FDA Medical Device Inspections

FDA Small Business
Regulatory Education for Industry (REdI)
Rockville, MD
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U.S. Food and Drug Administration

Poll Question #1

How many people are employed by your firm?

1. 1 to 9
2. 10 to 49
3. 50 to 99
4. 100 to 499
5. More than 500

Poll Question #2

How many times has your facility been inspected by the FDA?

1. Never
2. Once
3. 2-5 times
4. More than 5 times

Learning Objectives

1. Understand ORA's role within FDA
2. Learn how to prepare for your next inspection
3. Review the Quality System Inspection Technique
4. Discuss common problems seen during inspections
5. Learn what happens after the inspection

FDA Organization

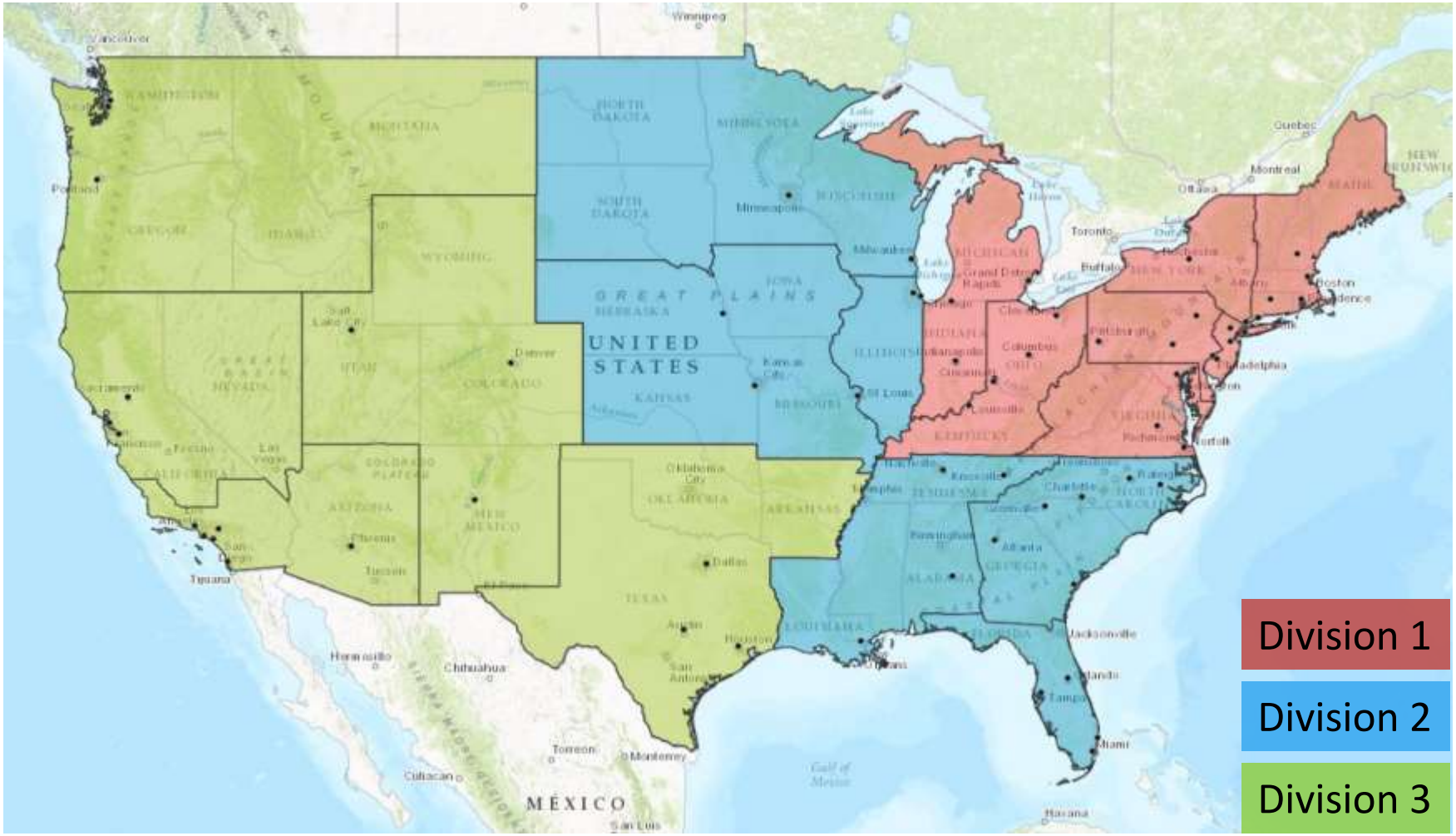
Center for Devices and Radiological Health (CDRH)	Office of Regulatory Affairs (ORA)
• Responsibilities include: – Premarket review – Postmarket surveillance – Policymaking and guidance development – Public communication and education	• Responsible for field activities such as: – Establishment inspections – Conducting investigations – Sample analyses – Import operations

