# Overview of Medical Device Law and Regulation

FDLI Introduction to Medical Device Law & Regulation

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FDLI

# Session Roadmap

- Sources of Law and Guidance
- Regulation as a Medical Device
- Organizational Structure and Other Agency Involvement

# I. Sources of Law and Guidance

# Sources -- Terminology

- Laws – Legally binding and enacted by the legislative branch
- Regulations – Legally binding and promulgated by the FDA
- FDA Guidance Documents – Non-binding and represents FDA's current thinking on a topic
- Case Law – Serves as precedent

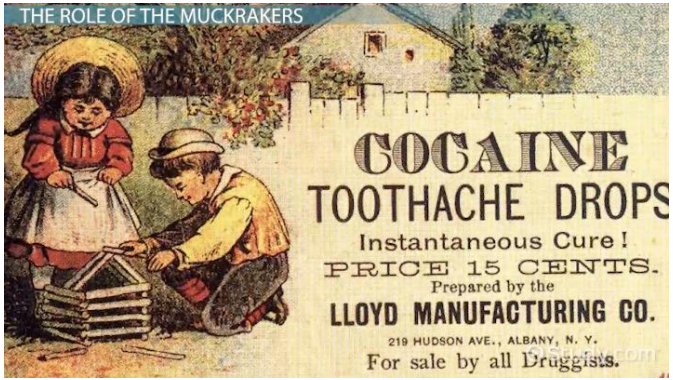
# Relevant Statutory Authority

## 1906 – Food and Drugs Act of 1906

*Created to prevent the "manufacture, sale, or transportation of adulterated or misbranded or poisonous or deleterious food, drugs, medications, and liquors..."*

## 1938 – Federal Food, Drug and Cosmetic Act

*Overhauled the public health system and strengthened FDA's regulatory authority*


# Key Amendments to the 1938 FDCA

## 1968 – Radiation Control for Health and Safety Act

*Authorized FDA's administration of a radiation control program*

## 1976 – Medical Device Amendments

*Enacted to ensure safety and effectiveness of medical devices*

## 1990 – Safe Medical Devices Act

*Expanded post-market regulation (e.g., tracing and post-market surveillance, adverse event reporting, mandatory recall authority) and defined substantial equivalence for purposes of 510(k) clearance*

## 1992 – Mammography Quality Standards Act

*Required accreditation and annual inspection of mammography facilities*

## 1997 – Food and Drug Administration Modernization Act

*Accelerated review of devices and regulated advertising of unapproved uses of approved drugs and devices*

## 2002 – Medical Device User Fee and Modernization Act

*Assessed fees as part of sponsors' medical device applications and established FDA's Office of Combination Products*

# Key Amendments to the 1938 FDCA

## 2007 – Food and Drug Administration Amendments Act

*Encouraged pediatric medical device research and added Unique Device Identification (UDI) system authority*

## 2012 – Food and Drug Safety and Innovation Act

*Expanded FDA's authority to collect user fees and promotes innovation to speed patient access to safe and effective products*

## 2016 – 21st Century Cures Act

*Further accelerated medical product development, established "Breakthrough Device" program, streamlined process for exempting devices from premarket notification requirement, and clarified regulation of digital health products*

