ORA Medical Device Compliance Update

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Overview

- FDA Locations, Employee Duties/Qualifications & Organizational Structure
- Inspection Process – General
- Inspection Outcomes and Post Inspection Activities
- Compliance Activities & Regulatory Actions
- Adequate Responses
- Resources for Medical Device Manufacturers

Center for Devices and Radiological Health (CDRH)

- Responsible for regulating firms who manufacture, repackage, relabel, and import medical devices sold in the United States.
- Mission includes:
  - Assuring continued access to safe, effective, and high-quality medical devices and safe radiation-emitting products
  - Providing understandable and accessible science-based information

Office of Regulatory Affairs (ORA)

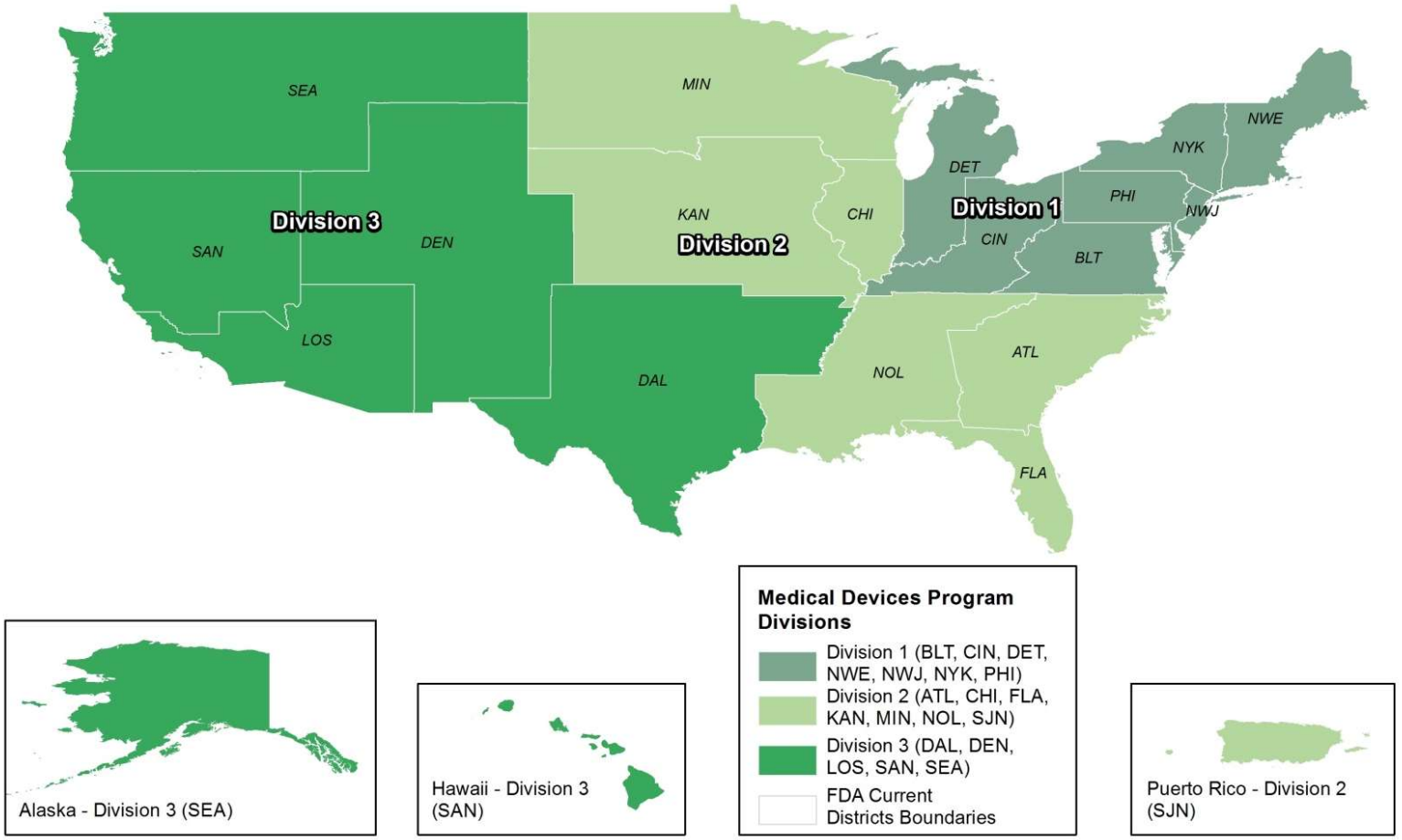
- Lead office for field activities.
- Supports the Centers by inspecting regulated products and manufacturers, conducting sample analysis, and reviewing imports.
- Mission includes protecting consumers and enhancing public health by maximizing compliance of FDA regulated products and minimizing risk associated with those products.

