Hogan Lovells

FDLI Introduction to Medical Device Law and Regulation

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Overview of Medical Device Law and Regulation

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Practices

Medical Device and Technology Regulatory

Education

J.D., Georgetown University Law Center, 2015

B.A., University of Virginia, 1998

With a background in biology and economics, Kristin Zielinski Duggan provides strategic advice to companies on scientific and U.S. Food and Drug Administration (FDA) regulatory challenges, while always keeping business needs in mind. For over 20 years, she has been counseling cutting-edge companies regarding the development and regulation of medical devices, pharmaceuticals, and combination products.

Kristin has a wealth of experience with the entire FDA regulatory process and agency interactions, from devising regulatory strategy for innovative products to pre-submission meetings; to assisting with preclinical and clinical programs and IDEs; to preparing regulatory submissions (510(k)s), de novo petitions and premarket approvals (PMAs); to appeals of agency decisions. Having prepared companies for dozens of advisory panel meetings over the years – including panel meetings to review 510(k) notices and PMAs, general issues panels, and classification panels – Kristin is a top thought leader in this area. She has been involved with all of the meetings of the Medical Devices Dispute Resolution Panel (MDDRP) to date.

Kristin also assists companies with compliance challenges, including 483 and Warning Letter responses, adverse events reporting, recalls, Department of Justice (DOJ) investigations, and product liability litigation, as well as with due diligence for investments and acquisitions.

Kristin's practice covers products in many therapeutic areas, including software products, cardiovascular products, orthopedic and gynecologic implants, plastic and reconstructive surgery devices, radiology devices, gastroenterology devices, wound care products, dental implants, endoscopes and minimally-invasive surgical solutions, and in vitro diagnostics.

Kristin previously served as Vice President for Strategic Consulting at a Washington, D.C.-based scientific consulting firm. Throughout her career, she has published and presented on various FDA regulatory issues. She is also an adjunct professor teaching an experiential seminar on FDA Regulation of Medical Products (Medical Devices, Drugs, and Biologics), which is part of the Executive Master of Science in Health Systems Administration (EMHSA) program at Georgetown University's School of Nursing and Health Studies.

Agenda

1 FDA Authority

2 Regulation as a Medical Device

3 Administrative Structure

4 Working with FDA


FDA Authority

Basic Legal History

- The Federal Food, Drug, & Cosmetic Act (FDCA), as amended, is the main law that governs medical devices
- 2006 - Food and Drug Administration (FDA) celebrated its 100th anniversary
- 1902 – Biologics Control Act required premarket license for biological products
  - A horse named “Jim” – used to create antibodies for diphtheria toxin – he got tetanus and 12 children died
- 1906 - President Teddy Roosevelt signed the Pure Food and Drugs Act (implemented by the Bureau of Chemistry under the U.S. Department of Agriculture)
  - Only enforcement, no premarket approval
- The Bureau, the oldest U.S. consumer protection office, eventually became the FDA under DHHS

FDA Authority - Statutes

- Federal Food, Drug, and Cosmetic Act of 1938 (FDCA)
  - Preceded by issue of toxic elixir sulfanilamide – 107 people died, many children
  - Provides for:
    - Premarket review of new drugs for safety
    - General oversight of medical devices
    - Inspection authority
    - Prohibited interstate shipment of misbranded/adulterated devices
    - Seizure, injunction, criminal penalties
- 1962 Drug Amendments
  - Preceded by thalidomide disaster (investigational drug only in U.S.)
  - Provided for:
    - Premarket review of drugs for both safety and effectiveness
      - Approval vs. notification
    - Required backward look at drugs that entered market between 1938-1962
    - No significant changes for devices
- Radiation Control for Health and Safety Act of 1968 (RCHS)
  - Radiation-emitting electronic products, device and not device
  - Reporting and record-keeping requirements and performance standards
  - Incorporated now into the FDCA §§ 531-542

FDA Authority - Statutes (cont.)

- 1976 Medical Device Amendments
  - Risk-based device classification process
    - Class I – Least risk
    - Class II – Intermediate
    - Class III – Highest risk
  - Premarket review of certain devices
    - Premarket notification – 510(k) Notification
      - "Substantial equivalence" to pre-1976 devices
    - Premarket approval – PMA
  - Postmarket Controls –
    - Establishment Registration
    - Device Listing
    - Medical Device Reporting (MDR)
    - Good Manufacturing Practices (GMPs)

FDA Authority - Statutes (cont.)

- Safe Medical Devices Act of 1990 (SMDA)
  - Definition of “substantial equivalence” for 510(k)
  - Added Reports of Corrections and Removals provision
  - Gave FDA mandatory recall authority
  - Added tracking and postmarket surveillance provisions
  - Authorized FDA to impose civil penalties for certain device-related violations
  - Required MDR reporting by user facilities
- Mammography Quality Standards Act of 1992 (MQSA)
  - Required all mammography facilities to be federally certified
  - Required certified facilities to undergo annual inspections by federal or state inspectors

FDA Authority - Statutes (cont.)

- Food and Drug Administration Modernization Act of 1997 (FDAMA)
  - Codified “least burdensome” principle for premarket review data requirements
  - Exempted most Class I devices from premarket review
  - “De novo” or “risk-based” classification – for low-risk devices classified as class III because they were found “not substantially equivalent” (NSE) to any identifiable predicate device.
  - Permitted accredited third-parties to conduct initial premarket review for certain devices
  - Eliminated automatic nature of tracking and postmarket surveillance requirements
  - Codified the “practice of medicine” principle for devices

FDA Authority - Statutes (cont.)

- Medical Device User Fee and Modernization Act of 2002 (MDUFMA)
  - User fees for premarket submissions
  - New regulatory requirements for “reprocessing” devices
  - Established Office of Combination Products
  - Permitted electronic labeling
- Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (Bioterrorism Act)
  - Designed to improve the ability of the United States to prevent, prepare for, and respond to bioterrorism and other public health emergencies
  - FDA responsible for carrying out provisions involving protection of the food supply and drug supply
    - Annual registration of foreign manufacturers shipping into the U.S.
- Medicare Modernization Act of 2003
- Project Bioshield Act of 2004
  - Medical products for use in emergencies

FDA Authority - Statutes (cont.)