## 2017 – Food and Drug Administration Reauthorization Act

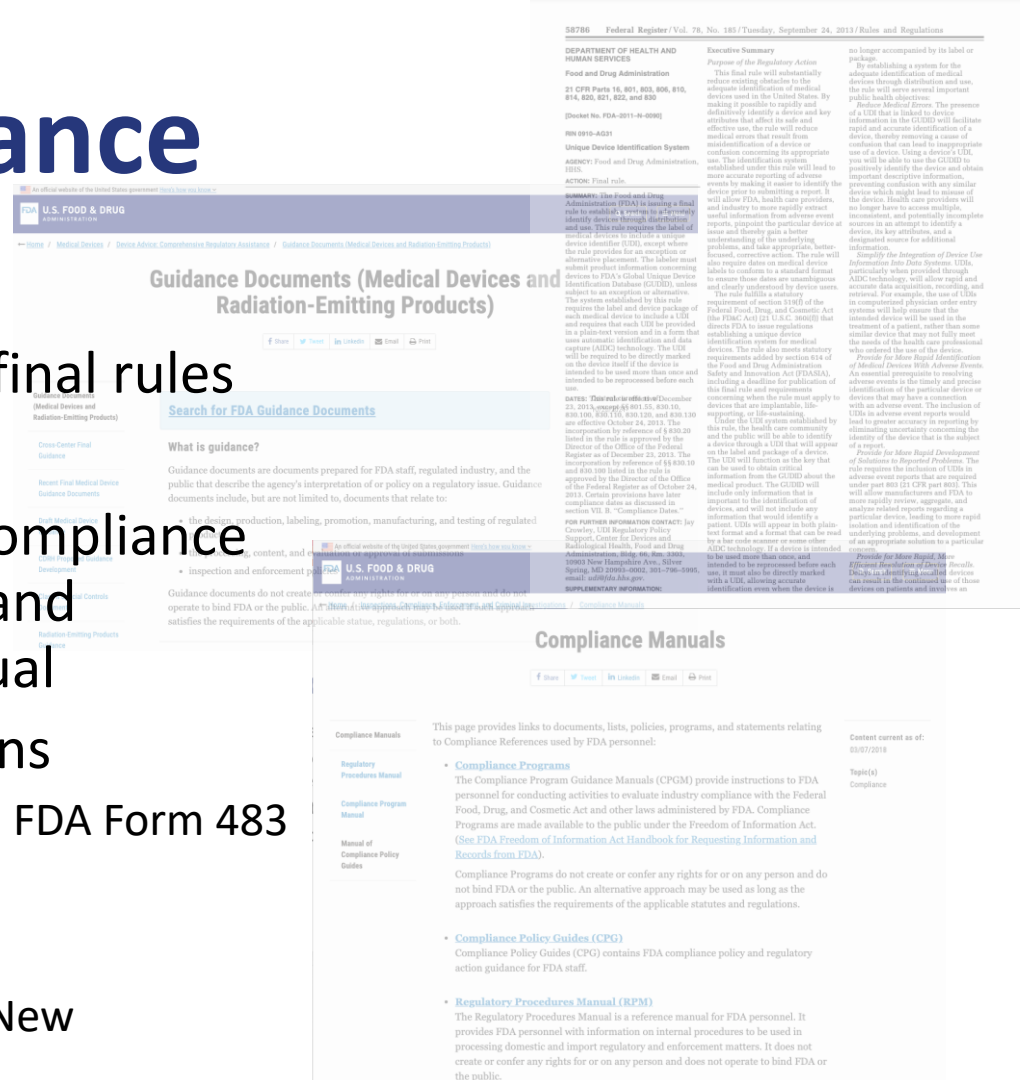
*Authorized risk-based inspection scheduling for device establishments and other process improvements and revised classification of device accessories vis-à-vis the parent device*

# Regulations

- Notice and Comment Rulemaking
- Final rules published in 21 Code of Federal Regulations (CFR)
- Selected device regulations in Title 21 of CFR:
  - Recalls (Part 7)
  - Labeling (Part 801)
  - Medical device reporting (Part 803)
  - Corrections and Removal reporting (Part 806)
  - Registration, listing, and 510(k) premarket notification (Part 807)
  - Investigational Device Exemption (Part 812)
  - Premarket Approval Applications (Part 814)
  - Quality System Regulation (Part 820)
  - Classification Regulations (Parts 862 to 892)

# Sources of Guidance

- FDA guidance documents
- Preambles to proposed and final rules
- Federal Register notices
- Compliance Policy Guides, Compliance Program Guidance Manual, and Regulatory Procedures Manual
- Prior FDA enforcement actions
  - Warning letters; Untitled letters; FDA Form 483 Observations; Recalls
- FDA website
  - Device Advice; Webinars; CDRHNew



# II. Regulation as a Medical Device

# II. Regulation as a Medical Device

- Definition of Device
- Device Classification and Examples
- Breakthrough Devices and the StEP Program
- Combination Products

# Definition of “Device”

“…an *instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory*, which is

A. recognized in the official National Formulary, or the United States Pharmacopeia, or any supplement to them,

***B.*** ***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

***C.*** ***intended 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. The term ”device” does not include software functions excluded pursuant to section 360j(o) of this title.”

