ORA Update
Denver District Office

Rocky Mountain Regulatory Affairs Society
January 11, 2017

LaTonya M. Mitchell
District Director, Denver District Office
Office Of Regulatory Affairs
A successful FDA is a critical factor for better public health in this changing world. I look forward to further building the FDA’s excellent workforce, while relentlessly focusing on the completion of priority projects and continuing to develop the science base that we need to give consumers and patients even more confidence that their food is safe and their medical products are safe and effective.

Robert Califf, MD  
FDA COMMISSIONER
Office of the Commissioner
Southwest Region
LaTonya M. Mitchell
District Director

Thomas R. Berry
Compliance Branch Director
5 Compliance Officers

Mark Harris
Investigations Branch Director
1 Deputy DIB
6 SCSOs
45 CSOs

www.fda.gov
• Pharmaceutical Quality
• Medical Devices and Radiological Health
• Human and Animal Food
• Products regulated by CBER
• Tobacco
• Bioresearch Monitoring
FISCAL 2016
THE YEAR THAT WAS
$333.2M

Paid Fines & Restitution

ORA FY 2016
$107.4M
Awarded Contracts & Grants
ORA FY 2016
www.fda.gov
41,356 Completed Inspections

ORA FY 2016

www.fda.gov
35,220 Analyzed Samples

ORA FY 2016

www.fda.gov
14,580
Warning Letters Issued

ORA FY 2016

www.fda.gov
9,178 Products Recalled

ORA FY 2016

www.fda.gov
Medical Device Inspections

RMRAS FDA Annual Update
Denver, Colorado
January 11, 2017

Kathleen Tormey
Bryan Love
Lauren Priest

U.S. Food and Drug Administration
Denver District Office
My Objectives...

- Describe inspectional tools
- Overview of the QSIT inspection
- After the inspection process
- Enforcement actions
- List of resources for industry
Inspectional Tools for Investigators

- Investigations Operations Manual (IOM)
- Quality System Inspection Technique (QSIT) Guide
- CPGM 7382.845 (Inspection of Medical Devices Manufacturers)
Inspectional Tools for Investigators

- Guidance Documents

- Quality System Regulation Preamble

- FDA Recognized Standards (e.g., ISO, IEC, and AAMI)
How are firms selected for inspection?

- Manufacturers of Class I, II and III devices selected using a risk-based approach:
  - Pre-Market and Pre-Clearance inspections
  - Manufacturers of Class III devices that have never been inspected
  - Compliance Follow Up/For Cause Inspections
  - Manufacturers of high risk devices
Purpose of the inspection

- To assess compliance with the Code of Federal Regulations, Title 21, Parts:
  - 820 (QS Regulation)
  - 803 (MDR)
  - 821 (Tracking)
  - 806 (Corrections and Removals)
  - 807 (Registration and Listing)

- To assess compliance with Electronic Product Radiation Control requirements
Pre-Announcement of Inspections

- General policy for Medical Device Inspections
- No less than 5 calendar days in advance
- The investigator may ask for your Quality Manual or other high-level procedures for pre-inspection review
What happens when the FDA investigator arrives at the site?

- We identify the top management official
- Present credentials
- Issue an FDA 482 “Notice of Inspection”
- Conduct an opening meeting
- Walk-through of the facility
Quality System Inspection Technique (QSIT)

Guide To Inspections of Quality Systems

www.fda.gov
What is QSIT?

- Design Controls
- Corrective & Preventive Actions
- Production & Process Controls
- Management
- Material Controls
- Equipment & Facility Controls
- Records, Documents, & Change Controls

www.fda.gov
What is QSIT?

- We review procedures then records
- QSIT uses the “establish” approach
  - To “establish” means to define, document (in writing or electronically), and implement
- We evaluate if procedures meet regulatory requirements, and whether firms are following their procedures.
What records are typically reviewed?

- **Management Controls**
  - Quality Manual
  - Quality Policy and Plan
  - Org Charts
  - Management Representative appointment and responsibilities
  - Evidence of Management Review Meetings
  - Evidence of Quality Audits

www.fda.gov
What records are typically reviewed?

- **Design Controls**
  - Design Plans
  - Design Inputs (requirements) and Outputs (specifications)
  - Evidence of Design reviews
  - Verification and Validation records
  - Risk Analysis
  - Production specifications (design transfer)
  - Change records (e.g., ECOs)
What records are typically reviewed?

- Corrective and Preventive Action (CAPA)
  - CAPA reports
  - Quality data sources and analysis (e.g., complaints, nonconformances (NCRs), service reports, returned products)
  - MDRs, Recalls and Tracking records
  - Process control charts as applicable (e.g., SPC charts)
What records are typically reviewed?

• Production & Process Controls
  ◦ Device Master Record
  ◦ Device History Records
  ◦ Calibration
  ◦ Maintenance
  ◦ Equipment qualification
  ◦ Process Monitoring

  ◦ Process Validation
  ◦ Environmental control
  ◦ Acceptance Activities
  ◦ Supplier evaluation
  ◦ Sterilization
  ◦ Software Validation
  ◦ Personnel training
  ◦ Servicing
What happens at the end of the inspection?