- Food and Drug Administration Amendments Act of 2007 (FDAAA)
  - Clinical trial registration and results reporting required for devices
  - Reauthorization of user fees - reduction in some fees and addition of others
  - Pediatric device provisions
- Patient Protection and Affordable Care Act of 2010 (ACA)
  - "Obamacare"
  - Biosimilar approval pathway established
  - Excise tax on medical devices (2.3%) (IRS rule)

FDA Authority - Statutes (cont.)

- Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA)
  - Reauthorized and amended the device user fee provisions
    - Substantive Interaction time
    - Total Time to Decision
  - Amended criteria for granting or denying investigational device exemptions (IDE)
  - Granted authority for clinical hold on an IDE study
  - Provisions on documentation and review of "significant decisions"
  - Provisions relating to device modifications for 510(k) devices; required withdrawal of draft guidance
  - Modified De Novo reclassification process to allow Direct De Novo
  - Authorized reclassification of devices by administrative order
  - Deadlines for Unique Device Identification (UDI) rule
  - Amendments regarding Humanitarian Device Exemption (HDE), Custom Devices, Health Information Technology, and more
- Pandemic and All-Hazards Preparedness Reauthorization Act of 2013 (PAHPRA)
  - Emergency Use Authorization

FDA Authority - Statutes (cont.)

- 21st Century Cures Act (2016)
  - Humanitarian Device Exemptions
  - Least Burdensome Device Review
  - Clarifying Medical Software Regulation
  - Combination Products Innovation
  - Additional device provisions
    - 510(k) exemptions—periodic review
    - Advisory panel procedures for classification, membership
    - Central versus local IRB review of multicenter studies
    - 1 year deadline to revise CLIA waiver guidance
    - Guidance on device modifications to be finalized
    - List of reusable devices where 510(k) is required to include cleaning information
    - Regulation of accessories based on intended use (not classification of parent device)
- Food and Drug Administration Reauthorization Act (FDARA) (2017)
  - Revise and extend the user fee programs for human drugs, biologics, generic drugs, medical devices, and biosimilar biological products

Additional FDA Authority: Code of Federal Regulations (CFR)

- Regulations
  - Issued by FDA under rulemaking authority granted by Congress
  - Implement or interpret provisions of the FDCA
  - Specific FDCA provisions direct FDA to issue certain regulations
- FDA general rulemaking authority: § 701(a):
  - The authority to promulgate regulations for the efficient enforcement of this Act, except as otherwise provided in this section, is hereby vested in the Secretary.
- Procedures for rulemaking in Administrative Procedure Act (APA), 5 U.S.C. §§ 551-559
- Federal regulations have the force of law
  - Are binding on FDA and the public
  - Penalties for violations

Code of Federal Regulations

- Promulgating Regulations
  - Rulemaking process:
    - Formal rulemaking: “on the record” rulemaking
    - Informal rulemaking: notice and comment
    - Direct Final Rule
    - Tentative Final Rule
- Federal Register notice
  - Text of the regulation
  - Preamble
    - Text explaining proposed rules
    - Text accompanying final rule that responds to public comments

Title	Volume	Chapter	Browse Parts	Regulatory Entity
Title 21 Food and Drugs	1	I	1-99	FOOD AND DRUG ADMINISTRATION, DEPARTMENT OF HEALTH AND HUMAN SERVICES
	2		100-169	
	3		170-199	
	4		200-299	
	5		300-499	
	6		500-599	
	7		600-799	
	8		800-1299	
	9	II	1300-1399	DRUG ENFORCEMENT ADMINISTRATION, DEPARTMENT OF JUSTICE
		III	1400-1499	OFFICE OF NATIONAL DRUG CONTROL POLICY

Code of Federal Regulations (CFR)

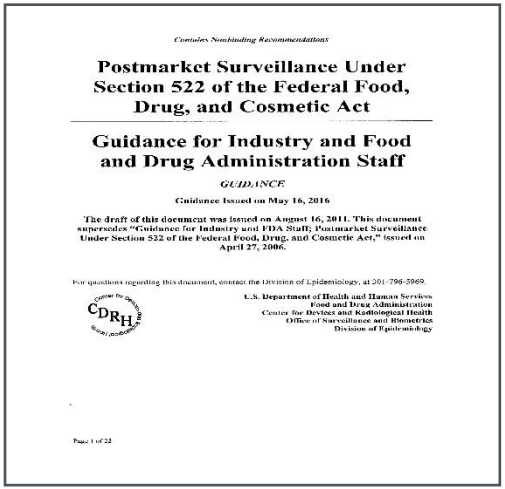
- 21 C.F.R. Parts 800-899
  - 801: Labeling
  - 803: Medical device reporting
  - 806: Reports of corrections and removals
  - 807: Registration and listing
  - 808: Preemption of state law
  - 810: Recalls
  - 812: IDEs
  - 814: Premarket approval
  - 820: QSRs
  - 822: Postmarket surveillance
  - 860: Classification procedures
  - 862-892: Classifications for devices of various types

Code of Federal Regulations (CFR) – Radiological Health

- 21 C.F.R. Parts 1000-1050
  - Records and Reports
  - Notification of defects or failure to comply
  - Repurchase, repair, or replacement of electronic products
  - Importation of electronic products
  - Performance Standards
    - General
    - Microwave and Radiofrequency
    - Lasers
    - Sunlamps
    - Sonic, infrasonic, ultrasonic

Additional Authority: Guidance

- Guidance Documents
  - Documents prepared for FDA staff, applicants/sponsors, and the public that describe FDA's interpretation of or policy on a regulatory issue
  - Constitute FDA's "current thinking" on a topic
    - Recommendations
    - Not legally binding on FDA or industry
  - Dissemination governed by "Good Guidance Practices," 21 C.F.R. § 10.115
    - Typically issued in draft
    - Comment period
- Shift from rulemaking to guidance documents



Contains Nonbinding Recommendations

Postmarket Surveillance Under Section 522 of the Federal Food, Drug, and Cosmetic Act

Guidance for Industry and Food and Drug Administration Staff

GUIDANCE

Guidance Issued on May 16, 2016

The draft of this document was issued on August 16, 2011. This document supersedes "Guidance for Industry and FDA Staff; Postmarket Surveillance Under Section 522 of the Federal Food, Drug, and Cosmetic Act," issued on April 27, 2006.