21 USC § 321(h)

# Software Functions

The term "device," does not include –

- Software for administrative support of healthcare facilities;
- "Healthy lifestyle" software that provides no diagnostic, prevention, or treatment function;
- Certain electronic patient records; or
- Software for transferring, storing, or displaying medical device or clinical laboratory test data but that does not support interpretation or analyze clinical data.

21 USC 360j(o)(1)(A)-(D)

Whether software that provides clinical decision support (CDS) qualifies as a device depends on the context and the software's intended function. CDS software would not qualify as a device if it is –

- Not intended to acquire, process, or analyze medical images from an *in vitro* diagnostic or signal acquisition system;
- Intended to display, analyze, etc. medical information about a patient or other medical information;
- Intended to support or provide recommendations to a healthcare professional about prevention, diagnosis, or treatment of a disease or condition; **and**
- Intended to enable such healthcare professional to independently review the basis for a recommendation that the CDS software presents.

21 USC 360j(o)(1)(E)

# Other Gray Areas

- Physical versus chemical reaction
- Exercise versus rehabilitation
- Wellness products

# Intended Use

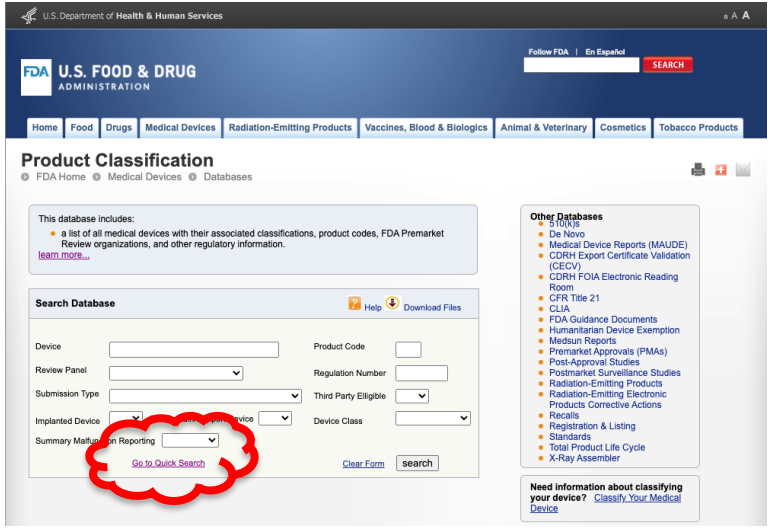
FDA may glean a product's intended use from:

- Manufacturer's explicit and implied claims made on the product's labeling, marketing materials, website, social media pages, etc.

Based upon a reasonable person standard

# Determining whether a product is a “device”

- Reference FDA’s Product Classification Database for existing product classifications
- Section 513(g) of FDCA:
  - Industry can request FDA’s views about classification and regulatory requirements applicable to a particular product
  - If product is a device, FDA will identify:
    - Applicable classification regulation
    - Class of device
    - What type of premarket review, if any, would be required
  - Decisions do not constitute FDA clearance or approval
- Pre-IDE Meeting



# Device Classification

Risk-based categorization that determines requirements:

**Class I (Lowest Risk)** – General Controls

**Class II (Medium Risk)** – General Controls + Special Controls (+ Premarket Clearance, unless exempt)

**Class III (Highest Risk)** – General Controls + Premarket Approval

- Devices intended for: life supporting or life sustaining uses; uses of substantial importance in preventing impairment of human health; or that present a potential unreasonable risk of illness or injury

Device types are classified by regulation. FDA has classified over 1,700 distinct types of medical devices (grouped into 16 medical specialties). *See* 21 CFR Parts 862-895.

