QA CONSULTING, INC.
MEDICAL DEVICE CONSULTING SERVICES

TMCx Accelerator Program: Medical Device Quality

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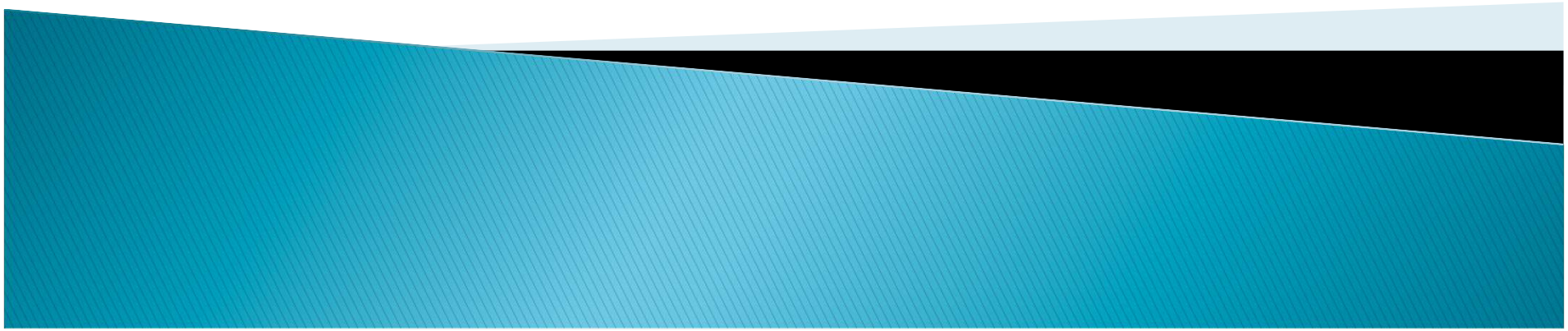
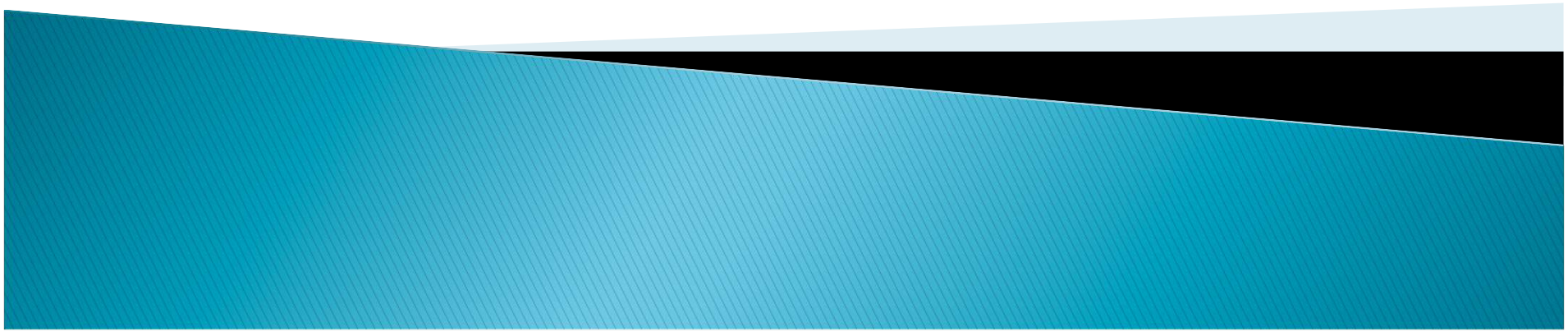
August 21, 2017



Outline

- What is a medical device?
- MDD and FDA Regulations
- Regulatory Requirements for a Quality Management System (QMS)
- Elements of a QMS
- FDA Inspections
- What is Next- ISO 13485:2016 and MDR replaces MDD

WHAT IS A MEDICAL DEVICE?



What is a Medical Device?

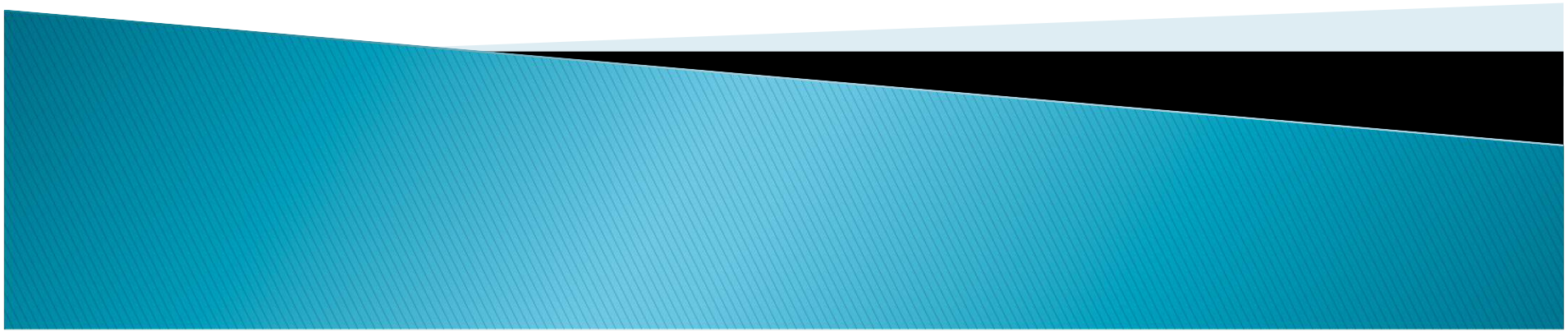
ISO 13485 section 3.11 defines a Medical Device as:

Any instrument, apparatus, implement, machine, appliance, implant, reagent for *in vitro* use, software, material or other similar or related article, intended by the manufacturer to be used, alone or in combination, for human beings, for one or more of the specific medical purpose(s) of:

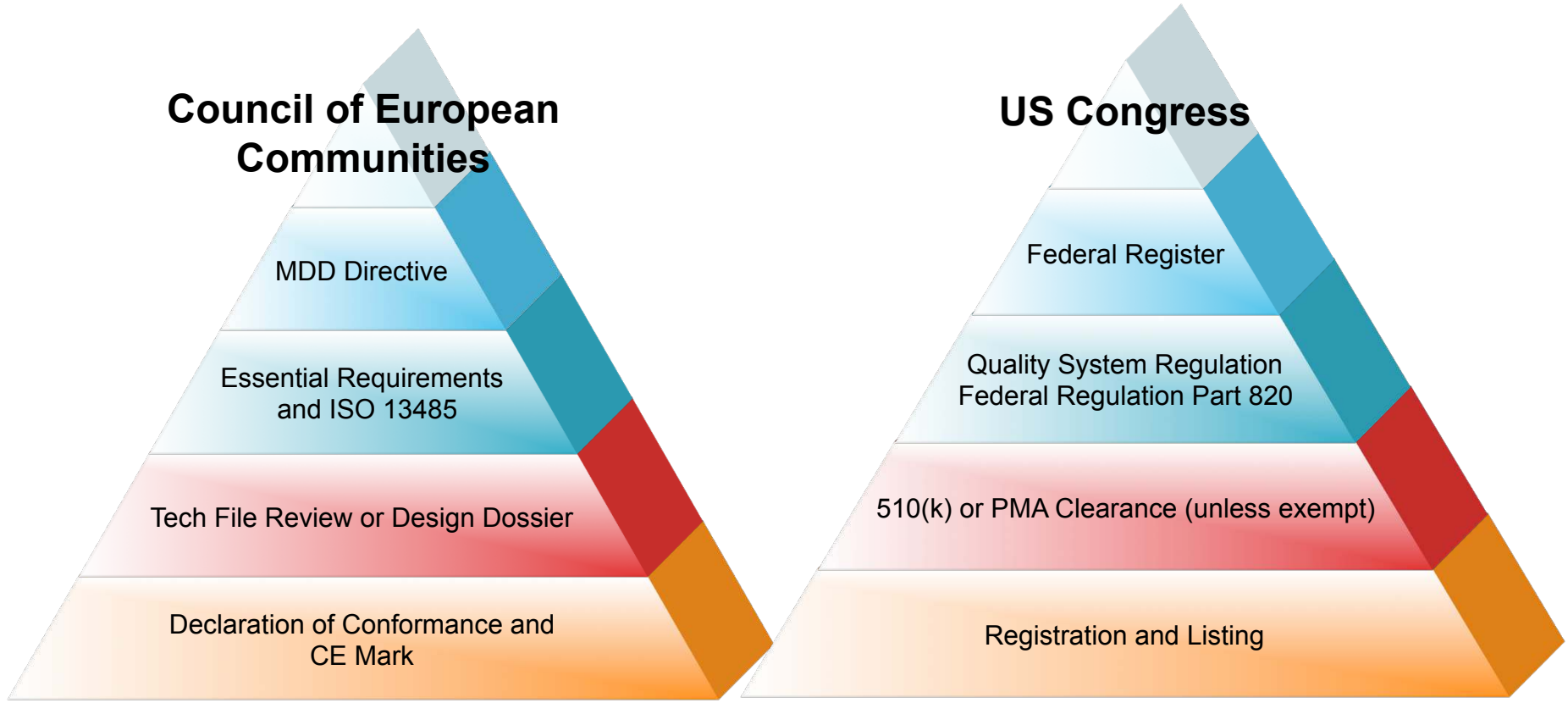
- Diagnosis, prevention, monitoring, treatment or alleviation of disease,
- Diagnosis, monitoring, treatment, alleviation of or compensation for an injury,
- Investigation, replacement, modification or support of the anatomy or of a physiological process,
- Supporting or sustaining life,
- Control of conception,
- Disinfection of medical devices,
- Providing information by means of *in vitro* examination of specimens derived from the human body,

and does not achieve its principal intended action by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means.

MDD AND FDA REGULATIONS



Relationship Between MDD & FDA Regulations



FDA is a Law Enforcement Agency with the Mission to Protect Public Health

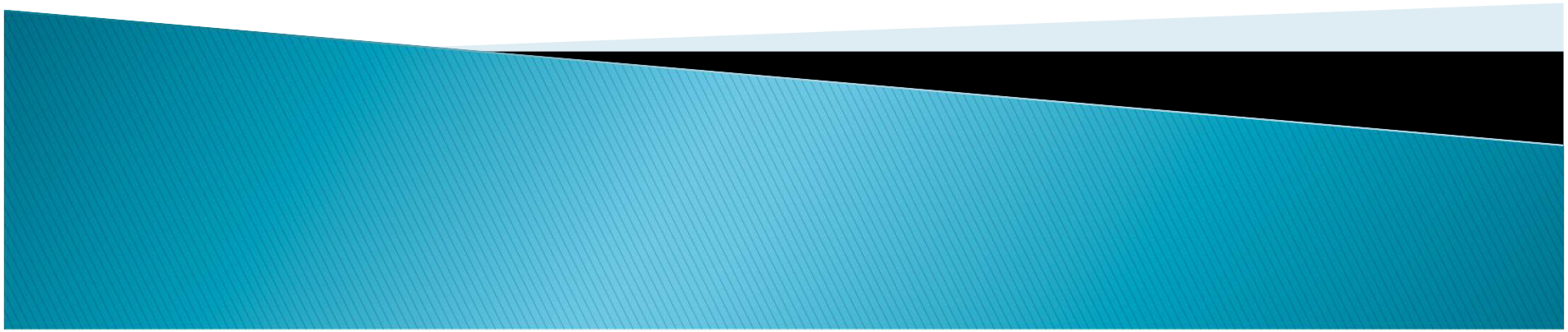
Manufacturers of finished medical devices and all entities subject to inspection are included under Section 301 of the general adulteration and misbranding provisions of the FD&C Act

Only manufacturers of finished medical devices must adhere to Quality System Regulations (QSR)