For questions regarding this document, contact the Division of Epidemiology, at 301-796-5969.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Office of Surveillance and Biometrics
Division of Epidemiology

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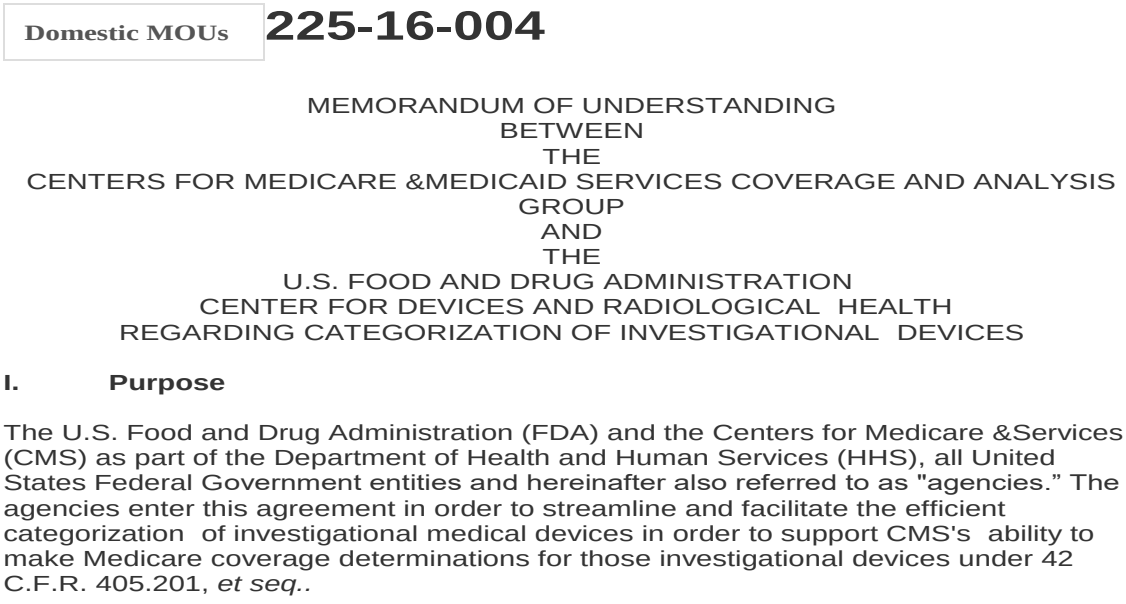
Additional Authority (cont.)

- FDA Regulatory Procedures Manual (RPM)
  - Reference manual for FDA personnel
  - Internal procedures for regulatory and enforcement matters
  - No force of law and not binding
- Compliance Policy Guides (CPGs)
  - Explain FDA policy on regulatory issues related to FDA laws or regulations
  - Advise field inspection/compliance staff on FDA standards and procedures to be applied when determining industry compliance
  - May derive from a request for an advisory opinion, from a petition from outside the Agency, or from a perceived need for a policy clarification by FDA personnel

Additional Authority (cont.)

- Memorandum of Understanding (MOU)
  - E.g., FDA-CMS parallel premarket review
  - E.g., FDA-CMS investigational device categorization



Domestic MOUs **225-16-004**

MEMORANDUM OF UNDERSTANDING
BETWEEN
THE
CENTERS FOR MEDICARE &MEDICAID SERVICES COVERAGE AND ANALYSIS GROUP
AND
THE
U.S. FOOD AND DRUG ADMINISTRATION
CENTER FOR DEVICES AND RADIOLOGICAL HEALTH
REGARDING CATEGORIZATION OF INVESTIGATIONAL DEVICES

I. Purpose

The U.S. Food and Drug Administration (FDA) and the Centers for Medicare &Services (CMS) as part of the Department of Health and Human Services (HHS), all United States Federal Government entities and hereinafter also referred to as "agencies." The agencies enter this agreement in order to streamline and facilitate the efficient categorization of investigational medical devices in order to support CMS's ability to make Medicare coverage determinations for those investigational devices under 42 C.F.R. 405.201, *et seq.*.

Additional Authority (cont.)

- Letters to Industry
  - FDA provides information to the industry
  - FDA requests information from a company (e.g., inquiring about potential violation of the FDCA)
- Other
  - Warning letters and untitled letters
  - Safety Communications and other publicity
  - Speeches and other public statements
  - FDA website
- Case law


Regulation as a Device -
Definition of a Device

What Is a “Device”?

Definition of a “Device”

- If a product is labeled, promoted or used in a manner that meets the definition in 201(h) of the Federal Food Drug & Cosmetic (FD&C) Act it will be regulated by FDA as a “medical device” and is subject to premarketing and postmarketing regulatory controls.

- Definition is:
  - “an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent . . . including a component part, or accessory which is”:
    - recognized in the official National Formulary, or the U.S. Pharmacopoeia, or any supplement to them,
    - intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or
    - intended to affect the structure or any function of the body . . . which is not dependent upon being metabolized for the achievement of any of its primary intended purposes.”

Definition of a “Device”

- Type of Product
  - Instrument, machine, implement, apparatus, contrivance
  - Implant
  - In vitro reagent
  - “Any component, part, or accessory”
  - Software
    - Accessory to another device
    - Freestanding
- Intended Use
  - Diagnosis of disease or other conditions
  - Cure, mitigation, treatment, or prevention of disease
  - Affect the structure or any function of the body
- Mechanism of Action
  - Does not achieve its primary intended purposes through chemical action within or on the body, and
  - Is not dependent upon being metabolized for the achievement of its primary intended purposes

21st Century Cures Modifies Device Description

- Modified statutory definition to exclude:

Administrative Software	Health and Wellness	Electronic Health Records	MDDS + Functionality	Clinical Decision Support
Examples •Billing •Scheduling	Must be unrelated to medical purposes	If created by a healthcare provider, and fits within the Health IT certification under section 3001(c)(5) of the Public 20 Health Service Act No analysis functions	Includes lab data and "findings" by a healthcare professional and associated "background information"	Must be transparent and not intended to be the sole basis for a determination. Not analyzing laboratory, imaging or sensor data.

