Overview of Medical Device Law and Regulation

McKenzie E. Cato
Hyman, Phelps & McNamara, P.C.
mcato@hpm.com

FDLI

Agenda

- Authority / Sources of Law
- Review of Key Statutes
- Regulation as a Medical Device
- Relevant FDA Offices and Other Agencies
- Appeals of FDA Decisions
- Working With FDA

Authority / Sources of Law

Statutes and Regulations

- **Laws / Statutes**
  - Legally binding
  - Executive/legislative branch
- **Regulations (implement laws)**
  - Issued by FDA (and other federal agencies)
  - Implementation of authority granted to the agency by statutes
  - Published in Federal Register
  - Codified in the Code of Federal Regulations (21 C.F.R.)

Case Law

- Courts may rule on questions of statutory interpretation or FDA authority
- These rulings become precedent for future cases within the court's jurisdiction

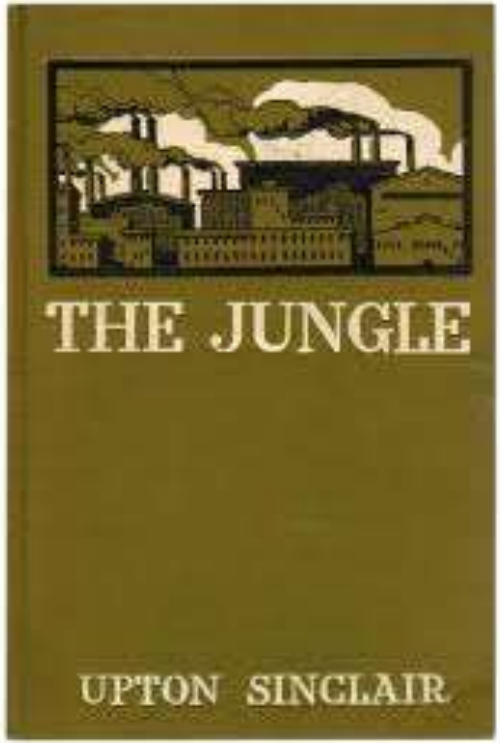
FDA Guidance and Policy

- **FDA Guidance Documents**
  - Represent FDA's current thinking on a topic (e.g., design, labeling, manufacturing, testing, processing, content and evaluation of submissions)
  - Non-binding
- **FDA Regulatory Procedures Manual (RPM)**
  - Reference manual for FDA personnel
  - Internal procedures for regulatory and enforcement matters
- **Compliance Policy Guides (CPGs)**
  - FDA compliance policy and regulatory action guidance for FDA staff on specific issues
- **Memoranda of Understanding (MOUs)**
  - Formal agreements between FDA and other federal, state, and local government agencies
  - FDA/CMS MOU regarding parallel review
- **FDA Website**

Review of Key Statutes

Pure Food and Drugs Act (1906)

- Prohibited adulterated and misbranded food, drinks, and drugs
- No requirement for premarket approval
- Political inspiration came partly from Upton Sinclair's The Jungle
- Attempts to change this law stalled until…



The Elixir Sulfanilamide Tragedy (1937)

- 107 people died from diethylene glycol ingestion from antifreeze that was used as solvent in a legally marketed sulfanilamide product manufactured by S.E. Massengill Company

Federal Food, Drug, and Cosmetic Act of 1938

- Premarket review of new drugs
- Inspection authority
- First law to address medical devices
  - Prohibited interstate shipment of misbranded/adulterated devices
  - No requirement for premarket review of devices
- Seizure, injunction, criminal penalties
- Gave FDA rulemaking authority

Radiation Control for Health and Safety Act of 1968

- Reporting and record-keeping requirements and performance standards for radiation-emitting "electronic products"
- Inspired by radiation leaking from TVs

1976 Medical Device Amendments

- Premarket Authority
  - Premarket notification and premarket approval for devices
  - Risk-based device classification process (Class I, II, III)
  - Registration and listing
- Postmarket Authority
  - Medical Device Reports (MDR)
  - Good manufacturing practices (GMPs)
  - Labeling
  - Banning devices
- Inspired in part by Dalkon Shield IUD causing major complications in approximately 90,000 women
- Still forms the basic structure of device regulation today

