AMDM Focus Meeting – 10/19/2023

FDA INSPECTIONS OF MEDICAL DEVICE FIRMS

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DISCLAIMER

Agenda

- FDA's Mission
- FDA's Program Alignment
- ISO 13485 Harmonization
- Firm Selection
- Types of Medical Device Inspections
- Types of FDA Personnel
- Inspection Process
- Inspection Outcomes
- Post-Inspection Activities
- Resources

FDA's Mission

"The Food and Drug Administration is responsible for protecting the public health by ensuring the safety, efficacy, and security of human and veterinary drugs, biological products, and medical devices; and by ensuring the safety of our nation's food supply, cosmetics, and products that emit radiation."

Source: FDA.gov (About FDA)

FDA's Mission

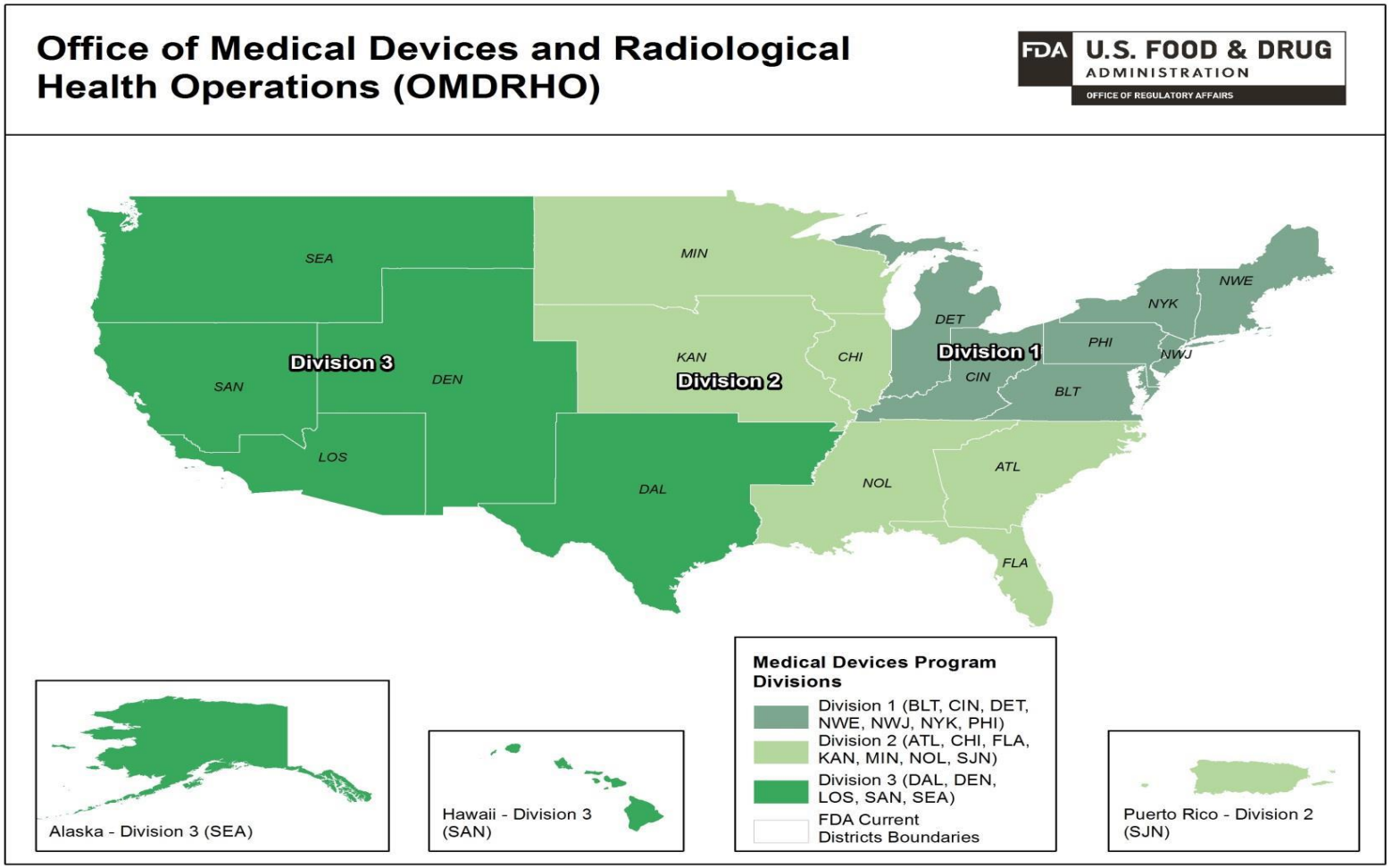
"FDA is responsible for advancing the public health by helping to speed innovations that make medical products more effective, safer, and more affordable and by helping the public get the accurate, science-based information they need to use medical products and foods to maintain and improve their health."