• Close-out meeting
  • Issue the FDA 483 “Inspectional Observations”
  • Explain the FDA 483 format and statements
  • Explain the annotation process
  • Discuss the observations
DEPARTMENT OF HEALTH AND HUMAN SERVICES  
FOOD AND DRUG ADMINISTRATION

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Industry Information: www.fda.gov/oc/industry

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO:

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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 OBSERVATION 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 (I) (WE) OBSERVED:
What are annotations to the 483?

- policy established by the FDA in 1997
- allows firms to comment on each Observation
- voluntary process

annotation options are:
- Promise to correct.
- Promise to correct by __.
- Promise to correct within __.
- Reported Corrected not verified __.
- Corrected and verified ___.
- Under Consideration (“agree to disagree”).

You have the opportunity to respond to the FDA 483 in writing to the FDA office within 15 business days of the end of the inspection!
What happens next?

- Investigator writes an “Establishment Inspection Report” (EIR)
- EIR is reviewed by the Investigations branch management
- Inspection is classified based on findings
- A copy of the EIR is sent to the facility (FMD-145)
How does FDA classify inspection reports?

- NAI – No action indicated
- VAI – Voluntary action indicated
- OAI – Official action indicated
OAI Cases

Investigator concludes the inspection and writes Establishment Inspection Report

Supervisor (SCSO) reviews EIR and submitted evidence and if significant violations will assign an OAI classification.

The Director of Investigations (DIB) will also review EIR/evidence and if he/she agrees with OAI classification will forward to Director of the Compliance (DCB).

The DCB will also review the case file and assign a Compliance Officer the case for further review.
OAI Case Processing

Lauren S. Priest
Medical Device Compliance Officer
U.S. Food and Drug Administration
Denver District Office
OAI Case Review

- After receiving a 483 during a violative inspection, a firm has the option to send in written response(s) to their local district office describing corrective actions taken.
- Responses received within 15 business days are reviewed by the district Compliance Department alongside the evidence collected by the investigator.
What should response include?

- Review of corrections to 483 items
  - Firm will work with the applicable Compliance Officer in written correspondence to provide documentation demonstrating corrections
  - Firm should supply actual updated procedures and a sample of records to demonstrate the new procedures have been corrected and implemented
  - Deficiencies will also be assessed during a follow up inspection
OAI Case Review

- Corrections are reviewed by local Compliance and possibly also CDRH
  - Firm may receive correspondence from local District Compliance personnel or from CDRH describing deficiencies with their responses.
What actions can FDA take to address OAI inspections?

- Advisory Actions such as:
  - Regulatory Meeting
  - Untitled Letter
  - Warning Letter
  - “It has come to our attention” letters
What actions can FDA take to address OAI inspections?

- Legal Sanctions such as:
  - Seizure
  - Injunction
  - Civil money penalties
  - Prosecution
Case Study

- After Inspection – Corrections to be reviewed by Compliance - Example
  - Firm was cited during the inspection for:
    - No Process Validation – 820.30
    - Inadequate CAPA procedure – 820.100
    - Missing complaint investigations – 820.198
    - Incomplete Risk Analysis – 820.30
Case Study

After Inspection – Corrections reviewed by Compliance - Example

- Firm was cited for Process Validation, CAPA, Complaints & Risk Analysis
- Firm sent several responses to the 483 in for review by Compliance to describe their corrections but ultimately a warning letter was issued
- Some reasons the responses were found deficient...
Case Study: What was missing?

- Process Validation response
  - Firm sent in a plan for developing their process validation and procedures over a timeline but did not address potential deficiencies of product currently in production or covering the timeline prior to validation being completed

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Case Study: What was missing?

- CAPA Response
  - Response stated firm opened a corrective action to improve their CAPA procedure... but no new procedure was included and no timeframe for when it would be drafted or approved was listed
Case Study: What was missing?

- Complaints Response
  - Not all complaints were addressed from those listed in the 483 and the firm did not include any reasoning for addressing some but not others
  - Firm did not conduct root cause investigations and provide the results for relevant complaints
483 Response (in general) was missing:

- Copy of new or updated procedures (especially for major subsystems)
- Plan to address product currently in house or in production potentially affected by unvalidated process
- Did not address all records mentioned in the 483
- Did not supply training records to demonstrate employees were notified of updated processes
Things to remember

- FDA can only verify corrections using the records you provide
- Provide documentation including procedures and a sample of records that demonstrate implementation of the correction
- If actions are planned, provide commitment dates
- Don’t forget training records!
- Opening a CAPA isn’t sufficient if further documented activities are not provided
Resources for Industry

- CDRH Learn (www.fda.gov/Training/CDRHLearn)
- Device Advice (www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/default.htm)
- Division of Industry and Consumer Education (www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/ContactDivisionofIndustryandConsumerEducation/default.htm)
- Medical Devices Databases (www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Databases/default.htm)
THANK YOU!