Safe Medical Devices Act of 1990

- Codified “substantial equivalence” for 510(k)
- Expanded FDA post-market regulation/enforcement
  - Device tracking
  - Reports of corrections/removals
  - New GMP requirements related to device design
  - Mandatory recall
  - Civil penalties
  - Required MDR reporting by user facilities
- Humanitarian Device Exemption

Mammography Quality Standards Act of 1992

- Required all mammography facilities to be federally certified
- Required certified facilities to undergo annual inspections by federal or state inspections

Food and Drug Administration Modernization Act of 1997

- Codified “least burdensome” concept for premarket review
- Exempted most Class I (low risk) devices from premarket review
- Permitted accredited third-parties to conduct initial premarket review for certain devices
- Codified the “practice of medicine” principle for medical devices
- Dispute resolution process

Food and Drug Administration Amendments Act of 2007

- Clinical trial registration and public results reporting required for devices
- Pediatric device provisions

Patient Protection and Affordable Care Act – 2010

- Imposed a 2.3% excise tax on medical devices
- Was in effect briefly (two suspensions)
- Permanently repealed December 2019

FDA Safety and Innovation Act of 2012

- FDA may not refuse to approve an Investigational Device Exemption (IDE) based on PMA or 510(k) standards
- Required FDA to prepare scientific and regulatory rationale for significant review-related discussion
- Clinical hold authority
- Simplified *de novo* pathway (no requirement for a Not Substantially Equivalent decision)

21st Century Cures Act – 2016

- Established “breakthrough devices” program for accelerating access to devices that provide more effective treatment/diagnosis of life-threatening or debilitating disease
- Exempted several categories of software products from the definition of “device” (e.g., Medical Device Data Systems)

Medical Device User Fee Reauthorization Legislation

- Medical device user fees first established in 2002 by the Medical Device User Fee Modernization Act (MDUFMA)
- The user fees were renewed in: 2007 (MDUFA II), 2012 (MDUFA III), 2017 (MDUFA IV)
- On September 30, 2022, Congress passed a 5-year reauthorization of the MDUFA agreement (MDUFA V)
  - Will be in effect for fiscal years 2023 through 2027

Other Important Statutes

- Public Health Service Act
  - Certain human cell and tissue products are regulated under Section 361 of the PHS Act
  - Some human cell and tissue products are alternatively regulated as medical devices (e.g., if more than minimally manipulated)
- Administrative Procedure Act
  - Governs the process by which federal agencies develop regulations
  - Provides that federal agencies may not act in an arbitrary and capricious manner

Regulation as a Medical Device

Definition of Medical Device

- An "instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article…which is"
  - Recognized in the National Formulary or United States Pharmacopeia;
  - Intended for use in "diagnosis…or in the cure, mitigation, treatment, or prevention of disease"; OR
  - "[I]ntended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes"
- FDCA § 201(h)

Device or Not a Device?

- FDA has classified over 1700 distinct types of medical devices
- FDA has established procedures for obtaining information about classification and regulatory requirements for a device: 513(g) process

Device vs. Consumer Product

- Regulatory status depends on the "intended use" of the product
- Cotton balls and swabs ("Q-tip")
  - Consumer product: For applying make-up
  - Device: Applying medication to a body surface or absorbing body fluids
- Exercise equipment
  - Consumer product: For general health and fitness
  - Device: For rehabilitation of injuries
- Cell Phone/Mobile Apps
  - Consumer product: For communication purposes
  - Device: For use as a stethoscope

Gray Area Products

- Physical vs. chemical action
- Medical software
  - 21st Century Cures Act
- Wellness products
  - Exercise vs. rehabilitation
- Mobile medical applications
  - E.g., meditation apps for relaxation vs. apps for diagnosis or treatment of Generalized Anxiety Disorder

In Vitro Diagnostics

- IVDs are a subset of devices
- Defined in 21 C.F.R. § 809.3(a)
  - *In vitro diagnostic products* are those reagents, instruments, and systems intended for use in the diagnosis of disease or other conditions, including a determination of the state of health, in order to cure, mitigate, treat, or prevent disease or its sequelae. Such products are intended for use in the collection, preparation, and examination of specimens taken from the human body.

