FDA Medical Device Inspections

FDA Small Business
Regulatory Education for Industry (REdI)
Atlanta, GA
May 10, 2017

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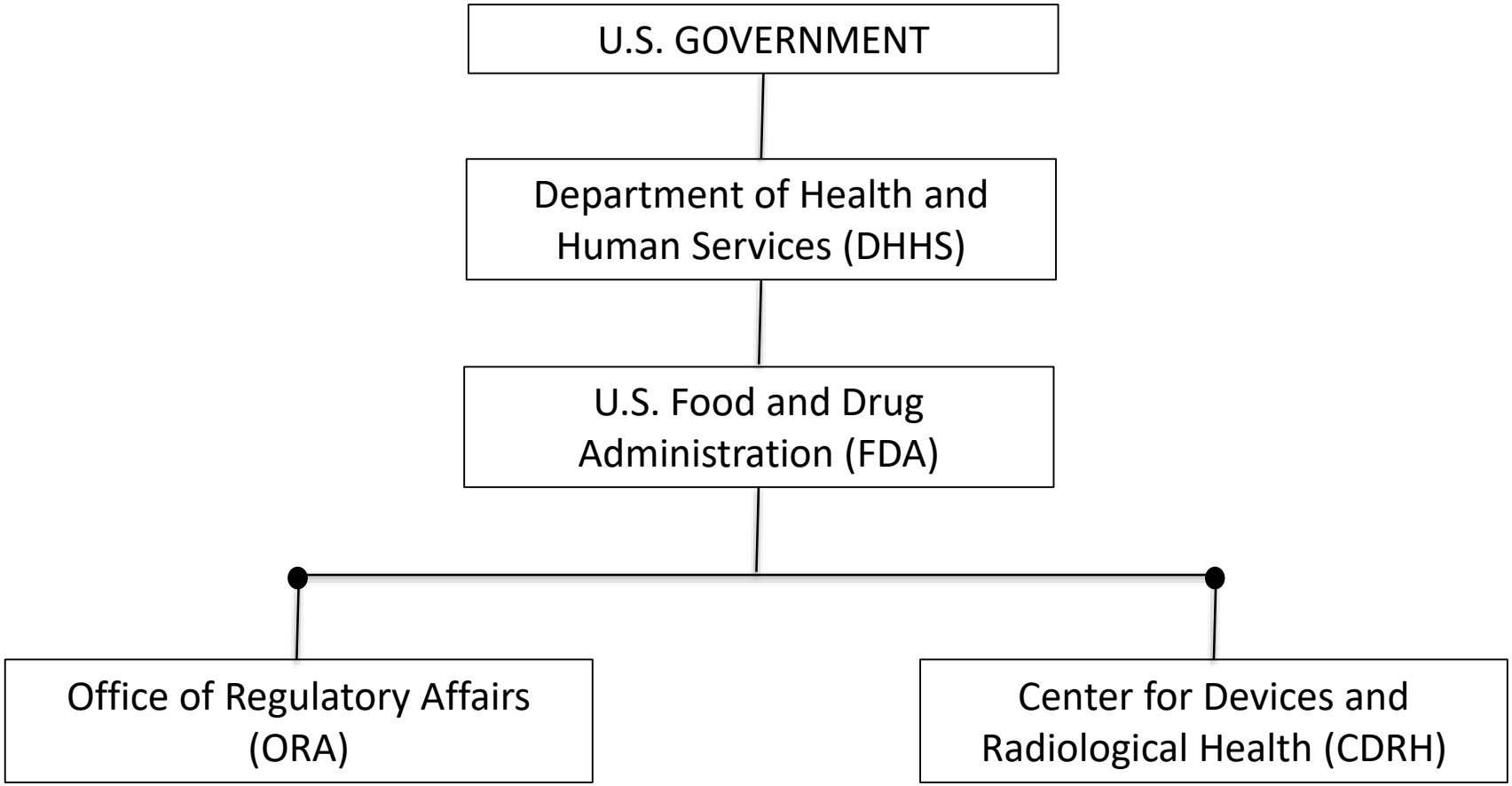
Office of Regulatory Affairs
U.S. Food and Drug Administration

Learning Objectives

- Understand the FDA organizational structure and mission
- Learn about FDA Medical device inspections and what to expect from your Investigator
- Review the Quality System Inspection Technique (QSIT)
- Know what happens after an inspection

Introduction Organization



Introduction – FDA 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 electronic radiation.

Introduction – FDA is Responsible for

promoting 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.