Source: FDA.gov (About FDA)

FDA's Program Alignment

- On May 15, 2017, the FDA reorganized its operations and staff by program (Human and Animal Food, Drug, Medical Device, BIMO, Biologics, Imports)
- No more regions and districts
- Each program has various Divisions and Groups

FDA's Program Alignment



Source: ORA

Prepared by Office of Regulatory Affairs (ORA) Division of Planning, Evaluation & Management (DPEM), Program Evaluation Branch, 2017

FDA's Program Alignment

- Office of Medical Device and Radiation Health Operations (OMDRHO)
- Headed by the Program Director (Anne Reid)
- Three Divisions (East or Div 1, Central or Div 2, and West or Div 3)
- Also includes Foreign Cadre and MQSA (Mammography Quality Standards Act)

FDA's Program Alignment

OMDRHO Division 3

- Covers 16 States – AK, AR, AZ, CA, CO, HI, ID, MT, NM, NV, OK, OR, TX, UT, WA and WY
- Program Division Director – Shari Shambaugh
- Investigations Branch Director – Trang Cox
- Compliance Branch Director – Jessica Mu
- 5 Investigation Branch Groups headed by Supervisory Investigators

ISO 13485 Harmonization

- CFR 21Part 820 has undergone amendment to harmonize it with ISO 13485:2016
- The FDA published the new rule on 02/24/2022 and it was open for public comment until 05/24/2022.
- The rule will become final in December 2023 and will become effective in December 2025.

ISO 13485 Harmonization

- You can locate the new rule in the Federal Register at:

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

Firm Selection

Firms are selected for inspection based on:

- Application for PMA
- Product complexity and risk to public health
- Inspection History
- Recalls
- Complaints
- Confidential information

Types of Medical Device Inspections

- Routine (Abbreviated or Comprehensive)
- For Cause
- Compliance Follow-Up
- PMA (Pre-Approval and Post-Approval)

Types of Medical Device Inspections

Routine

- QSIT (Quality System Inspection Technique)
- Abbreviated – CAPA plus one
- Comprehensive – All subsystems
- An Investigator may turn an abbreviated inspection into a comprehensive inspection

Types of Medical Device Inspections

For Cause

- Inspection triggered by recalls, complaints, confidential information, and/or observed trends

Compliance Follow-Up

- Follow-up to previous compliance actions (e.g. Warning Letter)

Types of Medical Device Inspections

Pre-Market Approval (PMA)

Pre-Approval

- Is the firm ready to market its medical device?

Post-Approval

- Is the firm adhering to making the device in accordance with the conditions specified in the PMA and complying with the requirements of the QS, MDR, C & R, etc. regulations?

Types of FDA Personnel

Investigation Branch Personnel

- Investigator (aka Consumer Safety Officer)
- Supervisory Investigator (aka Supervisory Consumer Safety Officer)
- Director of Investigations Branch

Note: Some FDA Personnel may be Public Health Officers (aka Commission Corp). They wear a uniform.

Types of FDA Personnel

Compliance Branch Personnel

- Compliance Officers
- Recall Coordinators
- Director of Compliance Branch

CDRH Personnel

- Subject Matter Experts
- Reviewers
- Branch Chiefs

Types of FDA Personnel

Other personnel that may become involved:

- OCI (Office of Criminal Investigations) Agents
- US Marshals
- State Regulators (e.g., California Department of Public Health)

Inspection Process

- Preannouncement
- Getting Ready for Inspection
- Initiation of Inspection
- The Inspection (Management Controls, CAPA, Design Controls, Production & Process Controls, MDRs, C&R, Registration & Listing, Labeling, etc.)
- Outcomes and Activities

Inspection Process

Preannouncement

- Typically given 5 days before initiation of a routine inspection
- Is not given for certain types of inspections (such as For-Cause)

Inspection Process

Preannouncement

What the Investigator is looking for?