Types of IVDs

- Diagnostic
- Monitoring patients who have a disease
- Screening for disease
- Prediction of effect of drug
- Prognosis of disease outcome
- Companion diagnostic, to help decide what drug to administer

Laboratory-Developed Tests (LDTs)

- Tests designed, validated, and performed in a single laboratory
- FDA takes the position that LDTs are medical devices, but that it will generally exercise enforcement discretion
  - Exception: LDTs that FDA determines are high-risk or to address significant public health concerns
- VALID Act
  - If enacted, would create a regulatory framework for LDTs and other IVDs
  - Risk-based system for targeting FDA oversight

Practice of Medicine

- FDA does not regulate the practice of medicine.
- “Nothing in this chapter shall be construed to limit or interfere with the authority of a health care practitioner to prescribe or administer any legally marketed device to a patient for any condition or disease within a legitimate health care practitioner-patient relationship.”
  - FDC Act § 1006

Device Classification

- FDA classifies devices into Class I, Class II, or Class III, depending on their risk
- Classifications provide the global framework for device regulation

Class I

- Subject to “general controls”
  - Establishment Registration
  - Device Listing
  - Labeling
  - Medical Device Reports (MDRs)
  - Quality System Regulation (some)
  - Recall reporting
- Most (but not all) are 510(k)-exempt
- Examples: manual stethoscope, tongue depressors, arm slings

Class II

- Moderate-risk devices
- Most (but not all) require a 510(k)
- Subject to Quality System Regulation and other general controls
- May be subject to Special Controls
  - Special labeling requirements
  - Guidance documents
  - Performance standards
  - Post-market surveillance
- Examples: endoscopes, powered wheelchairs, infusion pumps

Class III

- General and Special Controls apply
- Requires Premarket Approval (PMA)
  - PMA is more involved and costly than a 510(k); substantial administrative burdens both before and after approval
  - PMA must demonstrate reasonable assurance of safety and effectiveness
- Examples: cardiac ablation catheters, coronary stents

Determining Classification

- FDA's classification of device types is codified in classification regulations (required by the Medical Device Amendments of 1976)
- When assessing the classification of a device, look to the classification regulations to see if it fits within an existing device type
- A new, unapproved device is Class III by default unless/until:
  - It meets the definition in a classification regulation for a Class I device type
  - It is found to be "substantially equivalent" to an appropriate "predicate device"
  - It is classified by FDA as Class II through a *de novo* application

Breakthrough Devices

- Voluntary program for certain medical devices and device-led combination products
- Goal: Provide patients and health care providers with timely access to breakthrough devices by:
  - Speeding up their development, assessment, and review
  - While preserving statutory standards for premarket approval, 510(k) clearance, de novo authorization

Breakthrough Criteria

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)