Finished medical device manufacturers can require suppliers to adhere to the QSR under the purchasing control provision (820.50)

Broad Authority includes manufacturers of components as well as any entity holding components

REGULATORY REQUIREMENTS FOR A QUALITY MANAGEMENT SYSTEM (QMS)



Defining Quality Requirements

ISO 13485

QMS Requirement:

To consistently meet Customer and regulatory requirements

FDA QSR

QMS Requirement:

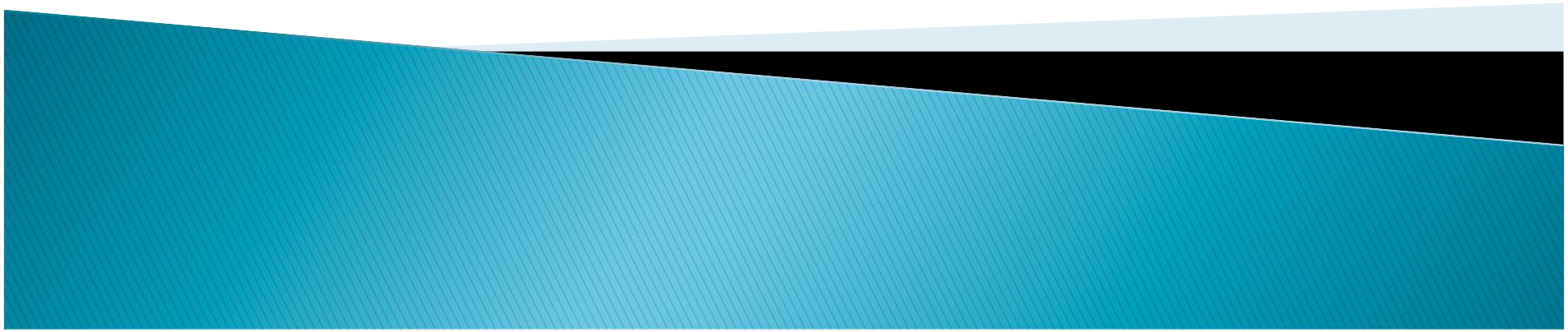
To consistently provide safe and effective medical devices

ISO 13485 – 5 Major Elements	21 CFR 820 – 15 Subsections
Section 4: Quality Management System	General Provisions
Section 5: Management Responsibility	Quality System Requirements
Section 6: Resource Management	Design Controls
Section 7: Product Realization	Document Controls
Section 8: Measurement, Analysis, and Improvement	Purchasing Controls
	Identification and Traceability
	Product and Process Controls
	Acceptance Activities
	Nonconforming Product
	Corrective and Preventive Action
	Labeling and Packaging Control
	Handling, Storage, Distribution, and Installation
	Records
	Servicing
	Statistical Technique

Associated Quality Regulations

- Medical Device Reporting (21 CFR 803)
- Vigilance Reporting (MEDDEV 2.12-1)
- Corrections and Removals (21 CFR 806)
- Unique Device Identification (21 CFR 830)
- Medical Device Tracking (21 CFR 821)

ELEMENTS OF A QMS



Key Points of QMS

QMS specifically requires measurement, analysis and improvement processes to:

- Demonstrate product conformity
- Demonstrate QMS conformity
- Maintain effectiveness of QMS

QMS General Terms

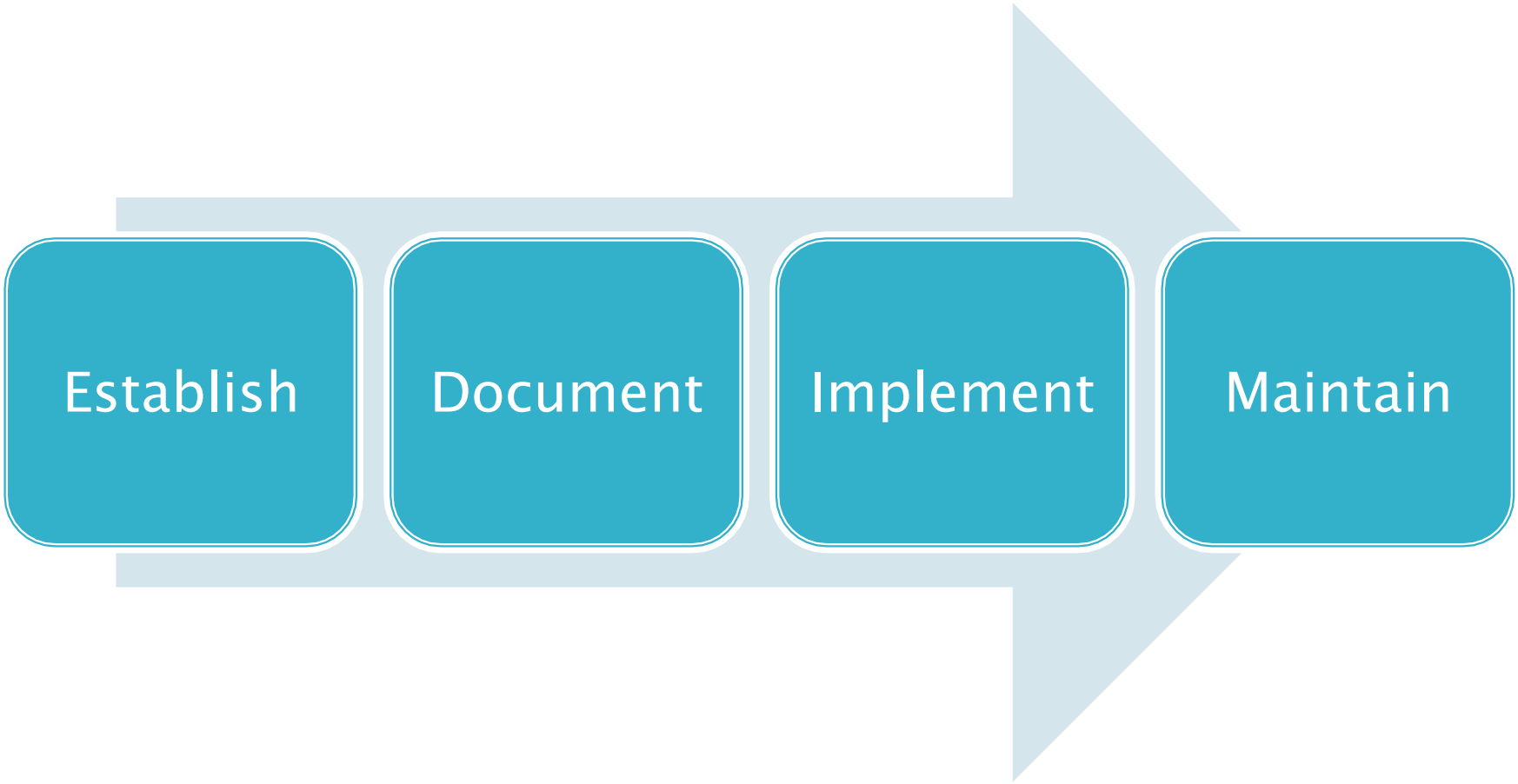
Shall: Mandatory
(Gotta)