ORA Program Divisions

- Office of Bioresearch Monitoring Operations (OBIMO)
- Office of Biological Products Operations (OBPO)
- Office of Medical Device and Radiological Health Operations (OMDRHO)
- Office of Pharmaceutical Quality Operations (OPQO)
- Office of Human and Animal Food Operations (OHAFO)
- Office of Enforcement and Import Operations (OEIO)
- Tobacco Operations Program

Office of Medical Device and Radiological Health Operations

Office of Medical Device and Radiological Health Operations (OMDRHO)



Why am I being inspected?

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 FDA Personnel

Investigation Branch Personnel

- Investigators (aka Consumer Safety Officer)
- Supervisory Investigators (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
- 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 can be credentialed by FDA

Inspection Process

- Preannouncement
- Getting Ready for Inspection
- Initiation of Inspection
- The Inspection (generally follows QSIT)
- Outcomes and Activities

How are inspections conducted?

- Quality System Inspection Technique (QSIT)*
  - Top-down, systems-oriented, inspections

    (instead of)
  - Bottom-up, problem-oriented, inspections

- http://www.fda.gov/downloads/ICECI/Inspections/InspectionGuides/UCM085938.pdf

*Guide to Inspections of Quality Systems – published 1999

Inspection Process – Quality System Inspection

Potential Inspection Outcomes

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

Form FDA 483
Inspectional Observations

- Used to report objectionable conditions or practices observed during an inspection

➢ On 483
  - GMP's
  - Adverse Event Reporting
  - Recall Issues

  (Significant findings only)

➢ NOT on 483
  - Registration & Listing
  - Pre-market (e.g., product lacks a 510(k) or PMA)
  - Labeling

FY17 vs FY18 Top 483 Observations

CFR Number	# of Domestic Observations	Topic
21 CFR 820.100(a)	400	CAPA SOP
21 CFR 820.198(a)	269	Complaints
21 CFR 820.50	138	Purchasing
21 CFR 820.75(a)	137	Process Validation
21 CFR 803.17	127	MDR SOP
21 CFR 820.90(a)	127	NCR
21 CFR 820.100(b)	115	CAPA documentation
21 CFR 820.30(i)	80	Design changes
21 CFR 820.22	78	Quality Audits
21 CFR 820.80(d)	67	Acceptance SOP

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21 CFR 820.90(a)	119	NCR
21 CFR 820.100(b)	86	CAPA documentation
21 CFR 820.22	78	Quality Audits
21 CFR 820.30(i)	76	Design changes
21 CFR 820.181	63	DMR

Inspection Outcomes

Inspection Classifications

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

Post-Inspection Activities

Firm actions:

- Make corrections to the observations through your CAPA process
- May voluntarily respond to FDA within 15 working days explaining corrections to observations

***Keep in mind:** Examples given in Form FDA-483 observations are just that – examples! You should not only correct the examples given in the Form FDA-483, but also make **systemic** changes to correct all other similar situations.