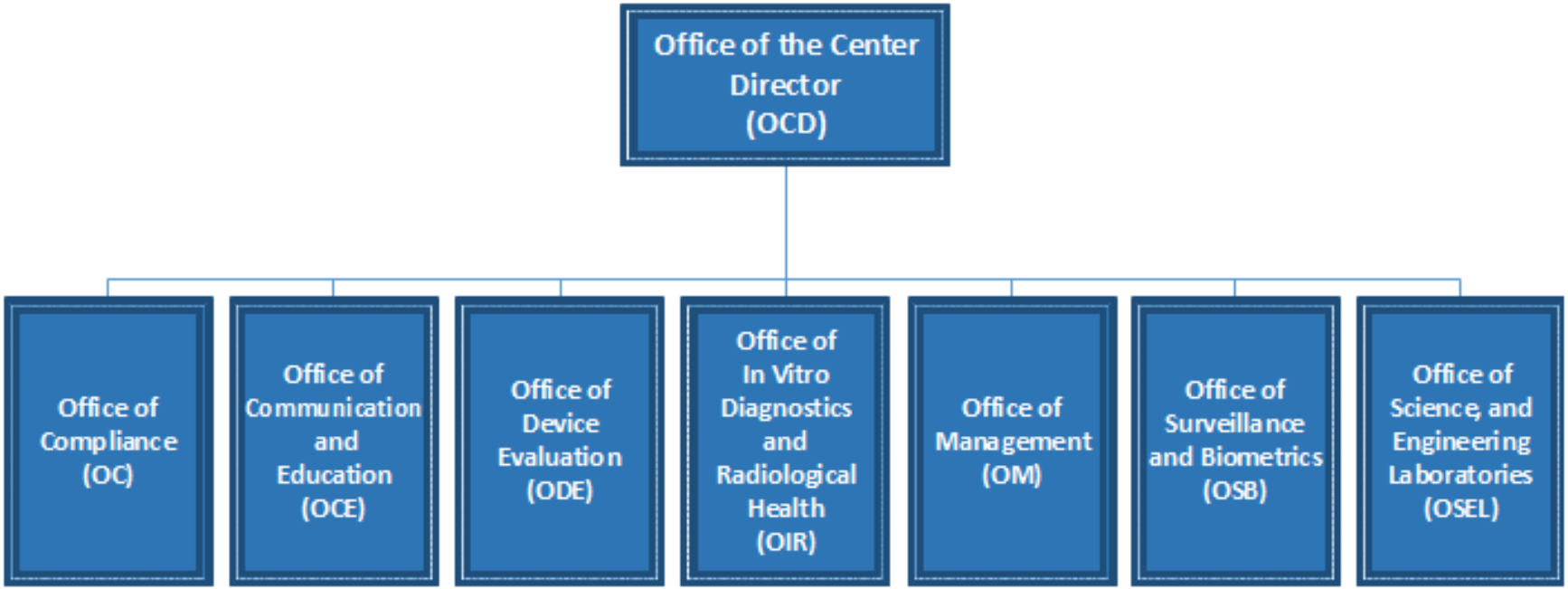
- Voluntary program for certain devices and device-led combination products that are reasonably expected to significantly improve the safety of currently available treatments/diagnostics
- Target diseases/conditions associated with morbidities and mortalities less serious than those eligible for the breakthrough program
- Benefits: Additional opportunities to interact with FDA's experts to address topics as they arise in the premarket review phase

SteP Criteria

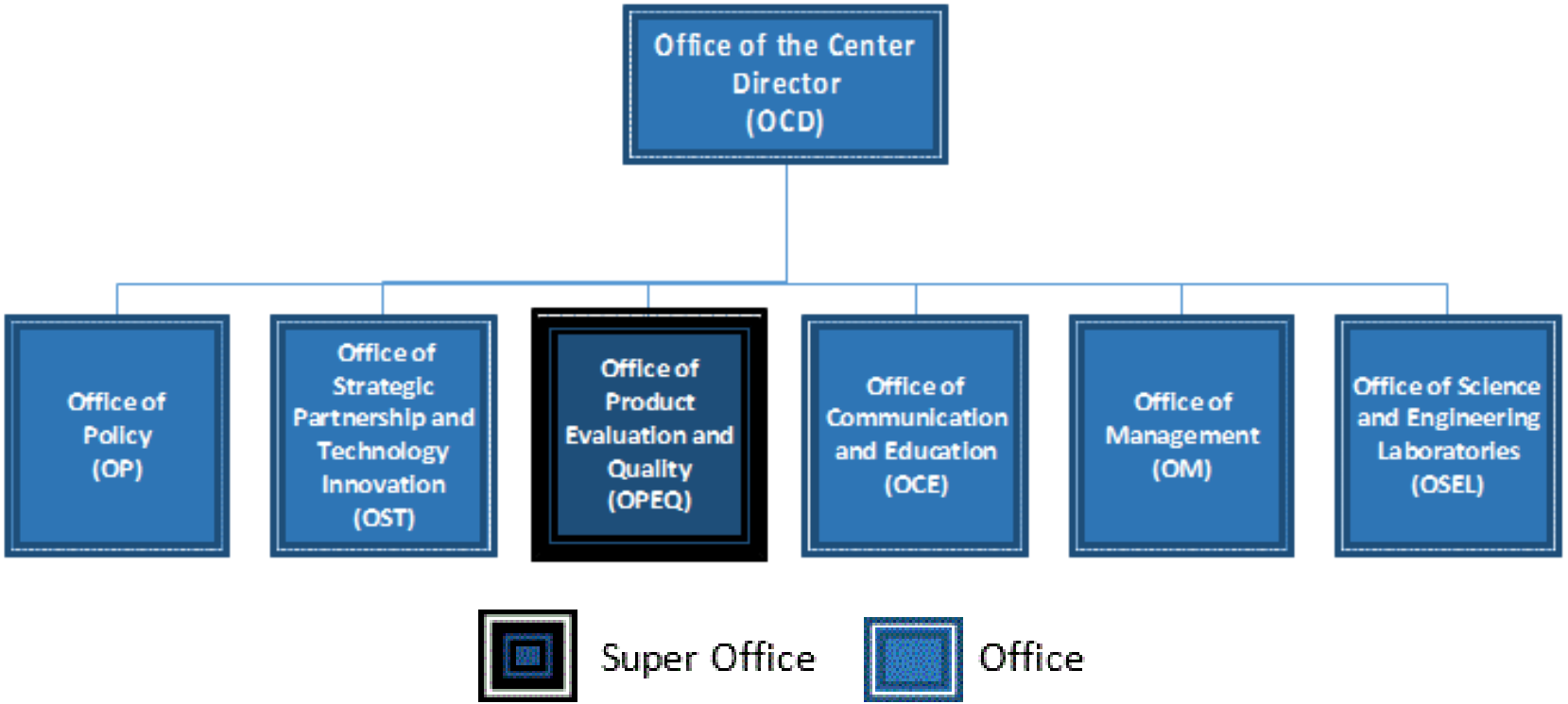
Criteria	Description
First Eligibility Factor	Not eligible for the Breakthrough Devices Program due to the less serious nature of the disease or condition treated, diagnosed, or prevented by the device
Second Eligibility Factor	Should be reasonably expected to significantly improve the benefit-risk profile 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