Should: Suggested
(Better)

May: Allowed
(Ought To)

Note: Explanation
(How To)

Quality Management System



Quality Management System

Organizations **shall** do 6 things:

1. Identify the processes required for the QMS and their APPLICATION throughout the organization
2. Determine sequence and interactions of these processes (process maps)
3. Effectively operate and control the processes
4. Make resources and information available to operate and monitor the processes.
5. Monitor, measure and analyze these processes
6. Implement actions to achieve your planned results and maintain effective QMS

Management Responsibility

- Executive Management Responsibilities
  - The CEO or President assesses the status of the quality system:
    - Opportunities for improvement
    - Need for changes to the quality management system, including quality policy and quality objectives
  - The CEO or President provides all resources needed to maintain the quality system and achieve quality objectives

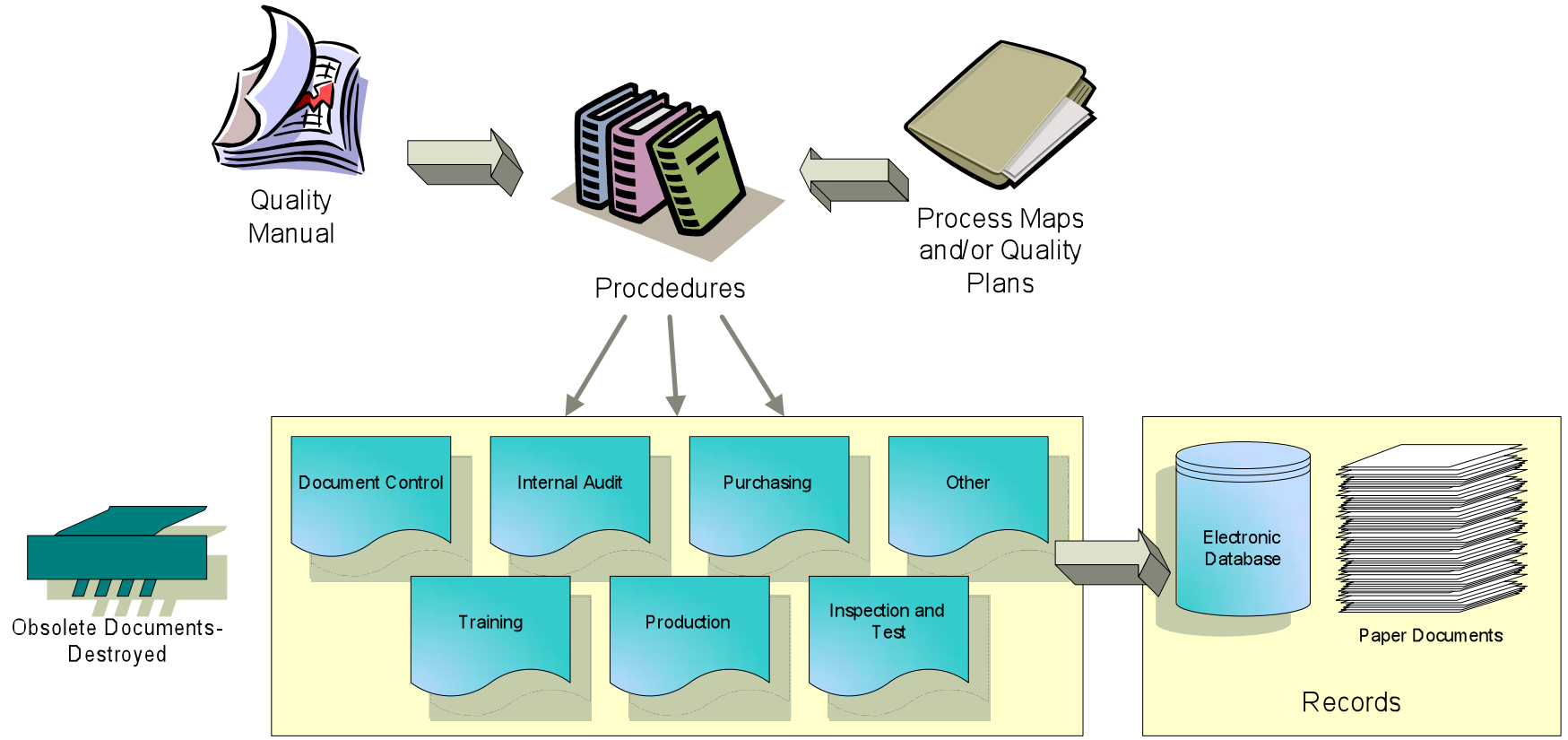
Management Review

- To assess suitability, adequacy, and effectiveness of QMS

Inputs	Outputs
• Results – audits, feedback and processes • CAPA Status • Follow up actions • Changes that could affect QMS • Improvement recommendation • New or revised regulatory requirements	• Improvements to system, process or products • Resource needs • MUST BE COMMUNICATED