ORA Organization

- **May 2017:** Reorganized from geographic to programmatic management model
- Seven new programs:
  1. Bioresearch Monitoring
  2. Biological Products
  3. Human and Animal Food
  4. **Medical Devices and Radiological Health**
  5. Pharmaceutical Quality
  6. Tobacco
  7. Imports

ORA Organization

Medical Device and Radiological Health Operations



Inspectional Objectives

- **FD&C Act:** Distribution of adulterated products in interstate commerce is prohibited
- **Adulterated:** Not manufactured in accordance with good manufacturing practices (GMPs)
- **Medical device GMPs:** 21 CFR 820

Primary Objective: Assess compliance with 21 CFR 820

Inspectional Objectives (cont.)

- Other regulations covered as applicable:
  - **21 CFR 803:** Medical Device Reporting
  - **21 CFR 806:** Corrections and Removals
  - **21 CFR 807:** Registration and Listing
  - **21 CFR 801:** Labeling
    - Includes Unique Device Identification

Inspectional Objectives (cont.)

- Other regulations covered as applicable:
  - **21 CFR 821:** Medical Device Tracking
  - **21 CFR 11:** Electronic Records
  - **21 CFR 1000-1050:** Electronic Product Radiation Control (EPRC)
  - **21 CFR 4:** cGMPs for Combination Products

Risk-Based Site Selection Process

- MDUFA inspections (*e.g.*, PMA)
- Initial inspections
- Class III > II > I device manufacturers
- Compliance follow-up
- For-cause inspections:
  - Consumer complaint / whistleblower
  - High recall / MDR frequency

Inspection Preannouncement

- **Purpose:** Facilitate the inspection
- **Eligibility:** Routine and PMA inspections
- Call five days in advance:
  - Set date/time
  - Inspection scope
  - Size of team
  - May request procedures

Prior to the Inspection: Investigator

- Review previous EIRs/FDA 483s
- FDA 483 responses
- Registration and listings
- 510(k)s and PMAs
- MDRs and recalls
- Relevant standards
- Procedures provided during preannouncement

Prior to the Inspection: Firm

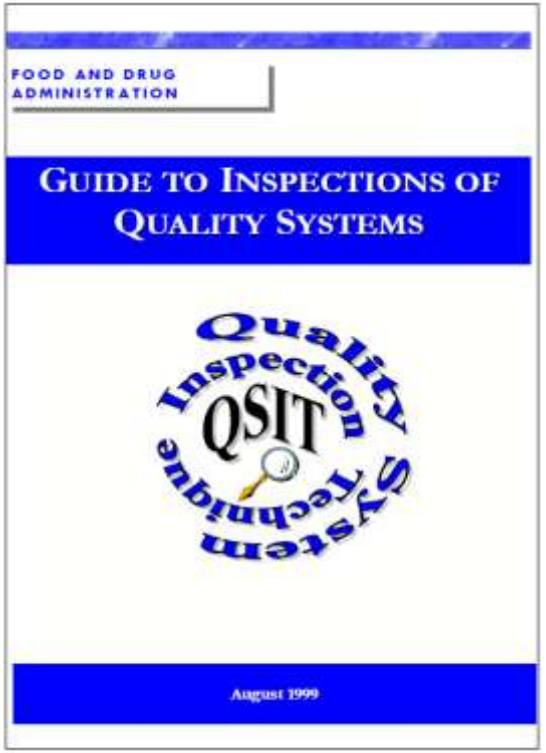
- Necessary documentation available?
- Coordinate inspectional resources:
  - Top management
  - Management representative
  - Subject matter experts (SMEs)
  - Scribes
  - Support staff