# General and Special Controls

General controls applicable to all medical devices (unless exempt by regulation) include:

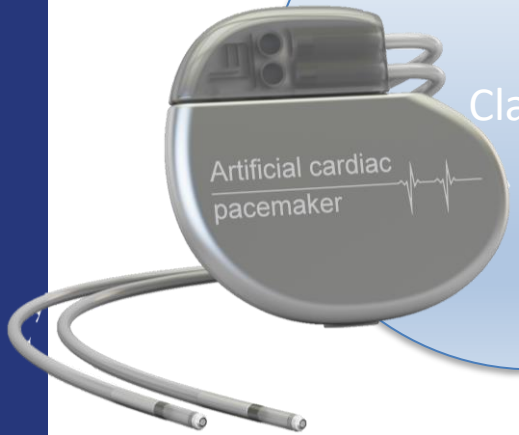
- Establishment registration, and Medical Device listing (21 CFR Part 807);
- Quality System (QS) regulation (21 CFR Part 820);
- Labeling Requirements (21 CFR Part 801);
- Medical Device Reporting (21 CFR Part 803);
- Premarket Notification (21 CFR Part 807);
- Reporting Corrections and Removals (21 CFR Part 806); and
- Investigational Device Exemption (IDE) requirements for clinical studies of investigational devices (21 CFR Part 812).

Special controls applicable to Class II devices might include certain performance standards, postmarket surveillance, patient registries, special labeling requirements, premarket data requirements, and FDA guidelines.