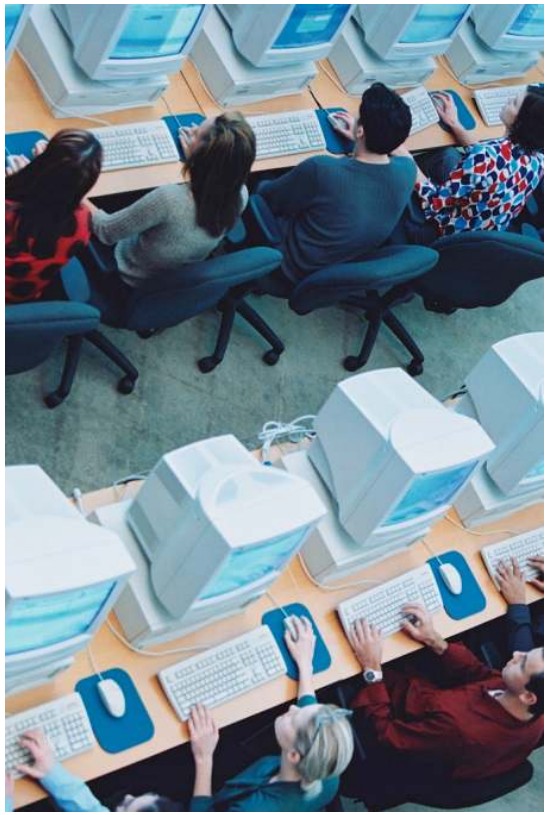
QMS Contents

Required Documented Procedures: Section 4.2



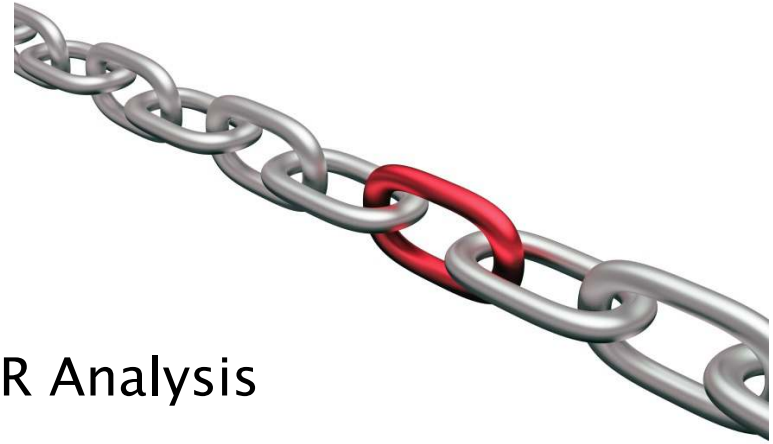
Training and Competence

- Necessary but not sufficient to be trained, one must demonstrate competence
- If special work environments are utilized, such as a cleanroom, operators and visitors must have specific training