Post-Inspection Activities

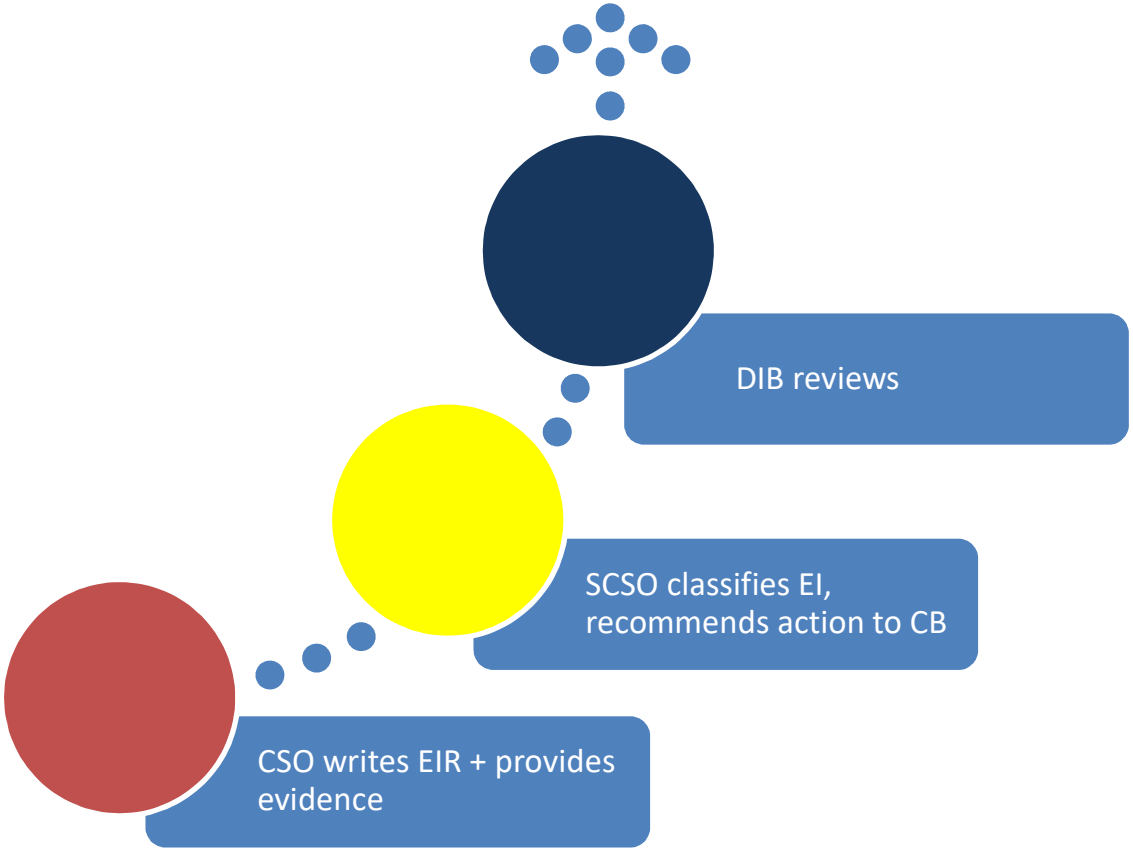
FDA Actions:

- Write up and review of EIR by Investigations Branch
- Review of EIR by Compliance Branch (for OAI or Compliance Follow-up)
- Review of EIR by CDRH (mainly for PMA Inspections)

*EIR: Establishment Inspection Report & Related documents

After the Inspection

Investigations Branch



After the Inspection

Compliance Branch: Compliance Officer & Director

Compliance Decision/Regulatory Strategy

Compliance Branch (CB) Operations

CB will review evidence to determine compliance with laws and regulations.

Potential Outcomes of Review:

- Downgrade based on firm's response
- Advisory Actions - Untitled Letters and Warning Letters
- Prepare recommendations for legal actions
- Coordinate enforcement actions and legal cases
- Recalls

FDA Enforcement Policy

- Basic Precept: The majority of persons want to comply with the law, and they will comply voluntarily when given information as to what is required and what violations appear to exist.
- Responsible persons will be given notice of their violative conduct and afforded an opportunity for correction provided that the situation does not present a danger to health, or does not constitute intentional, gross or flagrant violation.
  - The terms FDA uses to describe this practice are Prior Warning or Prior Notice

Potential OAI Outcomes

- Downgrade
- Advisory Actions
- Administrative Actions
- Enforcement Actions

Advisory Actions

- Untitled Letter
- Warning Letter

Untitled Letter

- Cites violations that do not meet the threshold for significance of a Warning Letter
- Does not include a statement that FDA will advise other federal agencies of the issuance of the letter
- Does not evoke a mandated follow-up

- Requests (rather than requires) a written response from the firm within a reasonable amount of time

Warning Letter

- Gives individuals and firms an opportunity to take voluntary and prompt corrective action before initiation of an enforcement action
- Provides “Prior Notice” for other actions (e.g. court enforced)
- Describes violations of FD&C Act / 21 CFR
- Direct reference by ORA for GMPs
- Some require Center Concurrence – 501(k)/PMA, labeling/claims, novel technologies

- The use of Warning Letters and prior notice are based on the expectation that most individuals and firms will voluntarily comply with the law.