# Guess. That. Class!

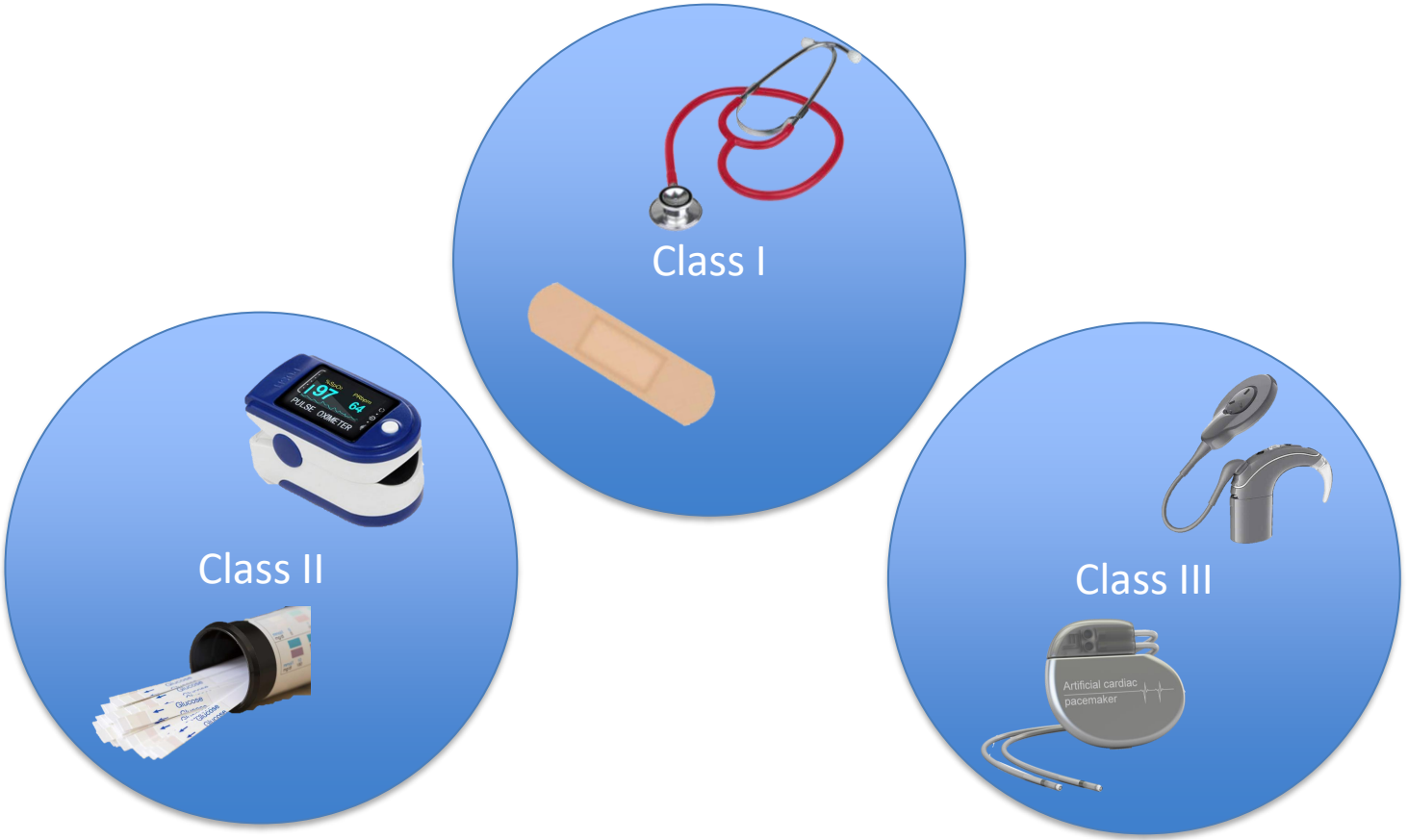
Class I


Class II




Class III

# Guess. That. Class!



# Reclassification Process

- FDA may on its own or in response to a petition change a device classification
- FDA may reclassify devices by administrative order rather than by regulation
- Order must be published in the Federal Register, after:
  - Publication of proposed reclassification order
  - Meeting of device reclassification panel
  - Consideration of public comments

# Premarket Review

**IN GENERAL**

Class I – exempt from premarket submission requirements (except Reserved Devices)

Class II – require premarket notification submission (510(k)) (“Cleared”)

- “Substantial equivalence” to a legally marketed device (predicate)
- Same intended use, and
  - Same technological characteristics; or
  - Different technological characteristics that do not raise different questions of safety/effectiveness
- Proxy for safety and effectiveness (as safe and as effective as a legally marketed device)

Class III – Premarket Approval (PMA) application (“Approved”)

- One or more adequate and well-controlled clinical investigations
- Reasonable assurance of safety and effectiveness
- Benefit-risk evaluation

# De Novo Classification Request

- De Novo request pathway is available for novel medical devices that pose a low- to – moderate-risk (such that general controls alone or with special controls can reasonably assure safety and effectiveness for intended use) but where no legally marketed predicate device exists

- Requested either following a not substantially equivalent (NSE) determination or as a “direct de novo” request

# In Vitro Diagnostics

- FDA considers in vitro diagnostics (IVDs) to be devices
- FDA defines IVDs as:
  - "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."
- About 50% of IVDs are Class I, 42% are Class II, and 8% are Class III

- Historically, FDA has exercised enforcement discretion for laboratory developed tests, a type of IVD test

# Examples of IVDs

Class I

- Most analyte specific reagents (ASRs)
- General purpose reagents (except in a Class II or III kit)
- General purpose laboratory equipment
- E.g.,: isocitric dehydrogenase test system; prolactin test system; chymotrypsin test system

Class II

- Some ASRs
- E.g.,: hemoglobin A2 Assay; sickle cell test; herpes simplex virus serological assays; methadone test system

Class III

- Some ASRs
- E.g.,: total prostate specific antigen (PSA); automated PAP smear readers; hepatitis C virus test

# Breakthrough Devices and the StEP Program

- Voluntary program for medical devices that:
  - provide for more effective treatment or diagnosis of life-threatening or irreversibly debilitating diseases (**Breakthrough Device Program**)
  - are reasonably expected to significantly improve the safety of currently available treatments or diagnostics that target underlying diseases less serious than those eligible for the Breakthrough Devices Program (**Safer Technologies program (StEP)**)
- Eligibility:

Breakthrough Device – must represent breakthrough technology; have no approved or cleared alternatives; offer significant advantages over existing approved or cleared alternatives; **or** be in patients' best interests to become available