Device Classification

- FDA classifies devices into Class I, Class II, or Class III, depending upon their risk and novelty
- FDA has classified and described approximately 1,700 generic types of devices, and categorized them into 16 medical specialties (panels)
  - Clinical Chemistry & Clinical Toxicology
  - Hematology & Pathology
  - Immunology & Microbiology
  - Anesthesiology
  - Cardiovascular
  - Dental
  - Ear, Nose, and Throat
  - Gastroenterology-urology
  - General & Plastic Surgery
  - General Hospital & Personal Use
  - Neurological
  - Obstetrical & Gynecological
  - Ophthalmic
  - Orthopedic
  - Physical Medicine
  - Radiology

Other Products Regulated by CDRH

- Radiological Products
  - Lasers, sunlamps, etc.
  - Might or might not also be medical devices

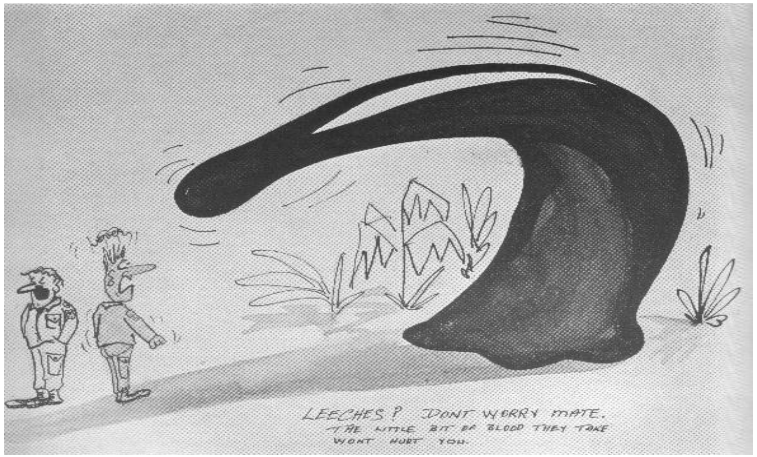
- Combination Products
  - Device/Drug
  - Device/Biological Product
  - Device/Drug/Biologic
  - Device + Device ≠ Combination Product

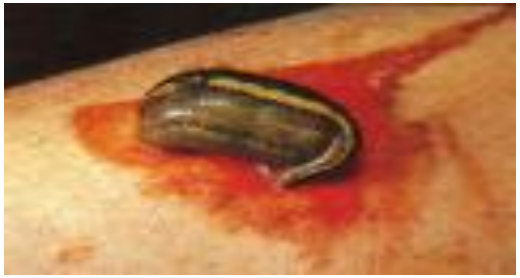
Some Devices Are Regulated by the Center for Biologics (CBER)

- Products regulated as devices
  - Product is reviewed under the device provisions of the FDCA
  - Generally applies to:
    - Products used in the collection and processing of blood (e.g., blood bank software)
    - In vitro diagnostic devices used to test for the presence of substances that are considered to be biologics (e.g., viruses -- HIV diagnostic tests)
- Products licensed as biological products
  - Generally applies to products to test the blood supply (e.g., to test blood for blood type or for HIV, HCV)

Is this a Medical Device?

Leeches





When Does A Product Become A Medical Device?

- A single product could be either regulated or unregulated depending on intended use:
- Examples:
  - **Heart Rate Monitor** –
    - Regulated – monitor patient health
    - Unregulated – use in fitness
  - **Pulse Oximeter** –
    - Regulated – evaluate oxygen saturation for medical condition
    - Unregulated - use by mountain climbers

“Enforcement Discretion” – Low-Risk Devices

- FDA can exercise discretion and refrain from enforcement of requirements to register & list, gain premarket clearance, comply with QSR, etc.

- Examples:
  - Guidance document on mobile medical applications (certain types of applications)
  - Draft guidance on general wellness products

Software and Mobile Medical Apps

- Freestanding software can be a “device” that is subject to FDA clearance/approval
- Mobile apps are being released that can be used in medical diagnosis, storage of data from a device, storage of digital images, storage of personal health information, etc.
- FDA has issued a guidance document describing when a mobile app will be considered a “mobile medical app”
  - Modifications to the MMA guidance due to 21st Century Cures were published in a separate guidance
- Some mobile medical apps subject to FDA regulation; some subject to FDA “enforcement discretion”
- http://www.fda.gov/medicaldevices/digitalhealth/mobilemedicalapplications/default.htm

FDA Mobile Medical Applications Guidance

- Examples:

Not a Medical Device

- Generic tools like magnifying glass or notes application
- Reference texts
- *Tracking and trending health data for patient's use*

Medical Device, but "Subject to Enforcement Discretion"

- Automate simple tasks for health care providers
- Video games for physical therapy
- *Remote display of ICU bedside monitoring data*

** Italics signifies changes due to 21st Century Cures*

Actively Regulated Medical Device

- Motion sensor for sleep apnea
- Radiation therapy dose calculation
- Remote display of ICU bedside monitoring data

FDA General Wellness Guidance

- Enforcement discretion for two categories of products intended only for general wellness:
  - Maintaining or encouraging a general state of health or a healthy activity (*now excluded by statute*)
  - Associates healthy lifestyle with helping to reduce the risk or impact of a disease/condition
- Only low-risk products - cannot be invasive, pose a risk to user safety, raise novel questions of usability, or raise questions of biocompatibility
- Examples:
  - Product X plays music to relax an individual and "manage stress," without reference to anxiety disorders or any other disease/condition;
  - Software Product Y tracks caloric intake and helps users manage an eating plan to maintain a healthy weight and balanced diet, which may help in living well with high blood pressure and type 2 diabetes;

Function-by-Function Approach to Digital Health Devices

- July 2020 FDA released final guidance: *Multiple Function Device Products: Policy and Considerations*
- FDCA regulates articles (e.g., drug, device) based on the intended use(s) of the article
  - 21st Century Cures directs FDA to regulate software **by function**
  - Article may have more than one "function," which could be the same as the intended use or a subset of the intended use
- For example, product may have multiple functions, some of which are device functions and some of which are not:
  - Intended use: predict and prevent heart attacks in at risk patients
  - Device functions: wearable sensor that measures physiological data to predict heart attack, alert patient, and recommend immediate actions
  - Non-device functions: diet recommendations; medication reminders; heart rate and activity tracking and trending; HCP communication portal
- FDA will focus review (and postmarket obligations) on regulated functions in an integrated product

