 CFR 820 Proposed Rule

Purpose of the proposed rule:

- The action, if finalized, will harmonize key areas of a device manufacturer's Quality Management System and will more closely align the United States with many other regulatory authorities around the world
- The primary proposed change is to incorporate, by reference, ISO 13485:2016

21 CFR 820 Proposed Rule

Similarities and Differences of Proposed Rule from Current Regulation:

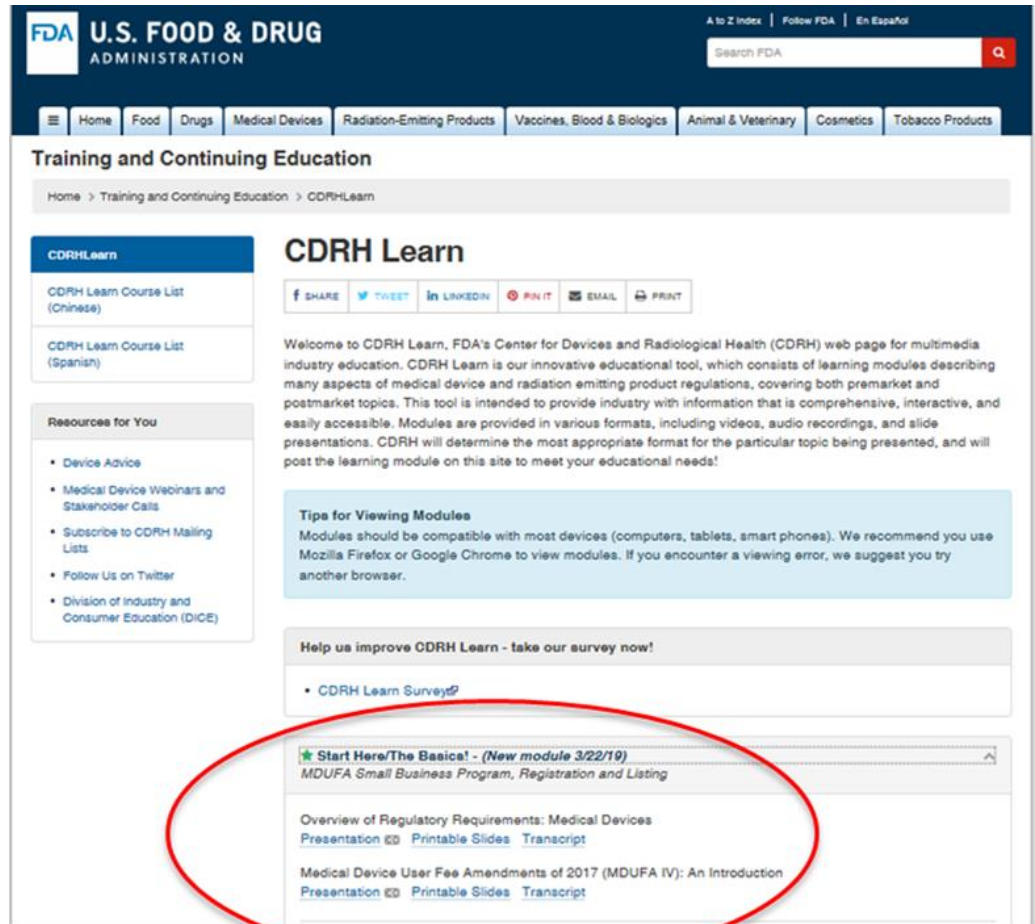
- **ISO 13485:2016 is very similar to current version 21 CFR 820, but is more explicit about incorporation of risk management**
- **Proposed rule would retain a similar scope, as well as certain definitions and requirement to ensure consistency and alignment between ISO 13485 and existing requirements in the FD&C Act and its implementing regulations**

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<https://www.fda.gov/Training/CDRHLearn/default.htm>

References



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Quality System (QS) Regulation/Medical Device Good Manufacturing Practices

<https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/PostmarketRequirements/QualitySystemsRegulations/default.htm>

References

The screenshot displays the FDA's official website. At the top, the FDA logo is on the left, and navigation links for 'A to Z Index', 'Follow FDA', and 'En Español' are on the right. A search bar is also present. Below the header is a horizontal menu with tabs for 'Home', 'Food', 'Drugs', 'Medical Devices', 'Radiation-Emitting Products', 'Vaccines, Blood & Biologics', 'Animal & Veterinary', 'Cosmetics', and 'Tobacco Products'. The 'Medical Devices' tab is selected. Below this, a breadcrumb trail reads: 'Home > Medical Devices > Device Advice: Comprehensive Regulatory Assistance > Postmarket Requirements (Medical Devices) > Quality Systems Regulation'. A blue button labeled 'Quality Systems Regulation' is visible. The main heading of the page is 'Quality System (QS) Regulation/Medical Device Good Manufacturing Practices'. Below the heading are social media sharing options for Facebook, Twitter, LinkedIn, Pinterest, Email, and Print. A list of links is provided: 'Introduction', 'Flexibility of the QS Regulation', 'Applicability of the QS Regulation', 'GMP Exemptions', 'Additional Quality System Information', and 'Quality System Regulation and Preamble'.