Relevant FDA Offices and Other Agencies

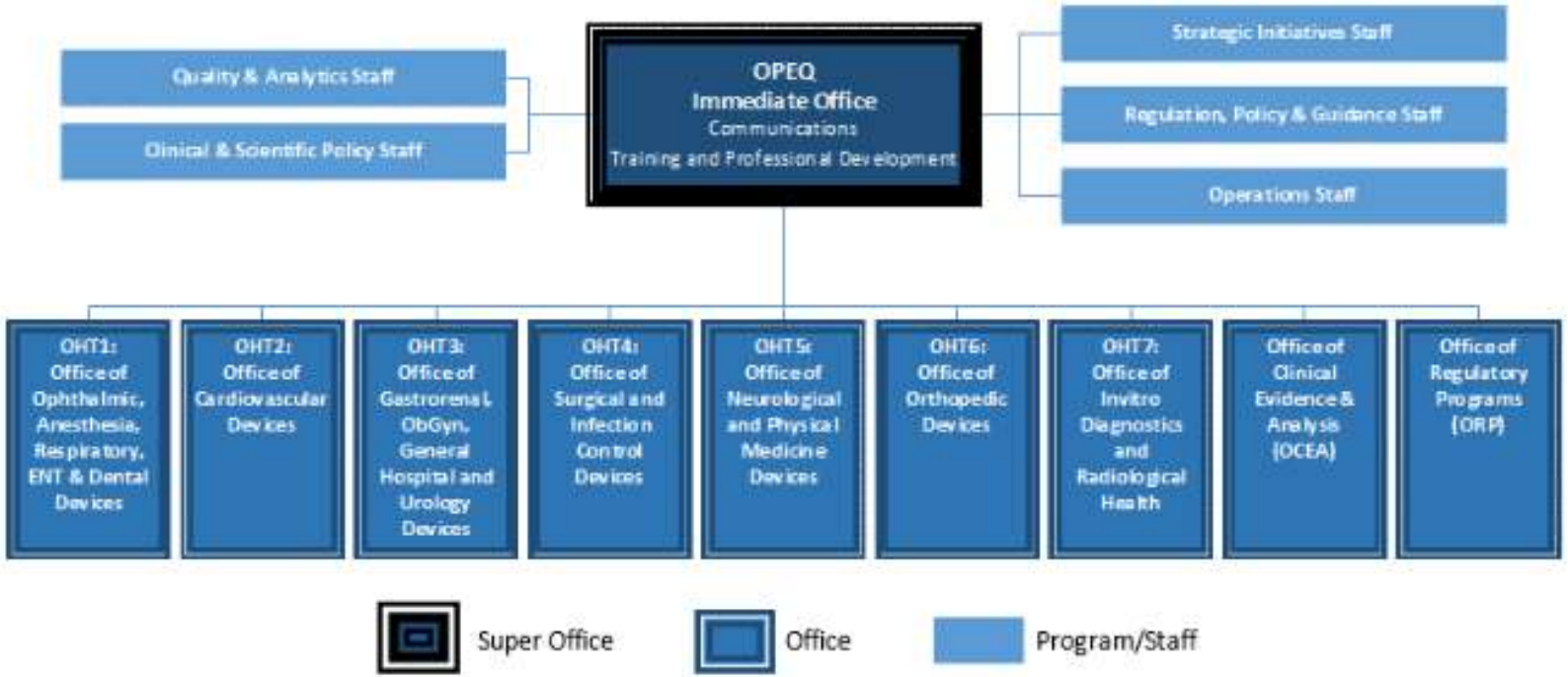
CDRH Reorganization: Original Structure (Pre-2019)