Laboratory Developed Tests (LDTs)

- Laboratory testing services are regulated under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) by CMS
- FDA asserted in the 1990s that it could regulate laboratory-developed tests (LDTs) as "devices" – but would exercise enforcement discretion not to regulate LDTs and instead to leave them to regulation under CLIA
- In 2010, FDA announced its intention to begin regulating LDTs under device authorities, including premarket clearance/approval of the tests, and regulation of laboratories as "device manufacturers"
  - Clinical laboratories object to this FDA plan
  - Device manufacturers assert that their IVD products and laboratory-developed tests should be regulated on a "level playing field" – that both should be regulated by FDA
- FDA issued two draft guidance documents (October 2014) describing a risk-based Framework for LDT regulation by FDA
- Following November 2016 election, FDA suspended efforts on LDT policy
- Legislation may yet be considered to address the issue of LDTs

Practice of Medicine Exception

- FDA does not regulate the practice of medicine
- Doctors can prescribe lawful drugs and devices for unapproved uses

Determining if Product Is a Device

- Research (competitors, regulations, guidance, FDA databases)
- Informal inquiries of FDA
- 513(g)

Regulation as a Device – Device Classification and Examples

Regulatory Basics: Classification

- Began prior to 1976, concluded a decade later
- Reviewed all devices on the market at the time of enactment, MDA
- Expert panel recommendation
- Final classification regulation

Regulatory Basics: Pre-amendments Devices

- Devices in commercial distribution on or before May 28, 1976
- Grandfather status
  - 510(k) not required for classes I, II
  - For class III devices, subject to 510(k) until FDA calls for PMA
  - Evidence of preamendment status

Class I Devices

- Low risk
- Examples: scalpel, tongue depressor, toothbrush
- Typically exempt from premarket review
- FDA can hold back some Class I devices for 510(k) – "Reserved devices"
- Subject to postmarket "general controls":
  - Prohibition against adulteration and misbranding
  - Registration and Listing
  - Quality System Regulation (GMPs)
  - MDR Reporting
  - Labeling
  - Reports of Corrections and Removals

Class II Devices

- Moderate risk, or higher-risk but well-known
- Examples: powered wheelchair, endoscope
- Typically subject to 510(k) premarket notification
- FDA has exempted some from 510(k)
- Subject to postmarket "general controls"
- May be subject to "Special Controls" – for example:
  - Guidance document
  - Special labeling requirements
  - Mandatory performance standards
  - Postmarket surveillance

Premarket Notification 510(k)

- Section 510(k) of the FDCA
- Show "substantial equivalence" of new device to a "predicate" device – §513(i) of the FDCA
  - Same intended use as predicate device; and
  - Either (a) Same technological characteristics as predicate; or (b) Different technological characteristics and does not raise different questions of safety and effectiveness
- "Predicate" Device
  - Pre-amendments device (pre-1976 Amendments)
  - Legally marketed class I or II device, whether exempt or 510(k)-cleared
  - A device that FDA has reclassified through de novo process
  - Class III device for which FDA has not yet called for PMA applications
  - Not a class III, PMA-approved device (unless down-classified)

Class III Devices

- High risk or novel
  - Implants
  - Life-supporting or life-sustaining devices
  - NSE determination is automatically Class III
- Examples: implantable defibrillator, cardiac ablation catheter, coronary stents
- Premarket approval application (PMA)
- Postmarket “general controls”
- Potentially subject to “conditions of approval”
  - Training of physicians
  - Postmarket surveillance
  - Postapproval study

Premarket Approval Application –"PMA"

- Data and information to provide "reasonable assurance" that the device is safe and effective for its intended use –
  - Labeling is key
  - Specific use and specific patient populations
  - Clinical data
- PMA must include: Device description, manufacturing process information, preclinical studies (bench, animal), clinical study data, software validation
- Commitment to post-approval conditions (e.g., postapproval study, registry)
- Restrictions on sale, distribution, or use (e.g., training, advertising)

Changing a Device's Classification

- "De novo" or "risk-based" classification
  - Created by FDAMA and amended by FDASIA
  - Allows for streamlined reclassification of low risk devices that have been "automatically" classified into Class III
  - Can petition for de novo after a "not substantially equivalent" decision following 510(k) review
  - Manufacturer can submit Direct De Novo (without first submitting 510(k)) where no predicate device

Changing a Device's Classification (cont.)

- Reclassification Proceeding
  - FDA may reclassify a device based upon "new information" about the device
  - Either on the agency's own initiative, or in response to a petition from an interested party
  - Reclassification previously required a notice-and-comment rulemaking and consultation with an advisory panel – lengthy process
  - FDASIA amendment authorized FDA to reclassify by an administrative order – streamlined process

Establishment Registration & Device Listing

- All establishments must register with FDA and must comply with listing requirements
- Adds to FDA inspection list
- Submitted electronically once per year, October 1 – December 31 (but FDA encourages ongoing updates)
  - $5,672 user fee for FY 2022
- Listing includes submission of:
  - The name and registration number of each establishment that performs a manufacturing operation on device
  - Proprietary name of device
  - Type of activity performed on device
  - Product codes (for 510(k) and PMA-exempt devices)
  - Premarket submission numbers if applicable

Quality System Regulations (QSR)

- Establishes basic requirements applicable to manufacturers of finished medical devices
- Applies regardless of where product was manufactured

  - Management responsibility
  - Quality Audits and Personnel
  - Design Controls and Document Controls
  - Purchasing controls
  - Identification and Traceability
  - Production and process controls
  - Inspection
  - Measuring and test equipment
  - Process validation
  - Receiving, in-process, and finished device
  - Acceptance actions
  - Labeling and packaging control
  - Handling, storage, distribution and installation
  - Recordkeeping
  - Servicing
  - Statistical Techniques

Medical Device Reporting (MDR)