Administrative Actions

- Administrative Detention

- Civil Money Penalties

Administrative Detention

- Detain devices up to thirty calendar days if, during an inspection, the FDA has reason to believe the devices are adulterated or misbranded.
- Intent is to protect the public by preventing distribution or use of violative devices until FDA has had time to consider the appropriate action to take and, where appropriate, to initiate a regulatory action.
- The action of choice, in most cases, is a seizure.
- Appeal process available.

Civil Money Penalties

- Used to eliminate the profit from violative activity and/or provide non-compliant individuals or firms with the financial incentive to correct violations

Judicial Actions

- SEIZURE – vs. “the product”

- INJUNCTION – vs. “the behavior & individuals”
- PROSECUTION – vs. “the individual”

Product Seizure

- United States (as plaintiff) files a complaint for forfeiture and warrant for arrest directing the US Marshall to seize the article (the defendant), which is in violation of the law.

- Used as a means to gain control over violative product

Injunction

- A civil process to stop or prevent violation of the law and to correct the conditions that caused the violations to occur
- Used when there is:
  - Current and definite health hazard requiring immediate action to stop the violations, OR
  - Significant amounts of product with recall refused and multiple seizures impractical, OR
  - Long-standing, chronic violations

Injunction

Injunctions are documented in a Consent Decree which:

- Establishes the court's jurisdiction
- Specifies the violative conduct to be ceased
- Provides for additional inspection authority
- Specifies other requirements (e.g., recall, product disposition, third party audits, provision for costs, etc.)

Prosecution

- A criminal action directed against the firm and/or responsible individuals
- A punitive action with view of punishing past behavior and obtaining future compliance
- For gross, flagrant, or intentional violations, fraud, or danger to health

Other: Recalls

- “Recall” for medical devices = a firm's **correction or removal** of product which would otherwise present a risk to health covered under Part 806
- **Correction** means the repair, modification, adjustment, relabeling, destruction, or inspection (including patient monitoring) of a device without its physical removal from its point of use to some other location.
- **Removal** means the physical removal of a device from its point of use to some other location for repair, modification, adjustment, relabeling, destruction, or inspection.