CDRH Reorganization: Current Structure



Office of Product Evaluation and Quality (OPEQ)



OPEQ Immediate Office

- Clinical and Scientific Policy Staff
  - Oversight and coordination for clinical review programs
  - Clinical expertise
- Quality and Analytics Staff
  - Oversee implementation of OPEQ quality management system
  - Ensure improvement of OPEQ policies/procedures
- Strategic Initiatives Staff
  - Drive strategic initiatives that cut across OPEQ offices
- Regulation, Policy and Guidance Staff
  - Provide advice and guidance to the OPEQ director on regulatory policies and guidelines
- Operations Staff
  - Human resource, travel, budget, facilities, and operational support

Office of Regulatory Programs

- Office within OPEQ responsible for developing policy and processes for core regulatory programs
- Divisions of Regulatory Programs (DRPs)
  - DRP1: Division of Submission Support
  - DRP2: Division of Establishment Support
  - DRP3: Division of Surveillance Support
  - DRP4: Division of Regulatory Systems, Tools, and Data Management

Office of Clinical Evidence and Analysis

- Office within OPEQ responsible for providing policy and program support regarding:
  - Clinical trials
  - Biostatistics
  - Real-world evidence
  - Epidemiological analysis
  - Outreach and collaboration with hospitals and other external stakeholders

Office of Science and Engineering Laboratories (OSEL)

- Scientists and engineers with a variety of expertise (e.g., microbiology, AI)
- Organized into approximately 20 program areas, running about 150 research projects through 4 main technical divisions:
  - Applied Mechanics
  - Biomedical Physics
  - Biology Chemistry and Materials Science
  - Imaging Diagnostics and Software Reliability
- Undertake regulatory research to accelerate access to innovative, safe and effective medical devices

Division of Industry and Consumer Education (DICE)

- Answers questions (by phone and email) from the medical device industry and consumers
- Develop educational resources for the FDA website to help the device industry understand FDA regulations and policies

Office of Regulatory Affairs (ORA)

- Lead office for all FDA field activities
- Inspects regulated products and manufacturers
- Reviews imported products offered for entry into the U.S.
- **Office of Medical Device and Radiological Health Operations (OMDRHO)**
  - Program Area of ORA's field operations dedicated to devices
- **Office of Criminal Investigations (OCI)**
  - FDA's criminal law enforcement arm
  - Conducts criminal investigations of illegal activities involving FDA-regulated products

FDA's Attorneys

- **FDA Office of the Chief Counsel (OCC)**
  - FDA division of the HHS Office of the General Counsel
  - Litigators, counselors, and support staff
  - Handle civil and criminal enforcement cases, defend challenges to FDA regulations, policies, and decisions
- **U.S. Department of Justice (DOJ)**
  - DOJ is responsible for prosecuting crimes that are investigated by FDA's OCI
  - **DOJ Consumer Protection Branch**:
    - Brings criminal and civil enforcement actions related to consumer health and safety (including medical devices)
    - Also defends FDA in civil litigation

Federal Trade Commission

- Prevents fraudulent, deceptive, and unfair business practices
- Regulates promotion and advertising of FDA-regulated products
- Promotional claims must be truthful, not misleading, and adequately substantiated with data
- Can take enforcement action against companies for unsubstantiated promotional claims

Federal Communications Commission

- The FCC can have some overlapping jurisdiction with FDA regarding:
  - Radiation-emitting products
  - Medical devices that incorporate wireless technology
  - Health information technology