Introduction Organization

Office of Regulatory Affairs (ORA)

- **Lead office for all agency field activities.**
- Inspects regulated products and manufacturers.
- Conducts sample analyses of regulated products.
- Reviews imported products offered for entry into the United States.

Center for Devices and Radiological Health (CDRH)

- Facilitates medical device innovation by advancing regulatory science.
- **Provides industry with predictable, consistent, transparent, and efficient regulatory pathways,**
- Assures consumer confidence in devices marketed in the U.S.

Introduction ORA Realignment

Moving from an historical **geographic** management model to a **program-based** management model for many functions. The five regions will sunset, and seven key programs will exist for operations:

- Bioresearch Monitoring
- Biological Products
- Human and Animal Food
- **Medical Devices and Radiological Health**
- Pharmaceutical Quality
- Tobacco
- Imports

Purpose of the FDA Inspection

To assess compliance with Title 21 of the Code of Federal Regulations (CFR) – including 21 CFR Parts:

- 820 (Quality System Regulation/ cGMPs)
- 803 (Medical Device Reporting)
- 806 (Corrections and Removals)
- 807 (Registration and Listing)
- 821 (Tracking)
- 801 (Labeling)/ 830 (Unique Device Identification)

Purpose of the FDA Inspection continued

…and as applicable:

- Electronic Product Radiation Control (EPRC) (21 CFR Parts 1000-1050)
- Combination Products (21 CFR Part 4)

Types of FDA Inspections

- Routine
- Compliance Follow-up*
- For Cause (due to a complaint, whistleblower, recall, etc)*
- Risk Based Work Plan (RBWP)
- Pre-Market/ Post-Market Approval (PMA)
- Medical Device Single Audit Program (MDSAP)

(*Inspections that do not require preannouncement from FDA.)

Inspection Personnel

FDA PERSONNEL:

- Independent/ Team
- Commissioned Corps/ Civil Service
- Investigator/ Consumer Safety Officer (CSO)
- Laboratory

Prior to the Inspection

FDA INVESTIGATOR:

- Preannouncement of inspection to the firm
- Procedures (especially Quality System Manual) may be requested for review ahead of time
- Search of ORA and CDRH databases
- Review of previous EIRs, FDA 483 responses, standards applicable to products, and firm's website

Prior to the Inspection

FIRM:

- Check registration status and update device listing
- Coordinate easy retrieval of documents
- Coordinate resources for the inspection (pertinent personnel, scribes, support staff, etc.)
- Ensure website has accurate information (and Does Not display FDA logo or contain statements which may imply FDA endorses product or firm)

Prior to the Inspection

The best way to prepare is to…always be prepared.

- Know applicable FDA regulations (and where they differ with ISO)
- Make sure Quality Manager/ Management Representative & all personnel have necessary training
- Conduct regular and adequate Internal Quality Audits
  - Quality procedures and processes must be reviewed to ensure they reflect current practices
  - An outside auditor may need to be brought in
- Have meaningful Management Reviews

Start of the Inspection

- Identify the top management official on site
- Show credentials
- Issue a Form FDA 482, Notice of Inspection
- Conduct an Opening Meeting
  - Reiterate reason for inspection
  - Review history of firm, products and operations, organization, and other general information
  - Interview Top Management/ Quality Management
- Perform an initial walkthrough of the facility