Start of the Inspection

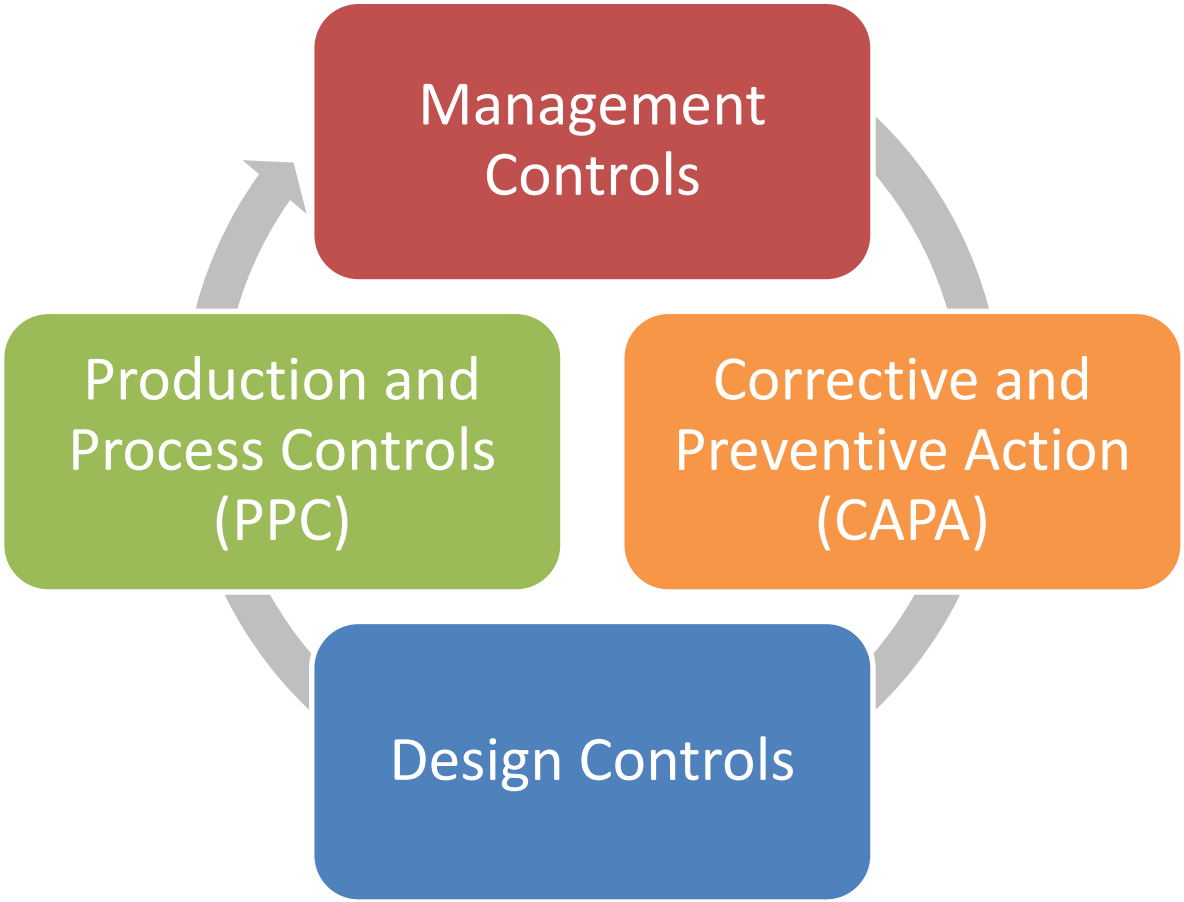
1. Identify top management official
2. Present credentials
3. Issue an FDA 482 (“Notice of Inspection”)
4. Conduct an opening meeting
5. Perform an initial facility walkthrough