- 21 CFR Part 803
- Mandatory requirements for manufacturers, importers, and device user facilities to report certain device-related adverse events
  - Deaths, serious injuries, and malfunctions
- Manufacturers and importers must submit reports to FDA electronically
- A "device user facility" is a hospital, ambulatory surgical facility, nursing home, outpatient diagnostic facility, or outpatient treatment facility, which is not a physician's office.
- Searchable MDR Database
  - https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMDR/Search.cfm (reports before July 31, 1996)
  - https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/Search.cfm (reports after July 31, 1996)

Breakthrough Devices Program

- The Breakthrough Devices Program is a voluntary program for medical devices that provide for **more effective** treatment or diagnosis of **life-threatening or irreversibly debilitating diseases or conditions**.
- The goal of the Breakthrough Devices Program is to provide patients and health care providers with timely access to these medical devices by speeding up their development, assessment, and review, while preserving the statutory standards for premarket approval, 510(k) clearance, and De Novo marketing authorization
- Breakthrough Designation request can be submitted any time prior to the marketing submission

Criteria	Description
First Criterion	The device provides for more effective treatment or diagnosis of life-threatening or irreversibly debilitating human disease or conditions
Second Criterion	The device also meets **at least one** of the following:
	a) Represents Breakthrough Technology
	b) No Approved or Cleared Alternatives Exist
	c) Offers Significant Advantages over Existing Approved or Cleared Alternatives
	d) Device Availability is in the Best Interest of Patients

Safer Technologies Program (STeP)

- The Safer Technologies Program (STeP) is a voluntary program for medical devices that are reasonably expected to significantly improve the **safety** of currently available treatments or diagnostics that target an underlying disease or condition associated with **morbidities and mortalities less serious than those eligible for the Breakthrough Devices Program**
- Has similar features to Breakthrough program:
  - Additional interaction mechanisms like sprint discussions and Data Development Plan review
  - Additional resources for IDE, PMA, etc.

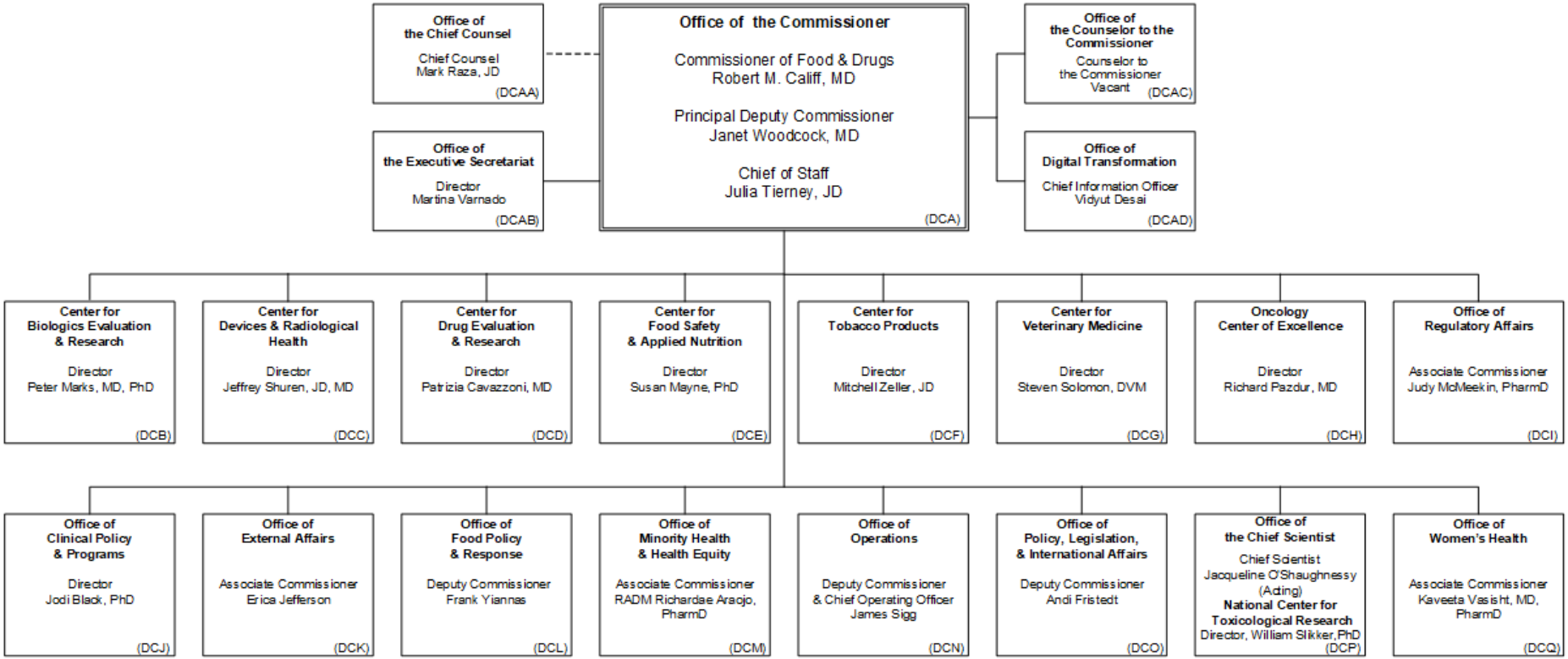
Criteria	Description
First Criterion	Not eligible for the Breakthrough Devices Program due to the less serious nature of the disease or condition treated, diagnosed, or prevented by the device
Second Criterion	Should be reasonably expected to significantly improve the benefit-risk profile of a treatment or diagnostic through substantial safety innovations that provide for **at least one** of the following:
	a) a reduction in the occurrence of a known serious adverse event
	b) a reduction in the occurrence of a known device failure mode
	c) a reduction in the occurrence of a known use-related hazard or use error
	d) an improvement in the safety of another device or intervention