During the Inspection

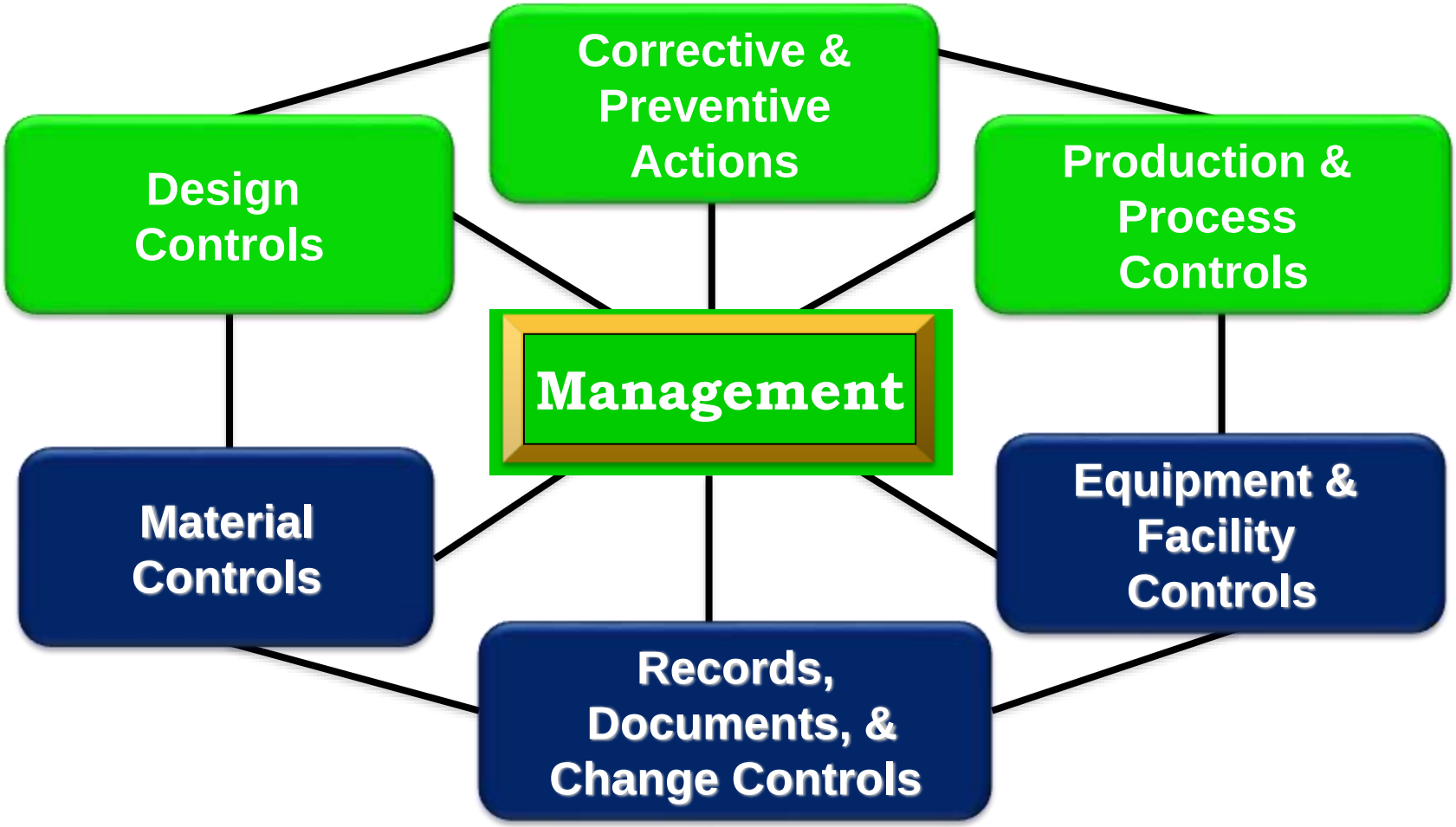
Quality System Inspection Technique (QSIT)

- Process for performing subsystem inspections based on a "top-down" evaluation of key elements of a firm's quality system
- To help determine whether a firm has established and maintained an appropriate quality system

Quality System Inspection Technique continued

- Begin with the evaluation of procedures, followed by understanding the firm's practices and ending with a review of records and raw data (for each process being investigated)
- **Are procedures established?** FDA's definition of establish means **define, document** (in writing or electronically)**, and implement (do)**.

The 4 Major Subsystems



Guide to Inspections of QS: Quality System Inspection Technique

Management Controls

Inspection begins and ends with the evaluation of this subsystem.

- Has management with executive responsibility ensured an adequate and effective quality system has been established and maintained?
- Has management **Documented** appointment of a Management Representative who has the responsibility to ensure the firm meets requirements to the Quality System Regulation and report on it's status to top management?

Management Controls continued

- Management Review (of the effectiveness of the firm's quality system)
  - Agenda, attendees, frequency
- Internal Quality Audit
  - Schedule, plan, frequency, qualified auditors (auditor independence)
- Records not requested during a **routine** inspection
  - Results of Management Reviews (MR); (Internal/ External) Quality Audit and Supplier Audit reports
  - **HOWEVER,** raw data that feeds into MR and any CAPAs opened as a result of Audits/ MR are reviewed

Design Controls

- New design and/or change in product design
- Review of design project or design change **(may include device software validation)**:
  - Design plan
  - Design inputs and Design outputs
  - Risk analysis
  - Design Verification and validation
  - Design reviews (Independent Reviewer)
  - Design transfer

Design Controls continued

- Verification – Do design outputs meet the design input requirements?
- Validation (Design) – Do device specifications conform with **predetermined** user needs and intended use(s)?
- Validation (Process) – Does product (or result of process step) conform to **predetermined** specifications?
- **Acceptance criteria must be stated up front.**
- **Validation using initial production units**

Corrective and Preventive Action

- CAPA subsystem is one of the most important quality system elements
- **Sources of quality data** identified and analyzed:
  - complaints, service records,
  - processes,
  - work operations,
  - quality audits (internal and external)
  - concessions, etc.