- Your firm's contact information is correct (right person and phone number)
- If the Investigator is unable to reach someone at the firm to preannounce, the Investigator will show up after making a good faith effort to make contact

Inspection Process

Preannouncement

What the Investigator needs to know:

- Building Address / Lobby Location
- Contact Person
- Cell Phone or Direct Number of Contact Person

Inspection Process

Preannouncement

- Investigator may tell you what documents and records you can assemble in preparation for the inspection
- Investigator will tell you the estimated duration of the inspection
- You may ask the Investigator questions to clarify the purpose and logistics of the inspection
- It is a good idea to get the Investigator's contact information in case you need to contact him/her before the inspection

Inspection Process

Getting Ready for Inspection

- Prepare a room where the Investigator can speak with firm representatives and review documents
- Prepare a brief presentation about your firm and product
- Gather documents such as Quality Manual, a list of SOPs, Organizational Charts, Facility Map, Process Flow Chart, etc. that are typically requested during an inspection
- Alert your Subject Matter Experts to be available during the inspection

Inspection Process

Getting Ready for Inspection

- Although you may supply lunch for your staff, Investigators cannot accept free lunches
- An Investigator typically leaves the firm during lunch, or may offer to pay for his or her own lunch if you are catering lunch
- An Investigator may have water, coffee, or other beverages as long as they are typically provided by the firm free of charge to the firm's employees
- Investigators cannot accept gifts of any kind

Inspection Process

Initiation of Inspection

- Notice of Inspection, Form FDA-482
- Credentials
- Purpose of Inspection

or

- Refusal
- Inspection Warrant

Inspection Process

Initiation of Inspection

What is the Investigator looking for?

- Most Responsible Person
- Quality Management Representative
- Introductions
- Background Information on Firm and Products
- Tour of the Facilities

Inspection Process

Initiation of Inspection

- Make sure that the Most Responsible Person (CEO, President, Plant Manager, etc.) is present at the opening of the inspection
- Provide the Investigator with a brief presentation about your firm's history, organization, and products

Inspection Process

The Inspection

- QSIT Subsystems
- Corrections & Removals (Recalls)
- MDRs
- Registration & Listing
- 510 (k) and PMA

Inspection Process

Inspection Process

QSIT Subsystems

- Management Controls
- Corrective Actions Preventive Actions (CAPA)
- Design Controls
- Production & Process Controls

The Investigator will cover some or all of the QSIT Subsystems depending on if it is an abbreviated or comprehensive inspection.

Inspection Process

Management Controls

Investigator's Goals:

To assess if your firm has a proper quality management organization that can address issues in your quality management system (QMS)

To assess if Executive Management is aware of the state of your QMS and is providing the necessary resources and support

Inspection Process

Management Controls

What is the Investigator looking for?

- Quality Policy & Objectives
- Management Review
- Internal Audits
- Organizational Chart / Responsibilities / Powers

Inspection Process

CAPA

Investigator's Goal:

To find if your firm has established procedures to assess and take effective corrective/preventive actions to address problems in your QMS

Inspection Process

CAPA

What is the Investigator is looking for?

- Data Sources / Trending (Complaints, Nonconformities, Literature)
- Investigation (Root Cause / Probable Cause)
- Corrective or Preventive Action Implementation
- Effectiveness Check (Plan, Criteria to be met, Next steps if ineffective, etc.)
- Timeliness

Inspection Process

Corrective Actions Preventive Actions (CAPA)

Complaints:

- An established complaint handling unit & procedure
- All data that meet the definition of a complaint are being handled as a complaint (e.g., “customer feedback”, service records, customer surveys)
- Sufficient information to do failure investigation
- Sufficient information to make MDR determination
- Timeliness
- Trending (Is a CAPA needed? Correction or Removal?)

Inspection Process

Design Controls

Investigator's Goal:

To assess whether the medical device is designed, verified, and validated to meet the user's requirements, and to find if design changes were developed and evaluated *prior* to implementation.

Inspection Process

Design Controls

What is the investigator looking for?

- Design History File (Inputs, Outputs, Verification, Validation, Transfer)
- Design Matrix, Risk Analysis, FMEA, Design Reviews
- Design Changes

Inspection Process

Production & Process Controls

Investigator's Goal:

To ensure that the medical device is manufactured according to a validated process on qualified equipment with materials sourced from qualified suppliers by trained personnel

Inspection Process

Production & Process Controls

What is the investigator looking for?