Quality System Inspection Technique (QSIT)

- Introduced in 1999
- Validated inspection method
- “Top-down” approach
- Target inspectional length is 4 to 5 days



QSIT: Four-Subsystem Approach



Routine Inspection Level

- **"Comprehensive" Inspections**
  - All four subsystems
- **"Abbreviated" Inspections**
  - CAPA + Design Controls **or** CAPA + PPC
  - Can be escalated if warranted

QSIT: Management Controls Coverage

- Quality policy
- Organizational structure
- Management review
- Quality audits

Management Controls

- By policy, FDA **won't** review:
  - Management review meeting minutes
  - Quality audit reports
- However, FDA **may** review:
  - Data that feeds into management review
  - CAPAs opened as a result of quality audits or management review

Common *Management Controls* Problems

- **Management review:**
  - Top management not in attendance or informed
  - Not meeting required frequency
- **Quality audits:**
  - Inadequate auditor training
  - Scope doesn't cover all applicable QSR elements
  - Auditing one self's work

CAPA Overview

- CAPA is the heart of an effective quality system!
- Squash small problems before they become bigger
- Determines direction for remainder of inspection

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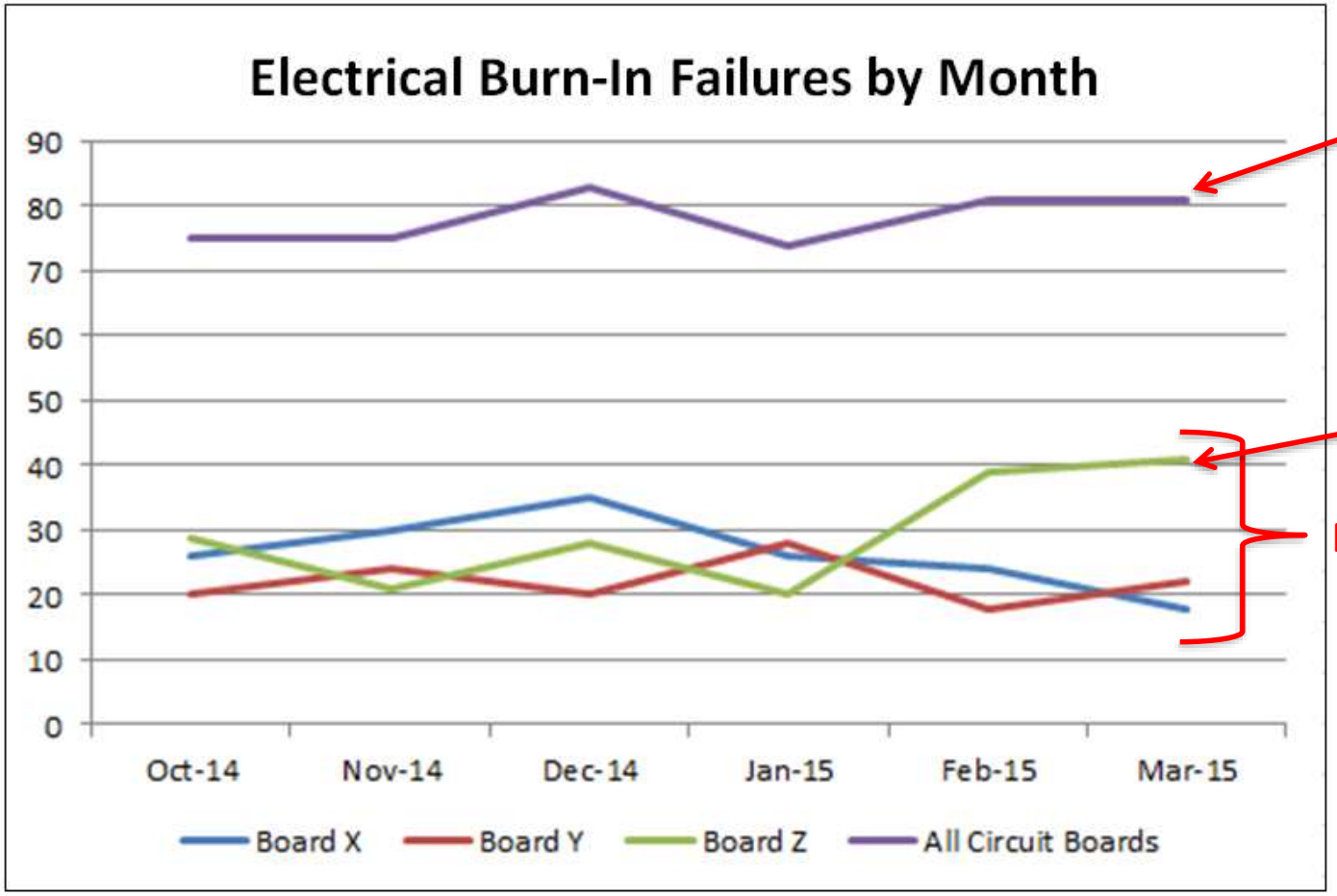
QSIT: CAPA Coverage