Corrective and Preventive Action continued

- Understand the difference between:
  - Correction (immediate)
  - Corrective Action (correct and prevent recurrence)
  - Preventive Action (prevent potential nonconformances)
- All CAPAs are effective and any actions taken were verified or validated (as applicable) prior to implementation; and that
- Actions do not adversely affect the finished device
- **CAPA satellite subsystems may also be covered**

CAPA Satellite
Corrections and Removals

- Review status of any Recalls, Market Withdrawals, Field Corrections
- Reported to FDA within 10 business days of making decision
- CAPA opened
- Health hazard evaluations
- Documented evaluation of corrections and removals determined to be non-reportable

Production & Process Controls

- New manufacturing process and/or change in process
- Critical manufacturing process **(may include software validation for an automated process); P&PC Satellite - Sterilization**
- Device History Record (DHR)
  - Documentation shows requirements of Device Master Record (DMR) are met
  - Include or refer to the location of labeling
  - Nonconformance/ Rework

P&PC continued

- Acceptance (incoming raw material; in-process and finished device)
  - Documented and dated
  - If not 100% verification, based on a valid statistical method
- Equipment Calibration/ Maintenance
- Environmental Controls

Purchasing Controls

- Document evaluation of suppliers (including contractors and consultants)
- Establish and maintain record of approved suppliers
- Clearly describe specified quality requirements for product and services
- Agreement to include requirement for supplier to notify manufacturer prior to making any changes

During the Inspection continued

- QSIT **may** be followed during Routine inspections, with some aspects used during other types of inspections
  - QSIT Level 2 (Comprehensive/ Baseline) covers all four major subsystems
  - QSIT Level 1 (Abbreviated) covers Corrective and Preventive Actions (CAPA) **plus** either Design Controls or Production & Process Controls (P&PC)
- Follow-up on issues cited during the previous device inspection

During the Inspection continued

- Perform multiple walkthroughs of facility
- Interview of personnel performing the work
- Point out issues observed in real time
- Provide daily briefings
- The firm is responsible for determining corrective actions for issues noted – Investigators are not consultants

Observations vs Discussion Items

- Observations
  - Documented on Form FDA 483, Inspectional Observations
  - FDA 483s can be requested by FOI Act
  - Corrections to FDA 483s reviewed during next inspection
- Discussion Items
  - Not placed on the FDA 483
  - Documented in final establishment inspection report (EIR)
  - Can lead to observations during next inspection

End of Inspection

- Conduct a Closeout Meeting
  - Discuss any discussion items
  - Discuss any observations issued on the FDA 483
    - Explain the annotation process – allows firm to provide a succinct statement for each observation
  - Firms are encouraged to respond to the FDA 483 within 15 business days
    - To the District Office for Domestic firms
    - To CDRH for Foreign firms [who may send an electronic copy of their response (in lieu of paper copy) – in English]

Form FDA 483

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
FDA CDRH White Oak Building 66, Room 2622 10903 New Hampshire Avenue Sliver Spring, MD 20993 Industry Information: www.fda.gov/oc/industry	05/08/2017 - 05/12/2017
	FEI NUMBER 1234567890

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: President & CEO

FIRM NAME	STREET ADDRESS
XYX, Inc.	123 Main Street
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
Any town, USA 12345	Manufacturer