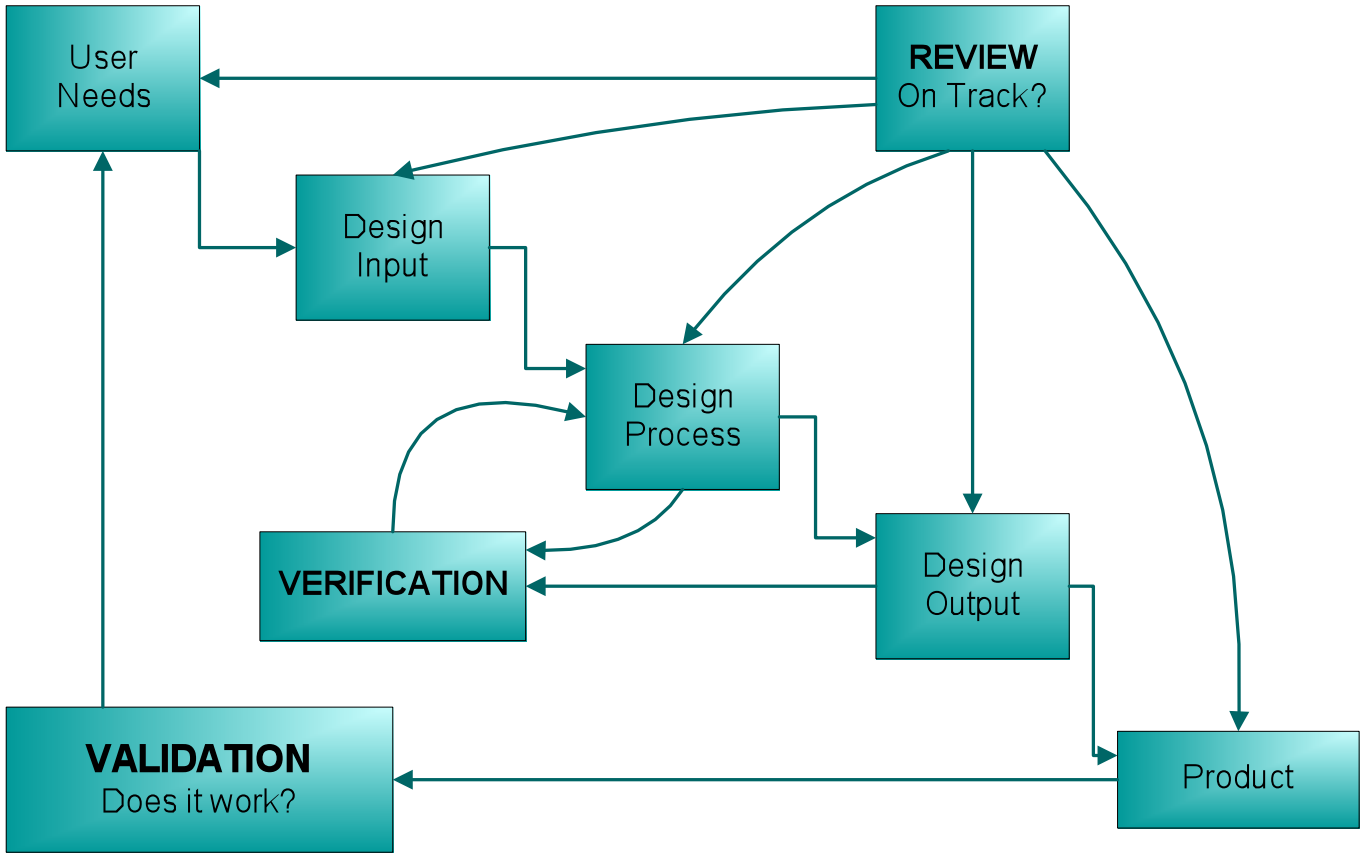


Risk Throughout Product Life Cycle

- Connect risk management activities
  - Design Controls
  - Change Controls
  - CAPAs
  - Post-Market Complaint and MDR Analysis
  - Nonconforming Materials
  - Supply Chain Controls
  - Production and Process Controls



Design Control

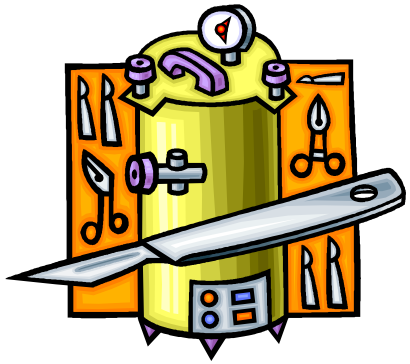


Supplier Management– Critical to Success

- Extent of control based on risk
- Evaluate suppliers based upon their ability to meet established criteria
- Applies to outsourced processes, intellectual property and consultants
- Must verify, inspect, test certifications and keep records showing products meet specifications

Production and Service

- Must have control
  - i.e. specifications, procedures, tools, maintained equipment, calibrated measuring equipment, identification, status, labeling
- Batch Records for Traceability
  - Who, what, where, when, how many
- Product Cleanliness and methods for contamination
- Installation, maintenance and servicing requirements that are controlled through product life cycle



Process Validation

- When does it apply?
  - Regulatory Risk:
    - When output cannot be verified by subsequent inspector or test

-OR-

  - Business Risk:
    - Verification is not sufficient or cost effective

Note: Process examples that must be validated: Sterilization, molding, cleaning. Reference GHTF/SG3/N99-10:2004 (Edition 2)

Monitoring and Measuring Equipment

- To ensure valid results
  - Procedures and records
  - Calibration (ISO 10012, ISO/IEC 17025)
  - Identified to calibration status
  - Protect from damage/deterioration
  - Adequacy of software used for calibration shall be verified

- If found out of conformance one must determine effect on product

Measurement, Analysis and Improvement

- Why?
  - To show product meets requirements
  - To show QMS meets regulatory and company defined requirements
  - Maintain effectiveness of QMS
    - Actual=plan?

Note: Regulations may include statistical technique such as FDA for sampling plan section 21 CFR 820.250

Measurement, Analysis & Improvement

- CAPAs
- Internal Audits
- Complaints
- Analysis of Data/Trending of Results
- Medical Device Reports/Vigilance Reports
- Monitoring Clinical Effectiveness
- Feedback to Management Review