Administrative Structure

HHS Organization

Department of Health and Human Services
Food and Drug Administration

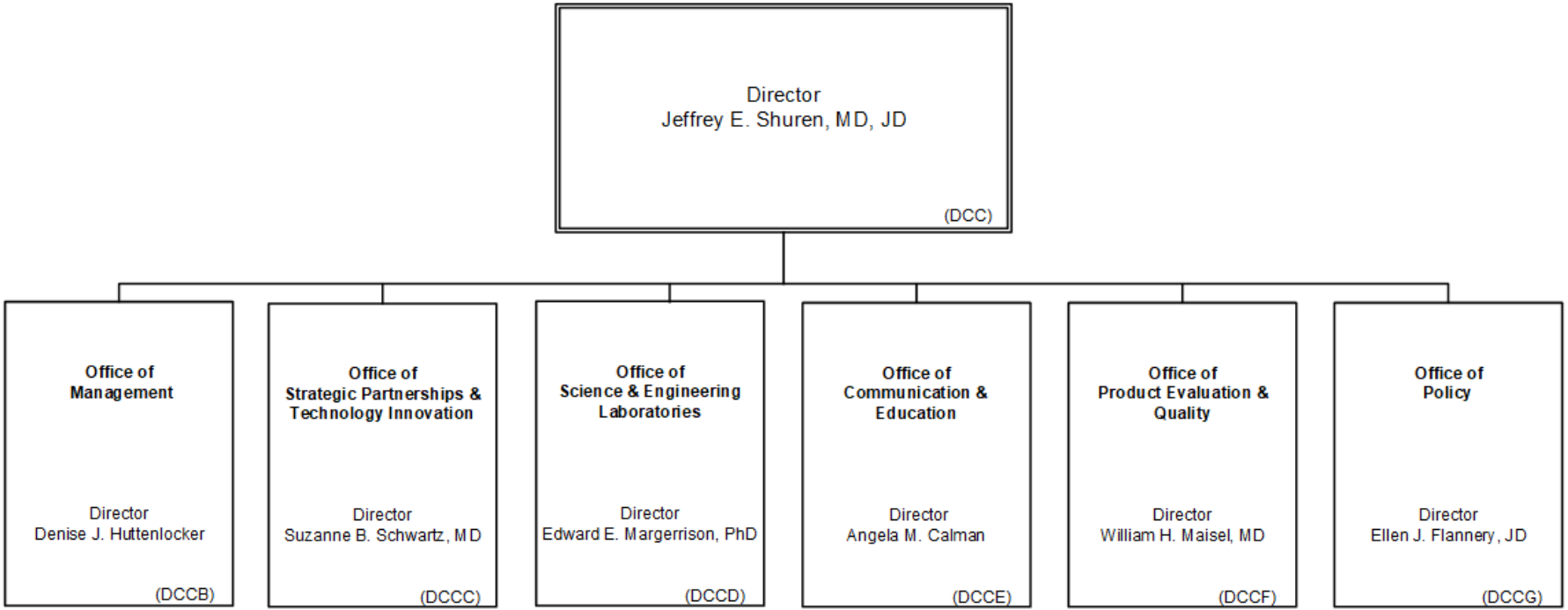
February 17, 2022



Legend:
- - - Direct report to DHHS General Counsel

June 2021

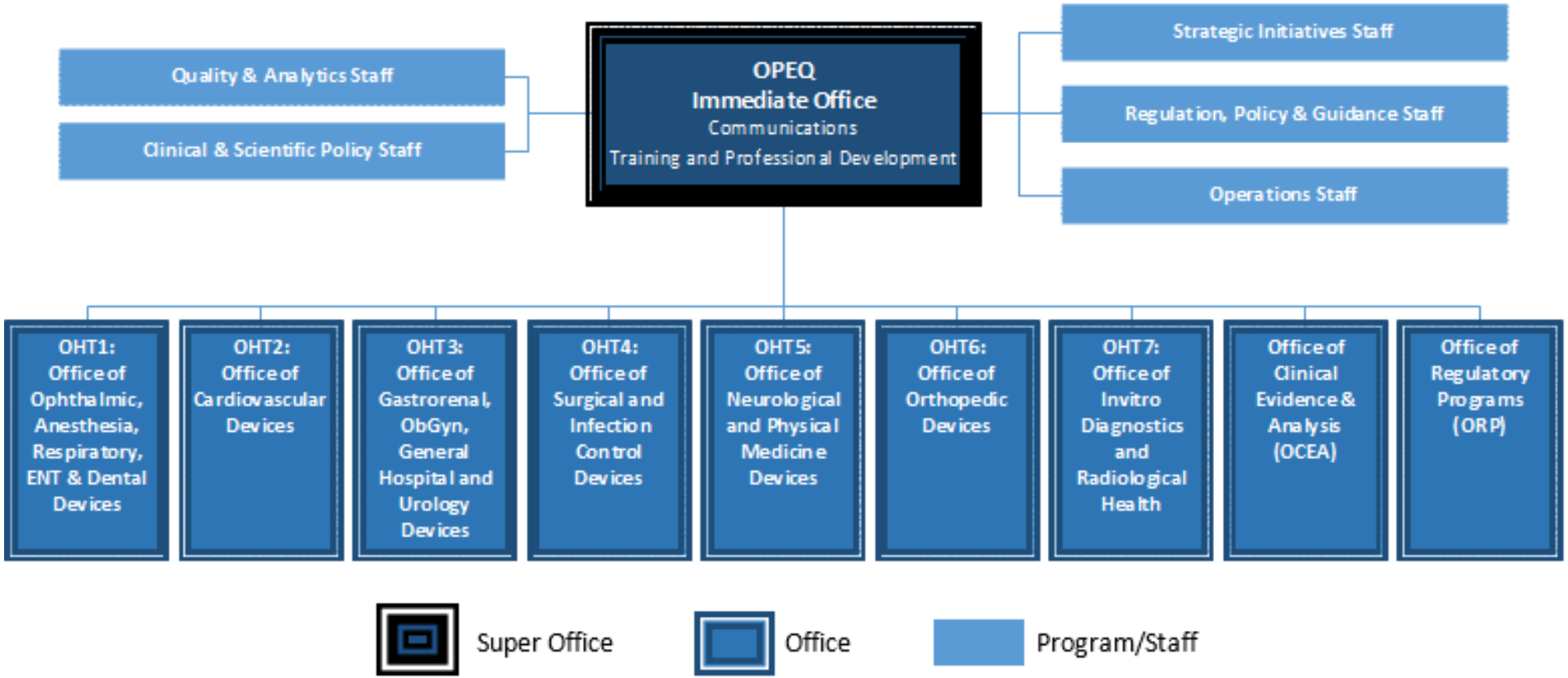
Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health



CDRH Reorganization

- **Established the Office of Product Evaluation and Quality (OPEQ)**
  - Combines the Office of Compliance, Office of Device Evaluation, Office of Surveillance and Biometrics, and the Office of In Vitro Diagnostics and Radiological Health
  - One super office focused on a Total Product Lifecycle approach to medical device oversight
  - Completed May 1, 2019
- **Established the Office of Policy**
  - Two teams, the Guidance, Legislation and Special Projects Team and the Regulatory Documents and Special Projects Team
  - Completed March 18, 2019
- **Established the Office of Strategic Partnerships and Technological Innovation**
  - Combines the Science & Strategic Partnerships, Digital Health, Standards, Health Informatics and Innovation teams
  - Completed March 18, 2019

CDRH OPEQ Organization



FDA Organization (cont.)