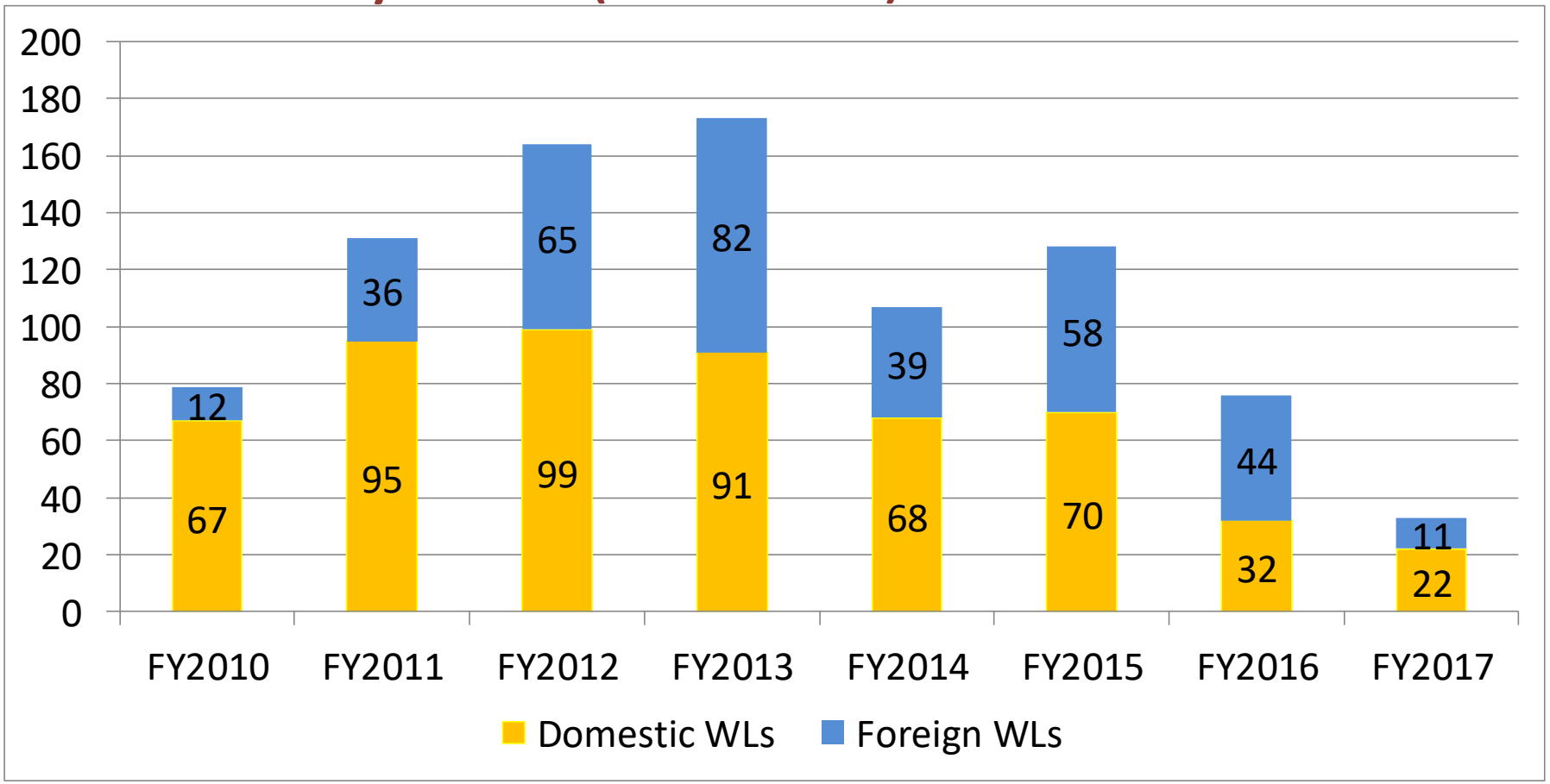
Other: Recalls

- Almost all recalls are voluntary, but FDA does have the authority to order recalls of food and devices under provisions in the FD&C Act.
- Recalls afford equal consumer protection but generally are more efficient and timely than formal administrative or judicial actions, especially when the product has been widely distributed.

Factors to Consider

- The Firm's compliance history
- The nature and impact of the violations
- The benefit & risk(s) associated with the product
- Documentation & adequacy of the firm's corrective action- systemic and effective
  - Ongoing or promised corrective action does not preclude the issuance of a Warning Letter or other regulatory action
  - Timeframe for the corrective actions
  - Ensures sustained compliance with the law or regulations

Domestic and Foreign WLs with Quality System (CFR 820) Citations



FY2018 Domestic Compliance Data

- Approximately 23 Warning Letters issued by ORA Device Field Compliance (OMDRHO issuing office)
- One injunction
- No seizures

FY2019 Domestic Compliance Data

- Approximately 18 Warning Letters issued by ORA Device Field Compliance to date (OMDRHO issuing office)
- No injunctions
- One seizure including devices from a multi-jurisdictional warehouse

*Data through 6/30/2019

*Furlough period: 12/22/2018 – 1/25/2019

Post Inspection Case Flow Example

- Inspectional Close Out/FDA 483(IB):

  - GMPs (on 483) and labeling evidence (discussed)

- FDA 483 response (Firm)

  - 15 business days and voluntary but your response may not be considered if not received within that timeframe

- Violations of the Act (CB)

  - GMPs causing adulteration

  - Labeling claims exceeding clearance: brochure, IFU, website, social media causing misbranding

Case Flow Example

- Regulatory Action - WL

- 15 business days response requested

Post-Regulatory Action

- Firm prepares response including corrective actions to WL
- Firm may decide to bring in a Consultant

- Firm works with CB providing timelines of systemic corrective actions

Case Flow Example

Post-Regulatory

- Re-inspection

- Other Potential Action
  - Regulatory meeting
  - 510(k) / Labeling status?