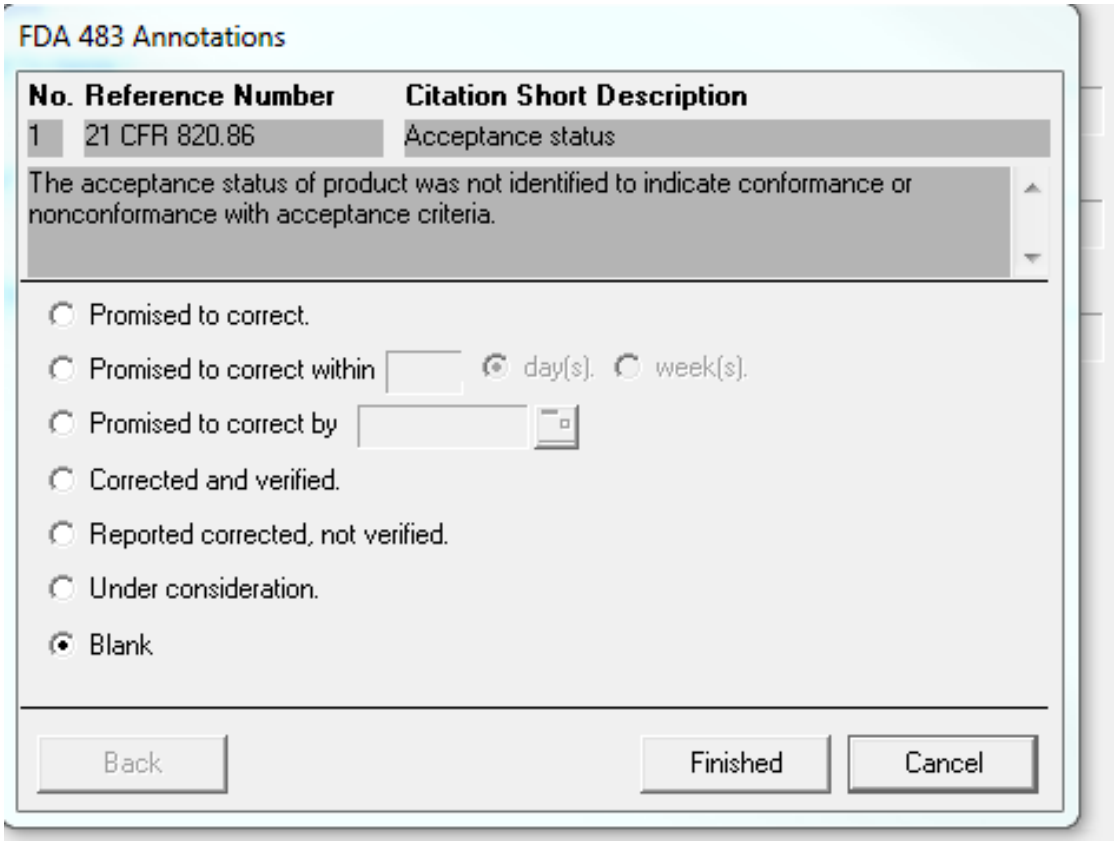
THIS DOCUMENT LISTS OBSERVATIONS MADE BY THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OF YOUR FACILITY. THEY ARE INSPECTIONAL OBSERVATIONS; AND DO NOT REPRESENT A FINAL AGENCY DETERMINATION REGARDING YOUR COMPLIANCE. IF YOU HAVE AN OBJECTION REGARDING AN OBSERVATION, OR HAVE IMPLEMENTED, OR PLAN TO 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 (I) (WE) OBSERVED:

OBSERVATION 1

Annotations



"Corrected and verified" and "Reported corrected, not verified" would be chosen by the Investigator after review of corrective actions (if warranted).

After the Inspection

- Investigator writes an Establishment Inspection Report (EIR)
- ORA Investigations Branch endorses EIR and provides final inspection classification for:
  - NAI (No Action Indicated)
  - VAI (Voluntary Action Indicated)
- ORA Compliance Branch (CDRH for Foreign firms) provides final inspection classification for:
  - OAI (Official Action Indicated – regulatory actions)

After the Inspection continued

- A copy of the EIR is sent to firm (FMD 145 copy) for NAI and VAI classified Routine inspections only
- For all other classifications and non-Routine inspections, firm must make a Freedom of Information Act (FOIA) request to receive a copy of the EIR – there may be a fee

Visit: https://www.fda.gov/RegulatoryInformation/FOI/default.htm

Where to find additional info?

Division of Industry and Consumer Education (DICE)

- (800) 638-2041
- (301) 796-7100
- DICE@fda.hhs.gov

Address:

Division of Industry and Consumer Education

CDRH-Center for Devices and Radiological Health

U.S. Food and Drug Administration

10903 New Hampshire Avenue

Silver Spring, MD 20993

www.fda.gov

- CDRH Learn
- QSIT Guide
- eMDR – Electronic Medical Device Reporting
- Unique Device Identifier (UDI) Basics
- Medical Device Single Audit Program (MDSAP) Q&A
- Freedom of Information
- Office of Regulatory Affairs Organization

FDA U.S. FOOD & DRUG ADMINISTRATION

Questions?

Please complete the session survey:

surveymonkey.com/r/DEV-D2S08

Call to Action

- Be prepared for you next FDA Inspection
- Use FDA Resources to learn about your regulatory requirements and responsibilities
- Communicate with FDA in a timely manner
- Know Investigators are doing their best to protect public health – and appreciate your cooperation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ADMINISTRATION