- Data analysis (*e.g.*, complaints, nonconforming product)
- CAPA records
- Complaint files and MDRs
- Corrections and Removals

Common *CAPA* Problems

- Inadequate quality data analysis



Firm's trend analysis

Adverse trend

My trend analysis

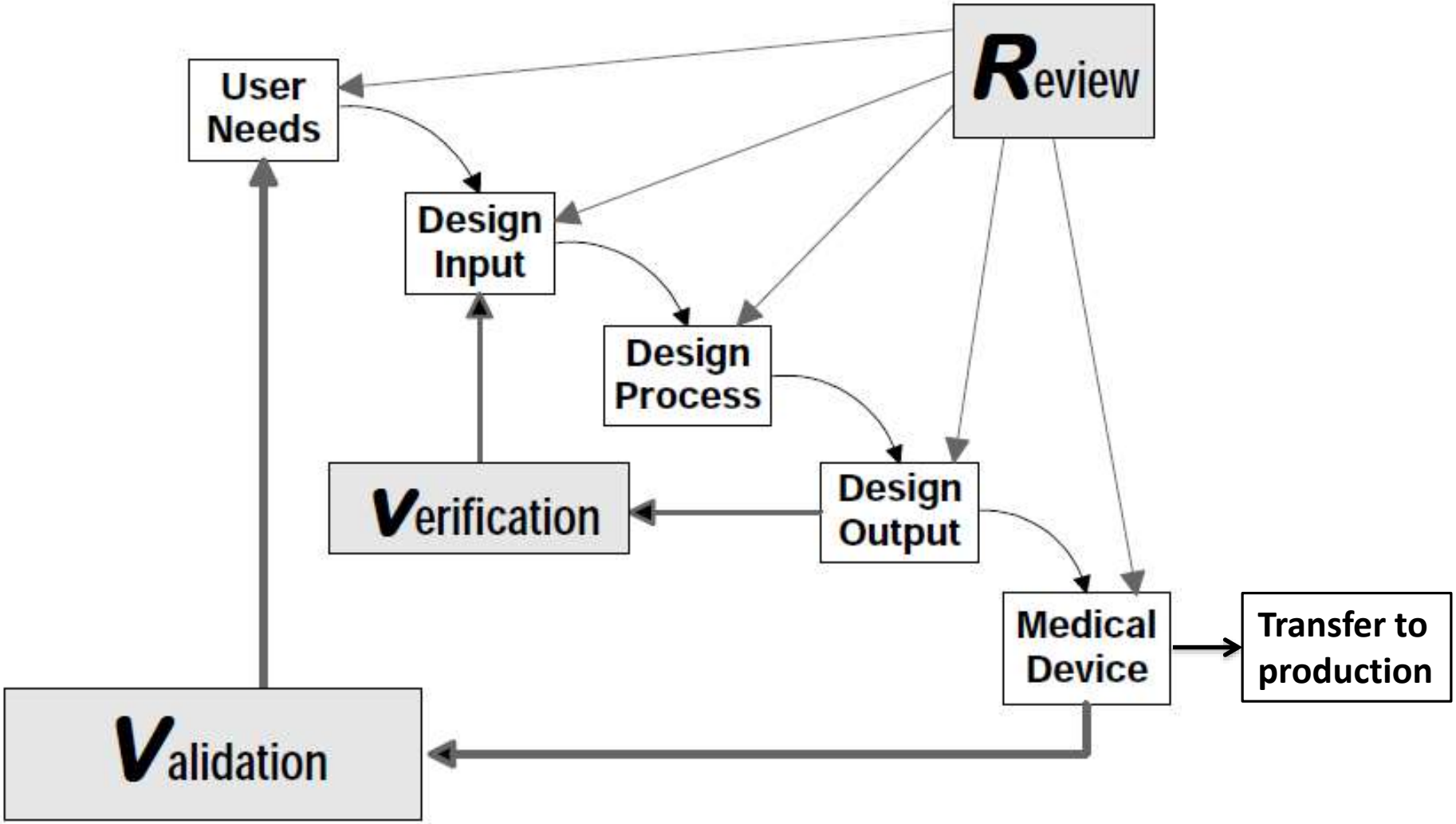
Common *CAPA* Problems

- Activities are not commensurate with risk:
  - Not opening CAPAs when warranted
  - Timeliness of open CAPAs
- Recurrence of quality problems
  - Inadequate root cause analysis
  - Inadequate corrective action V&V

Common *Complaint Handling* Problems

- Misunderstanding definition of complaint
  - "User error"
- Inadequate investigations
- Not evaluating for MDR reportability

QSIT: Design Controls Coverage



Common *Design Controls* Problems

- Ambiguous design inputs
- **Design V&V:**
  - Lack of predetermined acceptance criteria
  - Design changes with no/inadequate V&V
- **Risk Analysis:**
  - Failure to identify all hazards
  - Failure to utilize postmarket data

QSIT: PPC Coverage

- Select specific manufacturing process based on:
  - CAPA indicators
  - Risk of process to cause device failures
  - Process maturity
  - Use in multiple types of devices
  - FDA inspectional history

QSIT: PPC Coverage

- Manufacturing SOPs and training records
- Observe and interview personnel
- Relevant acceptance activities
- Control of nonconforming product
- Calibration and preventive maintenance

QSIT: PPC Coverage

- Environmental controls
- Process validation
  - IQ/OQ/PQ
  - Process monitoring
- DHR review
- Purchasing controls

Common *PPC* Problems

- Process not performed per SOP
- Poor DHR documentation
- Not operating within validated range
- Sampling plans not statistically valid
  - Acceptance activities
  - Process validation

Common *PPC* Problems

- **Process Validation**
  - Lack of predefined acceptance criteria
  - No documented rationale for worst-case conditions
  - Results do not align with production SOPs
- **Control of Nonconforming Product**
  - Failure to document
  - Concession without adequate justification