- The goal is always voluntary compliance

Optimizing Responses from Firm

- Address each observation/deficiency
- Comprehensive and accurate
- CAPA → Effectiveness check
- Consider risk to the patient
- Show evidence of correction and corrective actions
- Updated/revised SOPs, docs: show before & after versions, highlight changes, or provide revision history

Optimizing Responses from Firm

- Set realistic dates/provide timetable & meet timeframes
- Provide these documents to the email address provided
- Work with ORA Compliance Officer mentioned in the Advisory Action / letter received

Optimizing Responses from Firm

Things to remember:

- FDA can only verify using the records provided
- Provide documentation including procedures and a sample of records that demonstrate implementation of the correction
- Don’t forget training records!
- Opening a CAPA isn’t sufficient if further documented activities are not provided

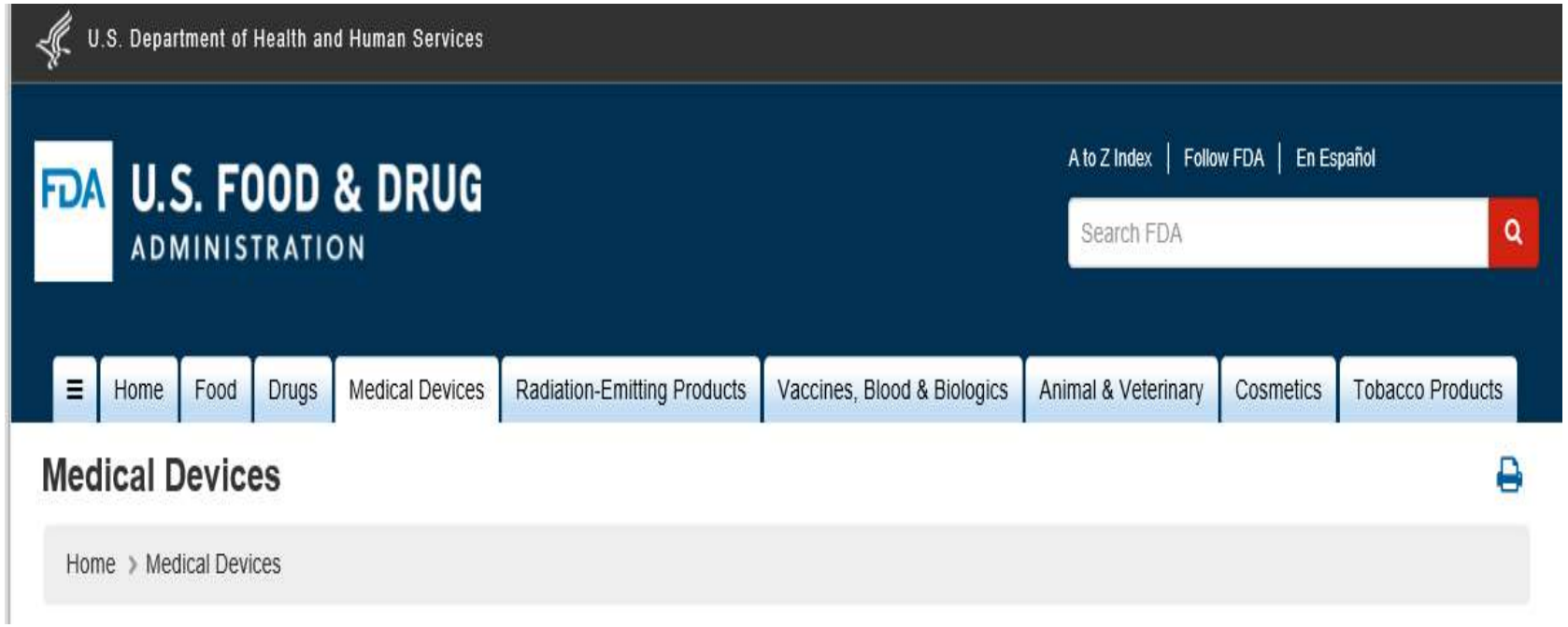
Optimizing Responses from Firm

Things to remember:

- Consider re-evaluating complaint rates at a reasonable timeframe after correction to assess adequacy
- If actions are planned, provide commitment dates
- Perform your own review cross cutting over various systems to determine how effective the correction was and provide that information to FDA to show your systemic correction

Resources to Know

Medical Devices (tab) at www.fda.gov



Device Resources

- Guidances http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/default.htm
- CDRH Learn http://www.fda.gov/Training/CDRHLearn/default.htm
- Device Advice http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/
- CDRH Small Business Contact DICE@fda.hhs.gov
- Ombudsman (e.g. dispute) ORAOmbudsman@fda.hhs.gov & CDRHOmbudsman@fda.hhs.gov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