StEP – must reduce the occurrence of a known serious adverse event; reduce the occurrence of a known device failure mode; reduce the occurrence of a known use-related hazard or use error; **or** improve the safety of another device or intervention

# Combination Products

*Drug + Device; Device + Biologic; Drug + Biologic; Drug + Biologic + Device*

- Comprised of two or more regulated components (drug, biologic, or device) that are physically, chemically, or otherwise combined

- Can take the form of:
  - A single entity
  - A co-packaged product
  - A cross-labeled product

# Examples of Combination Products

| | |
|---|---|
| **Single-entity combination product** | Device coated with a drug or biologic<br>• Drug-eluting stent<br>• Catheter with antimicrobial coating<br>• Condom with spermicide<br><br>Metered dose inhaler or prefilled syringe |
| **Co-packaged combination product** | Drug or vaccine vial packaged with delivery device (syringe)<br><br>A first-aid kit containing devices (bandages) and drugs (antibiotic ointments) |
| **Cross-labeled combination product** | Device and drug or biologic indicated for combined use (but not co-packaged)<br>• Ultrasound device and imaging drug<br>• Light-activated biologic labeled for use with a specific light source device |

# Combination Products: Lead Center

- FDA Office of Combination Products (OCP) serves as focal point for combination product and classification issues for FDA staff and industry
- Lead regulatory assignment depends upon "primary mode of action":

  *"the means by which a product achieves its intended therapeutic effect or action"*

  Device → CDRH; Drug → CDER; Biologic → CBER

- If PMOA is indeterminate, product is assigned to: the Center that regulates other products raising similar questions of safety and effectiveness, or if none, the Center with the most expertise related to the most significant safety and effectiveness questions presented by the product
- Lead Center has primary jurisdiction for premarket review and regulation
  - But FDA may use any agency resources it "deems necessary" to ensure safety and effectiveness
  - The non-PMOA Centers often collaborate or consult

# Combination Products: Formal Classification Determinations

- FDA Office of Combination Products (OCP) serves as focal point for combination product and classification issues for FDA staff and industry

- OCP handles Requests for Designation (RFD) of combination products
  - Sponsor submits a request to OCP for a determination of the regulatory identity of the product and the lead Center (21 CFR § 3.7; FDA Guidance)
  - RFD includes, among other things, the Sponsor's recommendation
  - FDA responds with a letter of designation, which is binding (as to the product described in the designation letter)
  - Sponsor can appeal with a Request for Reconsideration (RFR)

# Combination Products: Informal Classification Determinations

- Information Requests
  - Sponsor may engage with OCP in a “Pre-RFD” process

- Prior FDA determinations and OCP Guidance Documents
  - Prior determinations are not binding or determinative
  - Guidance, “Classification of Products as Drugs and Devices and Additional Product Classification Issues” (September 2017)
  - Intercenter agreements
  - RFD Jurisdictional Decisions, Jurisdictional Updates, Redacted RFD Decision Letters

# Regulation of Combination Products

- Drugs, devices, and biologics have different statutory and regulatory frameworks
- In general, as a legal theory, FDA has stated that all sets of relevant regulatory authorities apply to a combination product based on its constituent parts
- Thus, a combination product will be subject to at least two sets of legal authorities
- **BUT** FDA has attempted to streamline the process for compliance
  - One application that contains all information
  - Satisfying one set of authorities may be deemed to satisfy another

# Combination Products: CGMPs

- 21 CFR Part 4, Subpart A; FDA Guidance, Current Good Manufacturing Practice Requirements for Combination Products (Jan. 2017)

- Manufacturers of drug-device combination products can either:
  - Satisfy both sets of CGMP requirements; or
  - Satisfy one set, plus certain rules applicable to the other constituent part
    - Additional device requirements include: management responsibility, design controls, purchasing controls, corrective and preventive action, installation, and servicing
    - Additional drug requirements include: calculation of yield, tamper-evidence packaging requirements for OTC drugs, expiration dating, stability testing, and reserve samples