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Quality Systems Regulation

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- [Quality System Regulation and Preamble](#)

Link specific to 21CFR820 Quality System Regulation

<https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcr/CFRSearch.cfm?CFRPart=820>

References

CFR - Code of Federal Regulations Title 21

FDA Home Medical Devices Databases



The information on this page is current as of April 1 2018.

For the most up-to-date version of CFR Title 21, go to the [Electronic Code of Federal Regulations \(eCFR\)](#).

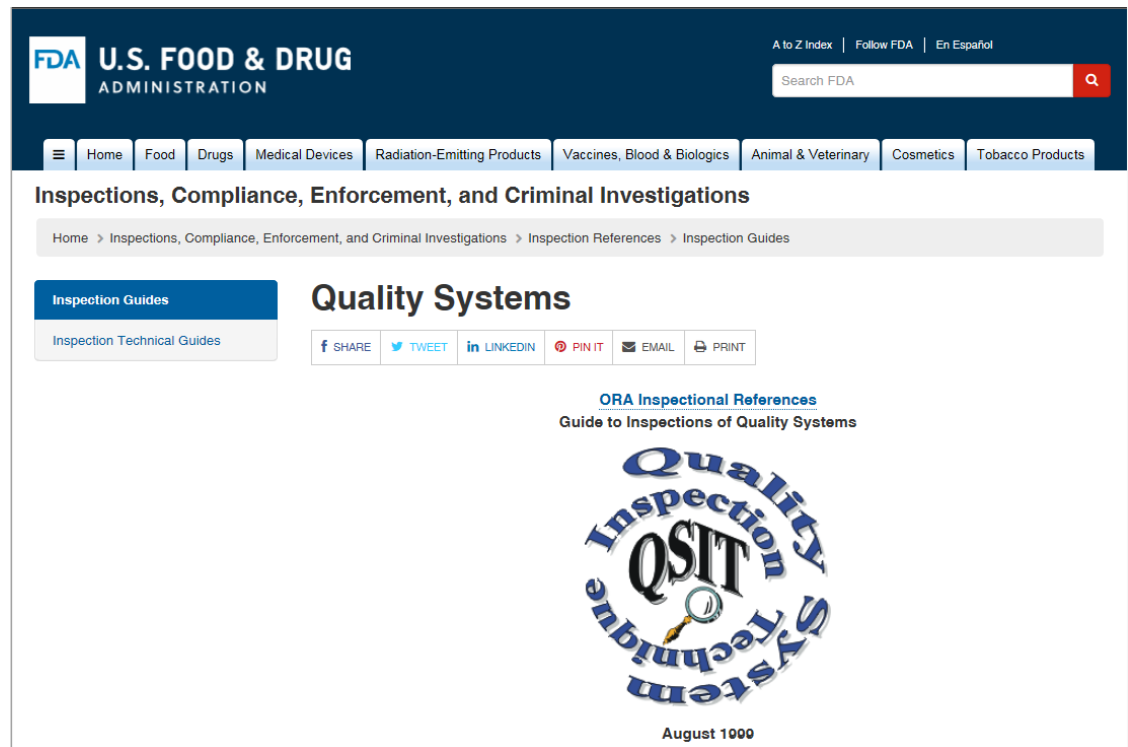
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TITLE 21--FOOD AND DRUGS
CHAPTER I--FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES
SUBCHAPTER H--MEDICAL DEVICES
PART 820 [QUALITY SYSTEM REGULATION](#)

QSIT

- <https://www.fda.gov/ICECI/Inspections/InspectionGuides/ucm074883.htm>

References



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820 Proposed Rule

Federal Register, including the proposed rule itself and instructions for submitting comments to the docket:

- <https://www.federalregister.gov/documents/2022/02/23/2022-03227/medical-devices-quality-system-regulation-amendments>

820 Proposed Rule website with additional information and Q&A:

- <https://www.fda.gov/medical-devices/quality-system-qs-regulationmedical-device-good-manufacturing-practices/proposed-rule-quality-system-regulation-amendments-frequently-asked-questions>

References

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