- Inspection of manufacturing areas
- IQ/OQ/PQ documentation
- Process Validations
- Calibration Records
- Device History Records / Lot History Records
- Training Records

Inspection Process

Production & Process Controls

What is the investigator looking for?

- Clean Room Certification
- Environmental Monitoring Records
- Deviations
- Nonconforming Material Reports
- Supplier Qualification Records

Inspection Process

Corrections & Removals

Investigator's Goal:

To find if the firm is assessing various data (complaints, CAPAs, NCMRs, etc.) and undertaking field actions when necessary, and doing them in compliance with the regulations.

Inspection Process

Production & Process Controls

What is the investigator looking for?

- Field Actions undertaken by the firm since the last inspection
- Did the company report the field action to FDA?
- Did the company retain the required information?
- Was the field action effective?

Inspection Process

MDRs

Investigator's Goal:

To find if the firm is gathering enough information and assessing its complaints in a timely manner to determine whether an MDR needs to be filed

Inspection Process

MDRs

What is the investigator looking for?

- Do complaint forms contain sufficient information to enable the firm to make an MDR determination?
- Is the firm making “good faith” efforts to gather the necessary information?

Inspection Process

MDRs

What is the investigator looking for?

- Are the risk ratings used to determine serious injury or death the same as the ones used in the firm's risk analysis, FMEA, and other design risk documents?
- Did the firm report the MDRs to the FDA within the required timeline?

Inspection Process

Registration & Listing

Investigator's Goal:

To ensure that the firm is registered correctly according to its activities, and that its products are listed for that registration

Inspection Process

Registration & Listing

What is the investigator looking for?

- The firm's registration correctly reflects its activities (manufacturer, initial importer, specifications developer, etc.)
- All of the firm's products are listed

Inspection Process

510(k) and PMA

Investigator's Goal:

To ensure that the firm's products are either cleared or approved, and that the firm is not making claims outside those that the FDA has cleared or approved.

Inspection Process

510(k) and PMA

What is the Investigator looking for?

- PMA supplements have been filed if there have been changes
- Claims on all labeling (product label, instructions for use, promotional materials, firm's website) reflects those that were cleared or approved by the FDA

Inspection Process

510(k) and PMA

A word about putting "FDA Cleared" on labeling

"Submission of a premarket notification … does not in any way denote official approval of the device. Any representation that creates an impression of official approval of a device because of complying with the premarket notification regulations is misleading and constitutes misbranding."

Source: 21 CFR 807.97 Misbranding by reference to premarket notification.

Inspection Process

Hints

- You can disagree with the Investigator; explain clearly why you disagree
- Never lie to an Investigator; if you do not know the answer, just say so
- Never fake documents; if you don't have it, just say so
- Do not stall an Investigator; it will raise suspicions in the Investigator's mind and prolong the inspection
- Do not "bug" or record an Investigator without disclosing that fact

Inspection Outcomes

- No observations
- Discussion items
- Inspectional observations – Form FDA-483
  - Annotation of Form FDA-483
- Affidavit

Inspection Outcomes

Inspection Classifications

- NAI – No Action Indicated
- VAI – Voluntary Action Indicated
- OAI – Official Action Indicated

Post-Inspection Activities

- Response Letter within 15 working days
- Review of Inspection by Investigations Branch
- Review of Inspection by Compliance Branch (especially for OAI and Compliance Follow-up)
- Review of Inspection by CDRH (especially for PMA or CDRH-directed Inspections)

Post-Inspection Activities

- Make corrections to the observations through your CAPA process
- Examples given in Form FDA-483 observations are just that - examples; do not only correct the examples given in the Form FDA-483, but make systemic changes to correct all other similar situations

Post-Inspection Activities

- FMD-145 Letter
- Untitled Letter
- Warning Letter
- Injunction
- Seizure
- Civil Money Penalties
- Criminal Prosecution

Resources

- Available at www.FDA.gov
  - Investigations Operations Manual
  - Compliance Program Manuals
  - Guidance Documents
  - CDRH Learn
  - DICE (Division of Industry and Consumer Education)

Resources

- Available on-line or in print
  - Food, Drug & Cosmetic Act
  - Code of Federal Regulations
  - Federal Register

FDA Inspections of Medical Device Firms

QUESTIONS?


FDA
U.S. FOOD & DRUG
ADMINISTRATION