State Involvement in Medical Device Regulation

- States, in addition to FDA, can regulate the manufacture and distribution of medical devices
- Many states require manufacturers and distributors to obtain licenses
  - Sometimes limited to in-state facilities
  - Sometimes required for out-of-state facilities that distribute devices in the state

Appeals of FDA Decisions

Supervisory Review (Appeals) 21 C.F.R. § 10.75

- (a) A decision of an FDA employee, other than the Commissioner, on a matter, is subject to review by the employee's supervisor under the following circumstances:
  - (1) At the request of the employee.
  - (2) On the initiative of the supervisor.
  - **(3) At the request of an interested person outside the agency.**
  - (4) As required by delegations of authority.

Supervisory Review (Appeals) 21 C.F.R. § 10.75

- (c) An interested person outside the agency may **request internal agency review of a decision** through the established agency channels of supervision or review. Personal review of these matters by center directors or the office of the Commissioner will occur for any of the following purposes:
  - (1) To **resolve an issue that cannot be resolved at lower levels** within the agency (e.g., between two parts of a center or other component of the agency, between two centers or other components of the agency, or between the agency and an interested person outside the agency).
  - (2) To **review policy matters** requiring the attention of center or agency management.
  - (3) In **unusual situations requiring an immediate review** in the public interest.
  - (4) As required by delegations of authority.

Supervisory Review (Appeals) 21 C.F.R. § 10.75

- (d) Internal agency review of a decision **must be based on the information in the administrative file**. If an interested person presents new information not in the file, the matter will be returned to the appropriate lower level in the agency for reevaluation based on the new information.

Examples of FDA Decisions that Can Be Appealed

- Requiring a PMA
- Issuing a not substantially equivalent (NSE) decision for a 510(k)
- Denying breakthrough designation
- Rejecting an investigation device exemption (IDE) application
- Designating a drug primary mode of action (combination product)

Supervisory Review Moves Up the Chain of Command

- *Example #1*:
  - 510(k) AI signed by Branch Chief → Division Director
- *Example #2*:
  - 510(k) NSE signed by Division Director → Director ODE/OIR
- *Example #3*:
  - RFD decision signed by Director of OCP → Associate Commissioner, Office of Special Medical Programs

Telescoped Appeals

- Rarely, appeal may skip a supervisory level to the next level
- Occurs when the signatory has already consulted with the supervisor, who is in agreement with the decision
- Could happen with a new policy question or complex scientific question
- Can be requested by the company appealing or telescoped by FDA on its own initiative

Deciding When to Appeal

- Context matters: product review vs. enforcement
- Helpful to find clear errors, not matters of judgment
  - If an issue of scientific judgment, the appeal is less likely to be successful
- May be better to answer FDA
  - Review team might be persuaded, making an appeal unnecessary

Final Appeals Guidance

- "Center for Devices and Radiological Health (CDRH) Appeals Processes" (March 2022)
  - Guidance provides general information about the various appeals processes available to individuals "who disagree with a decision or action taken by CDRH and wish to have it reviewed or reconsidered."
- "Center for Devices and Radiological Health Appeals Processes: Questions and Answers About 517A" (March 2020)
  - Shortened time frame for industry to appeal and for FDA to review "significant decisions" under 21 C.F.R. § 10.75, e.g., 30 days to appeal
  - Promise of quicker decisions makes appeals more attractive

Working With FDA

Reasons Device Companies Interact with FDA

- Getting information about regulatory requirements for a particular device
- Understanding regulatory requirements
- Resolving questions during FDA review of a 510(k), PMA, de novo, or IDE
- Responding to an enforcement action

Informal vs. Formal Interactions

- Company and FDA interactions may be more informal (e.g., phone call to lead reviewer)
- May also be formal interactions
  - Premarket submissions
  - Additional information requests and written responses
- Companies rely heavily on both informal and formal feedback received from FDA

Sources of Communication Issues

- Unclear communications leading to misunderstandings
- Inability or unwillingness to give guidance through informal means of communication
- Communication lapses due to changes in personnel
- Novel scientific issues or technology (lack of precedents)

Meetings

- Define the agenda
- Keep the goals focused
- Bring the right people
- Prepare and practice
- Anticipate FDA questions
- Keep good notes
  - Minutes will be the record of what happened
- Don’t talk too long