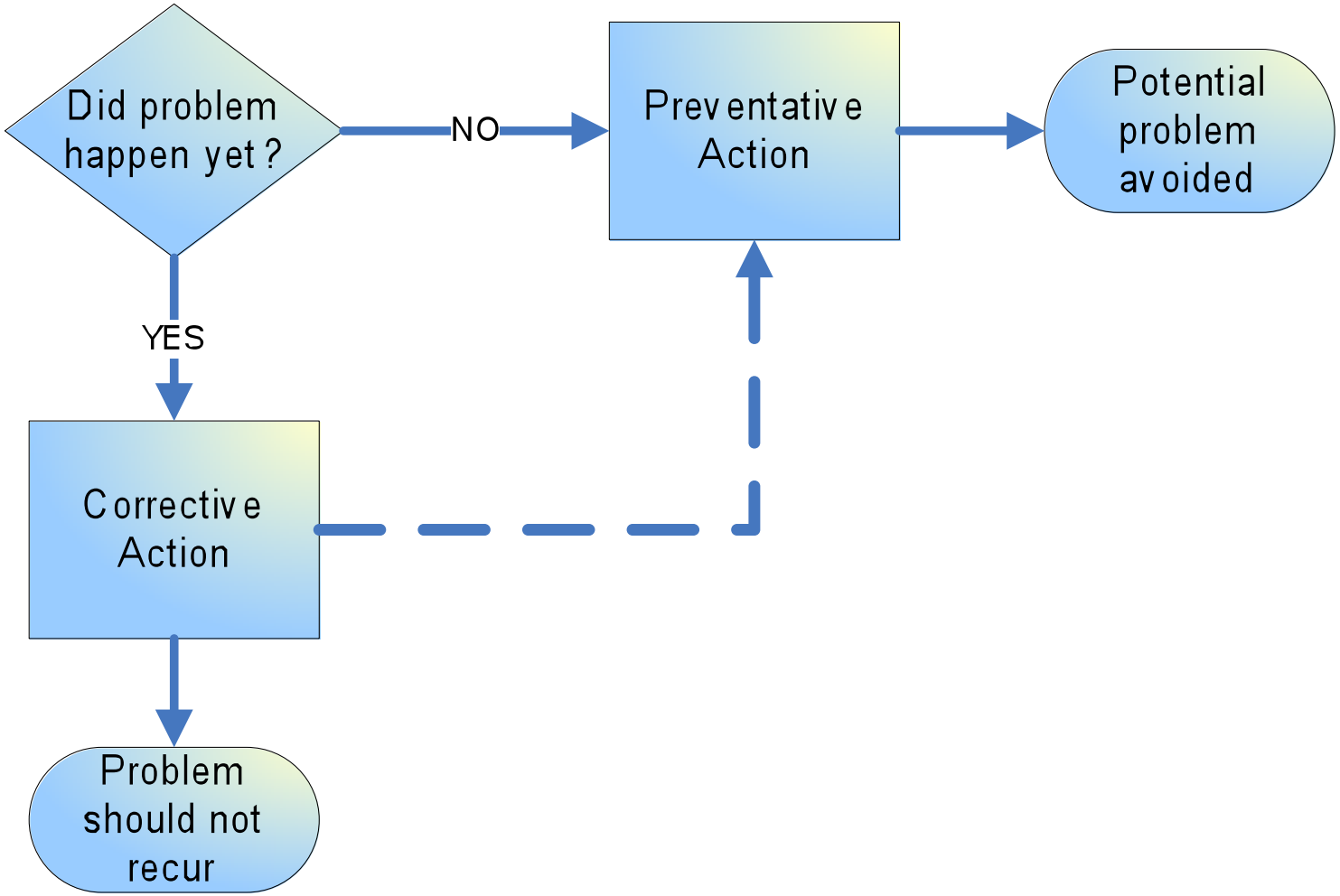
Monitoring and Measurement: Feedback

- Must determine whether customer requirements have been fulfilled (ref ISO 13485 7.2)
- Documented customer feedback system
  - Complaint Handling (ref 21 CFR 820.198, ISO 13485 8.2.2)
  - Device Vigilance Requirements (21 CFR 803, MEDDEV 2.12)
- Tools include surveys, site visits, focus groups, peer review journals, FDA, complaints, contracts, distributor and sales feedback, and service data.

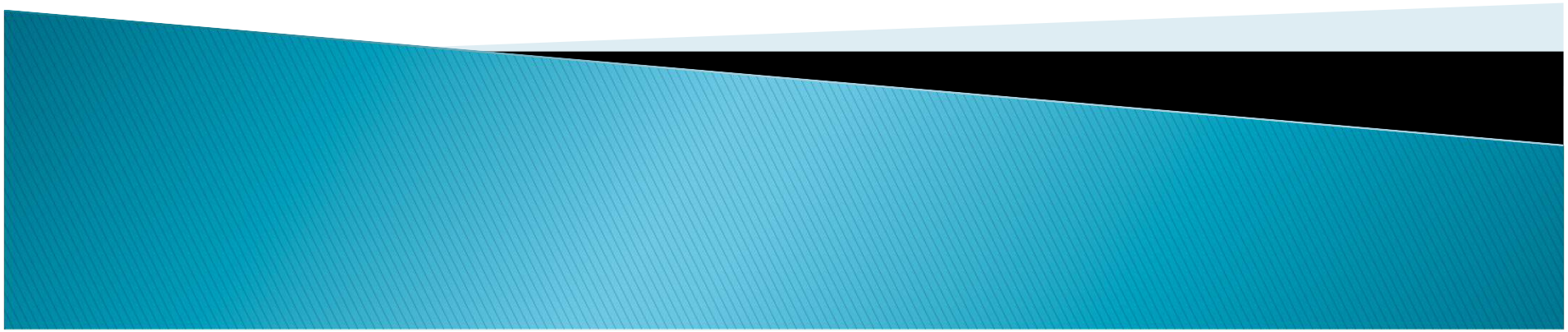
Nonconforming Product

- Identify, control, prevent unintended use
- Possible actions include:
  - Scrap
  - Accept by concession (needs regulatory signature)
  - Alternate use
- If rework is complete make sure it is tested to original specs