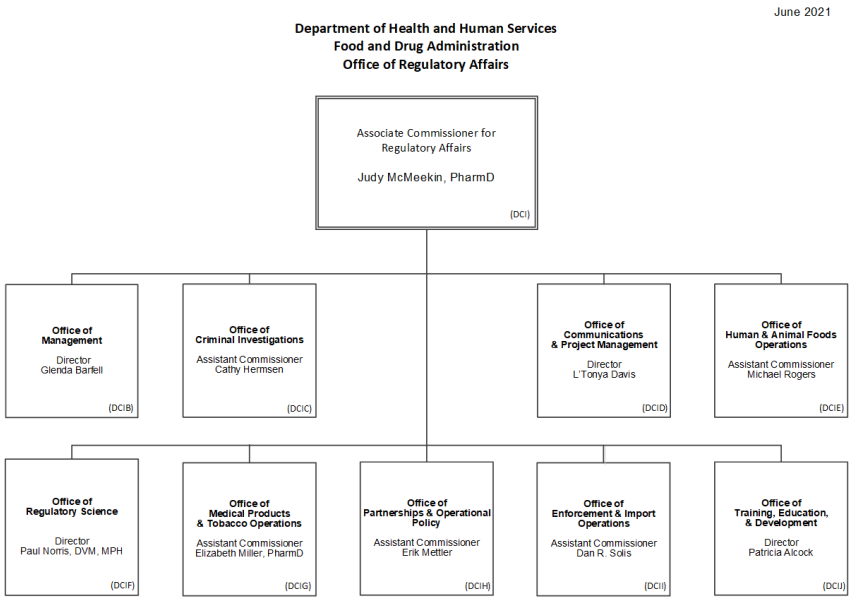
- Office of Combination Products
  - Focal point for combination product issues for agency reviewers and industry
  - Receives Request for Designation (RFD) submissions from industry and helps resolve jurisdictional questions
  - Assigns an FDA center to have primary jurisdiction for review of both combination products and single entity products where the jurisdiction is unclear or in dispute
  - Responsible for timely and effective premarket review of combination products by overseeing and coordinating reviews involving more than one agency center
  - Helps assure consistency and appropriateness of postmarket regulation of combination products
  - Develops guidance to clarify the regulation of combination products

FDA Organization (cont.)

- Office of Regulatory Affairs (ORA)
  - Lead office for all field activities of FDA
- Functions
  - Perform inspections
  - Collect samples
  - Analyze domestic/imported products
  - Initiate enforcement
  - Respond to emergencies
  - Work with state/local agencies to develop programs

Restructuring ORA

- Historical geography-based configuration moving to a program-based structure, aligning inspectors, compliance officers, and their managers into specialized programs within broader geographical zones.
- Personnel now grouped into the following product-based categories



Office of Criminal Investigations

- Directs, plans, and develops criminal investigation activities in coordination with other Agency components and with other Federal, State, and local law enforcement agencies
- Initiates and conducts criminal investigations under all statutes administered by FDA
- Provides recommendations to the Office of Chief Counsel on referrals of criminal cases to the Department of Justice for further investigation and/or prosecution, or directly to the U.S. Attorney when such direct reference is authorized
- Develops, reviews, and approves training programs for FDA's criminal investigators and related personnel
- Participates in Grand Jury investigations and serves as agents of the Grand Jury

The Enforcement Landscape

FDA

FEDERAL TRADE COMMISSION
FOR THE CONSUMER

Federal
Communications
Commission

Device Companies


Working with FDA

Seeking Guidance from FDA

- Non-binding views of FDA employees
  - "Best judgment" of employee
  - Does not bind FDA (per 21 C.F.R. § 10.85 (k))
- Meetings
  - Pre-Submission meeting
  - Formal Premarket Determination or Agreement Meeting
  - Other Meetings
- Formal opinion
  - FDCA § 513(g) – 513(g) Opinion on Classification
  - 21 C.F.R. § 10.30 - Citizen Petition
  - 21 C.F.R. § 10.85 - Advisory Opinion
- Appeals

What Companies Seek from FDA

- Predictability
  - Requirements
  - Timeframe
- Consistency and precedents
- “Level Playing Field”
  - Equal treatment
    - Compliance Burden
    - Enforcement Action (“Example” vs. “Singled Out”)
  - Non-enforcement against competitors
    - “Why should I comply?”
    - Competitive disadvantage
  - FDA’s choice of informal vs. formal action
- Confidentiality

Do's and Don'ts

- Do's:
  - Plan your marketing strategy before meeting with FDA and ask if it is appropriate
  - Prepare well organized and easy to follow submissions
    - Highlight key issues
  - Follow FDA advice when receiving feedback from the agency
  - Work interactively with the review team
  - Respond to all FDA comments received during the review
  - Use FDA Guidance documents to best prepare your submissions

Do's and Don'ts

- Do's (cont.)
  - Respect the time reviewers at FDA need to do their work
  - Always make sure that your tone and demeanor are professional and courteous
  - Make sure your actions are consistent with your own priorities
  - Heed FDA timeframes for response to a request
  - Understand that FDA is the final arbiter on the interpretation of the regulations

Do’s and don’ts

- Don’ts:
  - Become argumentative.
  - Make promises to provide data in the future.
  - Go over the review team’s head if you are unhappy with a decision until you have explored all options to resolving the issue.


Thank you!