Expectations During the Inspection

- **Transparency**
  - Communicate our concerns as we see them
  - Provide daily briefings
- **Cooperation**
  - Timely access to records and personnel
  - Be truthful and forthcoming
- ***We are not consultants!***

Observations vs. Discussion Items

- **Observations**
  - Documented on FDA 483
  - Publicly available (FOIA)
  - Corrective actions reviewed during next inspection
- **Discussion Items**
  - Not documented on FDA 483 (in EIR only)
  - Corrective actions reviewed during next inspection
  - Escalated to observations if not corrected

Inspection Close-Out Meeting

1. Communicate discussion items
2. Issue FDA 483 to top management
3. Explain annotation process
4. Discuss observations
5. Encourage written FDA 483 response within 15 business days

FDA 483

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER
300 River Place, Suite 5900
Detroit, MI 48207
(313) 393-8100 Fax: (313) 393-8139

DATE(S) OF INSPECTION
[redacted]

FEI NUMBER
[redacted]

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
[redacted]

FIRM NAME
[redacted]

STREET ADDRESS
[redacted]

CITY, STATE, ZIP CODE, COUNTRY
[redacted]

TYPE ESTABLISHMENT INSPECTED
Medical Device

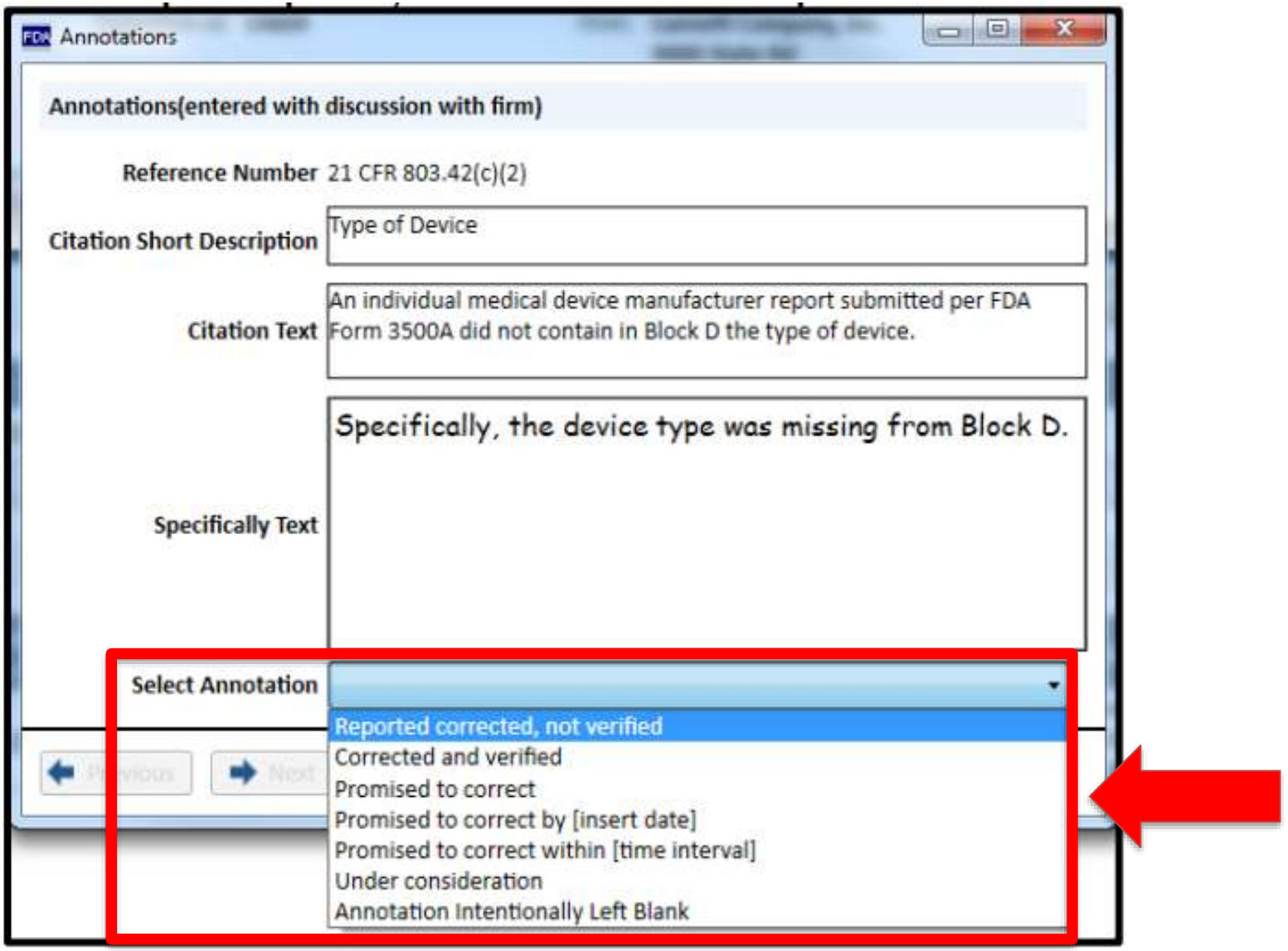
This document lists observations made by the FDA representative(s) during the inspection of your facility. They are inspectional observations, and do not represent a final Agency determination regarding your compliance. If you have an objection regarding an observation, or have implemented, or plan to implement, corrective action in response to an observation, you may discuss the objection or action with the FDA representative(s) during the inspection or submit this information to FDA at the address above. If you have any questions, please contact FDA at the phone number and address above.

