# THE QUALITY SYSTEM REGULATIONS

ROCKY MOUNTAIN REGULATORY AFFAIRS SOCIETY

# INTRODUCTIONS

# INTRODUCTION TO THE QUALITY SYSTEM REGULATION COURSE

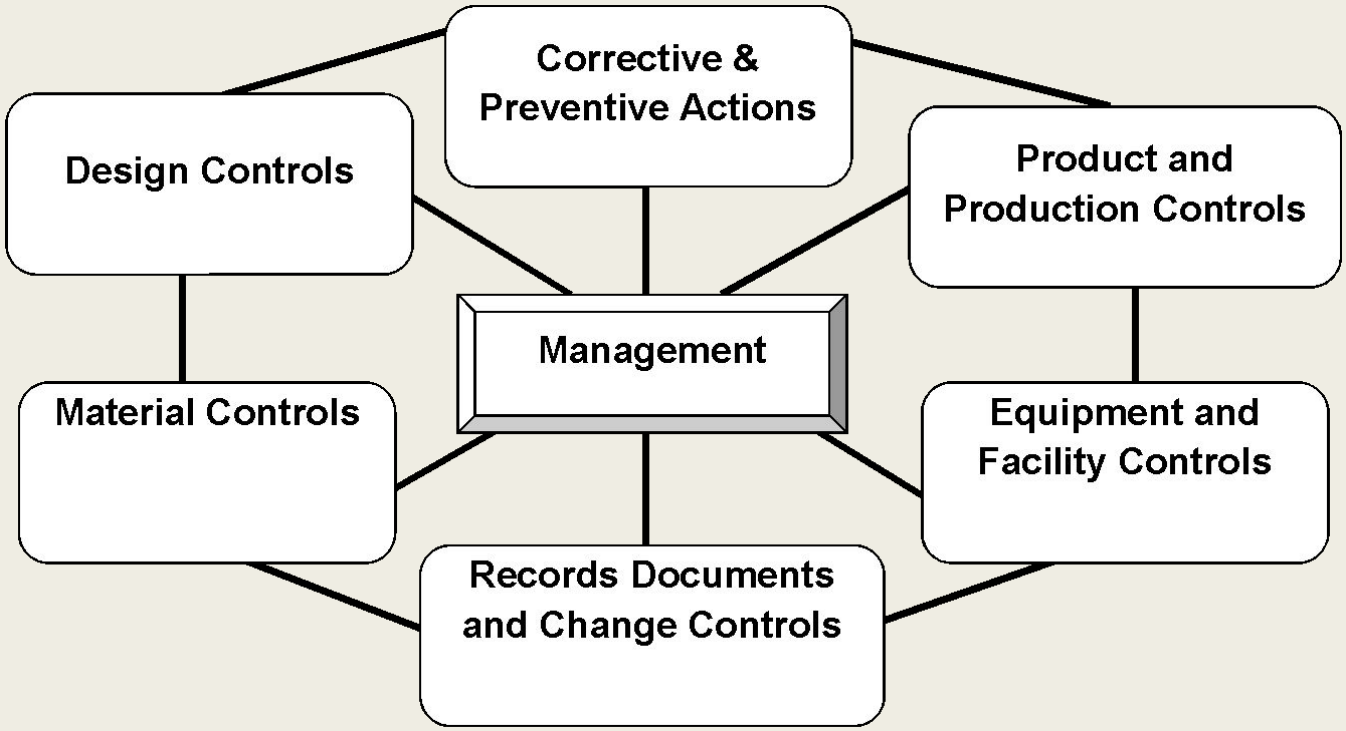
# Course Contents

- Overview course of 21 CFR 820 - Quality System Regulation
- Basic understanding and knowledge of the regulation
- Interpretation of the regulations

# Not included in Course Content

- **There are many FDA and international regulatory requirements beyond 21 CFR 820 that medical device companies must comply with:**
  - 21 CFR 4 cGMP Requirements for Combination Products
  - 21 CFR 11 Electronic Records; Electronic Signatures
  - 21 CFR 801 Labeling
  - 21 CFR 803 Medical Device Reporting
  - 21 CFR 806 Corrections and Removals
  - 21 CFR 807 Establishment Registration, Device Listings, 510(k) Premarket Clearance
  - 21 CFR 809 In Vitro Diagnostics
  - 21 CFR 810 Medical device recall authority
  - 21 CFR 812 Investigational device exemptions
  - 21 CFR 814 Premarket approval of medical devices
  - 21 CFR 821 Medical device tracking requirements
  - 21 CFR 822 Postmarket surveillance
  - 21 CFR 830 Unique Device Identification

# Quality System Regulation



# Quality System Regulation

- Definitions of “System”:
  - “A set of connected things or parts forming a complex whole.”
  - “A group of related parts that work together as part of an interconnecting network”
- The individual requirements of the regulation do not standalone.
- Requirements are interdependent, providing inputs and outputs to other requirements or subsystems.
- As we discuss each section of the regulation, we will point out how that section links with other requirements of the regulation.