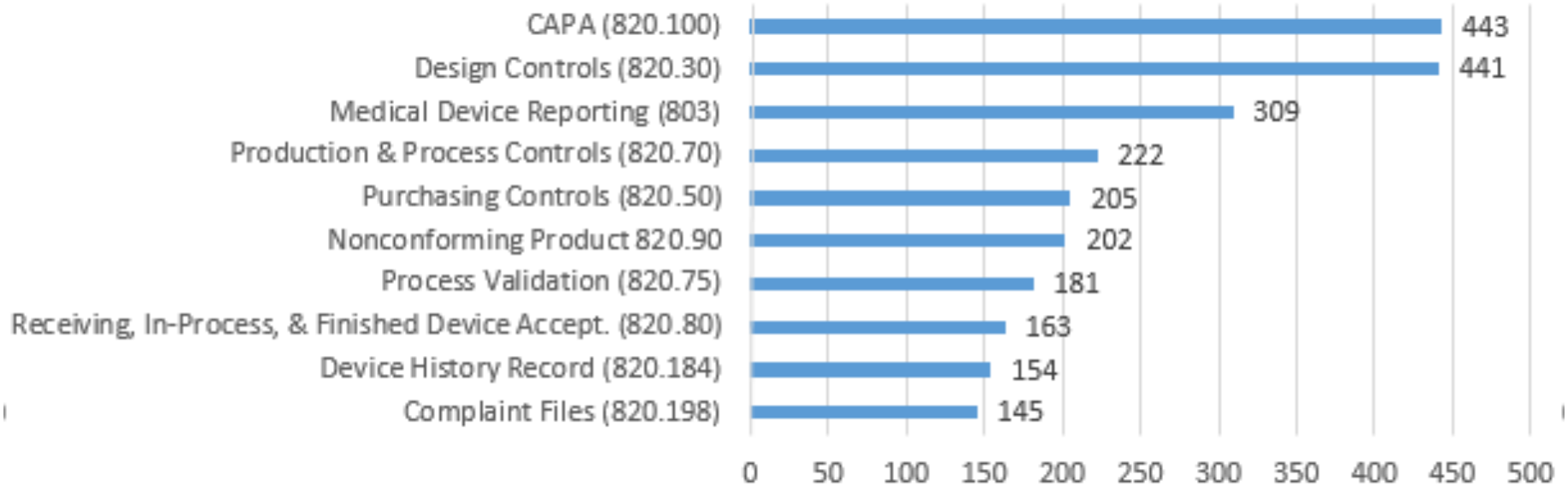
Corrective/ Preventive Action



FDA INSPECTIONS



2016 FDA-483 Top 10 CFR Sections Cited



FDA Inspection Outcome Summary

Hot Topics

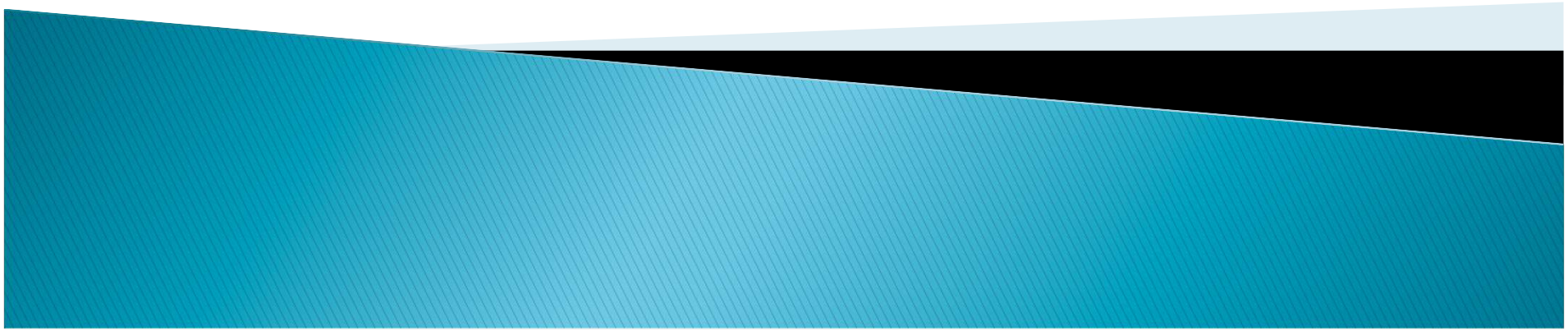
- Management Responsibility
- Risk – ***36 Citings in Preamble in QSR***
- Nonconforming Product
- Complaints and Medical Device Reports (MDRs)
- Supplier Controls

Triggers for Citings

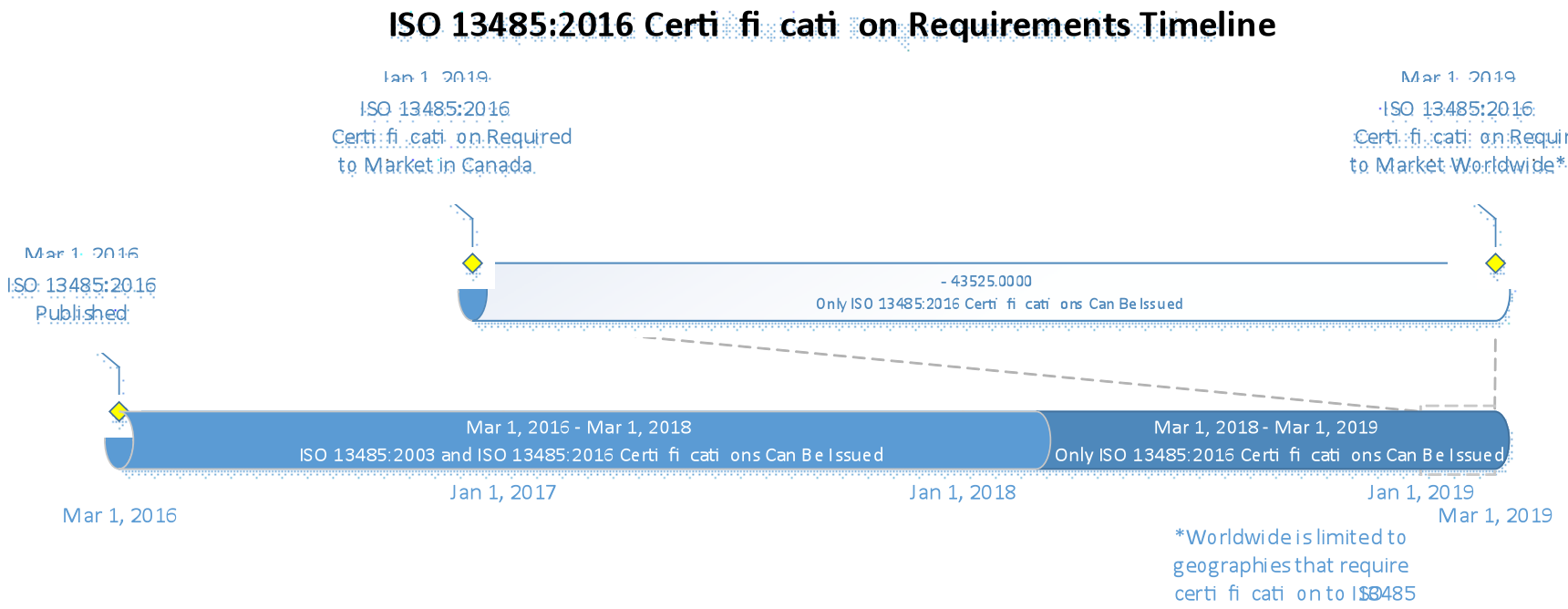
- Recalls without Health Hazard Analyses
- Lack of or inadequate rationale for no MDRs
- No clearance or a change to indications
- Absence of or inadequate supplier controls
- Lack of process validation prior to shipment
- Inadequate Management Oversight
- No evidence of quality planning
- Shipment of adulterated or misbranded product
- Risk management not integrated throughout product life cycle

WHAT IS NEXT?

ISO 13485:2016 and MDR Replaces MDD



ISO 13485:2016 Implementation



MDD Replaced in 2020

- Medical Device Regulation (MDR) and In-vitro Medical Device Regulation (IVDR) Published May 2017
  - These regulations replace EU Directives (MDD, IVDD, and AIMD)
- Must be applied to your QMS by:
  - MDR: May 26, 2020
  - IVDR: May 26, 2022

QUESTIONS?