The observations noted in this Form FDA-483 are not an exhaustive listing of objectionable conditions. Under the law, your firm is responsible for conducting internal self-audits to identify and correct any and all violations of the quality system requirements.

DURING AN INSPECTION OF YOUR FIRM WE OBSERVED:

OBSERVATION 1

Annotations



After the Inspection

- Investigator writes Establishment Inspection Report (EIR)
- Investigations Branch (IB) endorses EIR and recommends classification:
  - NAI (“No Action Indicated”)
  - VAI (“Voluntary Action Indicated”)
  - OAI (“Official Action Indicated”)

After the Inspection (cont.)

- If endorsed NAI or VAI:
  - IB finalizes classification (case “closed”)
- If endorsed OAI:
  - IB forwards EIR to Compliance Branch (CB)
  - CB determines need for regulatory action
  - CB finalizes classification
  - CB schedules follow-up inspection

Obtaining the EIR

- For routine NAI and VAI inspections…
  - Copy of EIR is sent to firm (FMD-145)
- Otherwise…
  - Firm must make FOIA request
  - There may be a fee
  - May be denied if case is not “closed”

Recap of Learning Objectives

1. Understand ORA's role within FDA
2. Learn how to prepare for your next inspection
3. Review the Quality System Inspection Technique
4. Discuss common problems seen during inspections
5. Learn what happens after the inspection

References

- ***Quality System Inspection Technique*** **(QSIT)**
  - www.fda.gov/downloads/ICECI/Inspections/InspectionGuides/UCM085938.pdf
- **CPGM 7382.845:** ***Inspection of Medical Device Manufacturers***
  - www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM244277.pdf
- **Preamble to 21 CFR 820**
  - www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/PostmarketRequirements/QualitySystemsRegulations/ucm230127.htm
- **Investigations Operations Manual**
  - www.fda.gov/ICECI/Inspections/IOM/default.htm

U.S. FOOD & DRUG ADMINISTRATION

Questions?

Please complete the session survey:

surveymonkey.com/r/DEV-D2S08

Call to Action

- Be prepared for your next FDA inspection
  - Understand your regulatory obligations
  - Perform thorough, meaningful quality audits
- Let's communicate and cooperate to promote more efficient inspections
  - Less burden on manufacturers
  - Better use of FDA resources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