# Quality System Regulation vs. ISO 13485

- Although the Quality System Regulation is “harmonized” with ISO 13485, the interpretation and compliance expectations of the FDA are different from your notified body.
  - FDA
    - Performs inspections for the purpose of determining compliance to federal regulations.
    - FDA Investigators carry badges.
    - FDA has many legal actions they can take to enforce compliance.
- Do not assume that having ISO 13485 certification and successful ISO audits means that you will meet FDA’s compliance expectations.

# Medical Device Single Audit Program (MDSAP)

The Medical Device Single Audit Program allows an MDSAP recognized Auditing Organization to conduct a single regulatory audit of a medical device manufacturer that satisfies the relevant requirements of the regulatory authorities participating in the program.

International partners that are participating in the MDSAP include:

- Therapeutic Goods Administration of Australia
- Brazil's Agência Nacional de Vigilância Sanitária
- Health Canada
- Japan's Ministry of Health, Labour and Welfare, and the Japanese Pharmaceuticals and Medical Devices Agency
- U.S. Food and Drug Administration

FDA will continue to accept MDSAP audit reports as a substitute for routine Agency inspections.

# QUALITY SYSTEM REGULATION BACKGROUND AND HISTORY

# Food and Drug Administration (FDA)

- Department of Health and Human Services (HHS)
  - Food and Drug Administration (FDA)
    - Center for Devices and Radiological Health (CDRH)
    - Office of Regulatory Affairs (ORA)

- Need Help? Contact DICE
  - **Phone:** 1(800) 638-2041 or (301) 796-7100
  - **Email: DICE@fda.hhs.gov**
  - The Division of Industry and Consumer Education (DICE) answers questions from the medical device industry and consumers of medical devices and radiation-emitting electronic products.

# FDA Enforcement Actions

- Inspection
- Voluntary Corrections
  - FDA-483 Notice of Observations
  - Untitled Letters
  - Warning Letters
- Mandatory Corrections
  - Mandatory Recall
  - Injunctions/ Seizures
  - Consent Decrees
- Legal Action
  - Civil Money Penalties
  - Criminal Indictments

# FDA Inspections and QSIT

- QSIT – Quality System Inspection Technique
- Inspectional process that is used to assess a medical device manufacturer's compliance with the Quality System Regulation and related regulations.
- 4 Major Subsystems
  - Management Controls (MGT)
  - Design Controls (DES)
  - Corrective and Preventive Actions (CAPA)
  - Production and Process Controls (P&PC)

# Regulatory Hierarchy

- Federal Laws
- Federal Regulations (CFR)
- Guidance Documents

# Federal Law

- Enacted by Congress
- Federal Food Drug and Cosmetic Act (FFD&C Act)
  - *Civil and Criminal act*
    - Violations of the Act can be tried in Civil or Criminal court
    - Both Companies and Individuals can be held liable for violations of the Act.

# Code of Federal Regulations (CFR)

- Implementation of Federal Laws
- Written by the governing agency
- Published in the Federal Register
  - Proposed Rule
    - Notice and Comment Period
  - Final Rule
  - Preamble to the Final Rule
    - 21 CFR 820 Quality System Regulation
    - Intent of Congress and FDA
    - Purpose of the Regulation
    - Response to Comments- provides insight into FDA interpretation

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

# Guidance Documents

- Guidance Documents are not legally binding documents
  - Guidance documents describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word should in Agency guidance documents means that something is suggested or recommended, but not required.
- Informative
- Express the Agency’s position
- Interpretation of the regulations
- Roadmap for compliance

# Quality System Regulation
## History

- The quality system regulations for medical devices were originally known as current good manufacturing practices (cGMP's).
- cGMP requirements for medical devices were first authorized by the 1976 Medical Device Amendments to the Federal Food, Drug, and Cosmetic Act.
- 21 CFR 820, prescribing cGMP requirements for medical devices, became effective in 1978.
  - Only governed the manufacturing of medical devices.
  - No authority over the design of medical devices.

# Quality System Regulation
## History

- Safe Medical Devices Act of 1990
  - Authorized revisions to cGMP
    - Design Controls
      - 44 percent of the quality problems that led to voluntary recall actions during 1983-1989 were attributed to errors or deficiencies in device design.
      - Over 90 percent of all software related device failures were due to design-related errors, generally, the failure to validate software prior to routine production.
    - Management Review
    - Harmonization with ISO 13485
  - Quality System Regulations (21 CFR 820)
    - Published October 7, 1996 , Effective June 1,1997

# Quality System Regulation

- The regulation is a framework that specifies the requirements that each manufacturer must incorporate into their quality management system.
- The regulation does not prescribe how to implement the requirements.
- Within the regulation framework, each manufacturer must develop a quality management system that is appropriate to their devices and business:
  - Risk class of the device
  - Type of device
    - Sterile/Process Controls (e.g. controlled environments, sterilization validation)
    - Software/Design Control (e.g. software development and validation)
  - Complexity of the device
  - Complexity of the manufacturing process
  - Size of the organization

# Helpful FDA Links

- Quality System Data Analysis:
  - *https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHTransparency/ucm199911.htm*
- Warning Letters:
  - *http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/*
- QSIT:
  - *https://www.fda.gov/files/Guide-to-Inspections-of-Quality-Systems.pdf*

# QUESTIONS?