# Combination Products: Post-Marketing Safety Reporting

- 21 CFR Part 4, Subpart B. Post-marketing safety regulations distinguish reporting requirements between “combination product applicants” and “constituent part applicants”

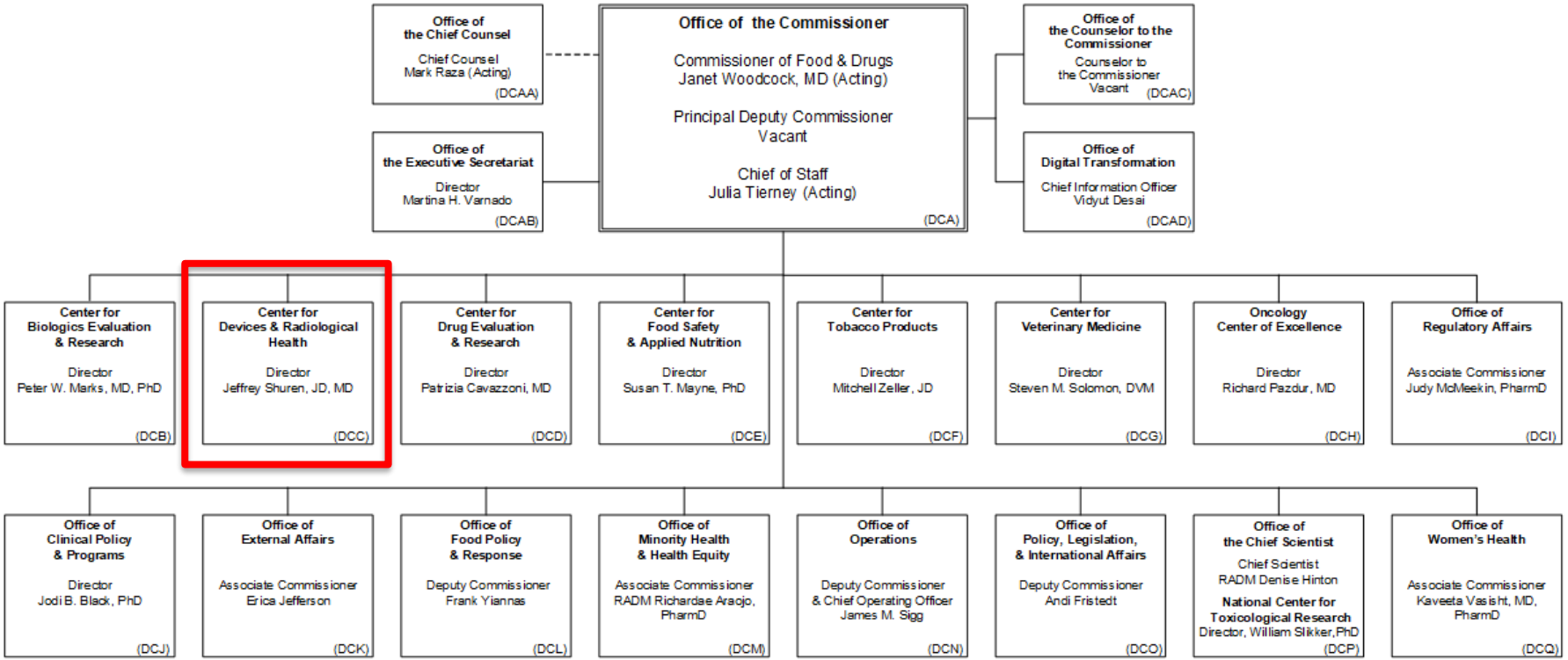
- Three basic duties:
  1. For both combination product applicants and constituent part applicants: reporting requirements associated with the application type (e.g., NDA, BLA, PMA, 510(k))
  2. For combination product applicants: specified, additional reporting requirements associated with any constituent parts
  3. For constituent part applicants: information-sharing requirements”

- Recordkeeping requirements

# III. Organizational Structure and Other Agency Involvement

**Department of Health and Human Services**
**Food and Drug Administration**

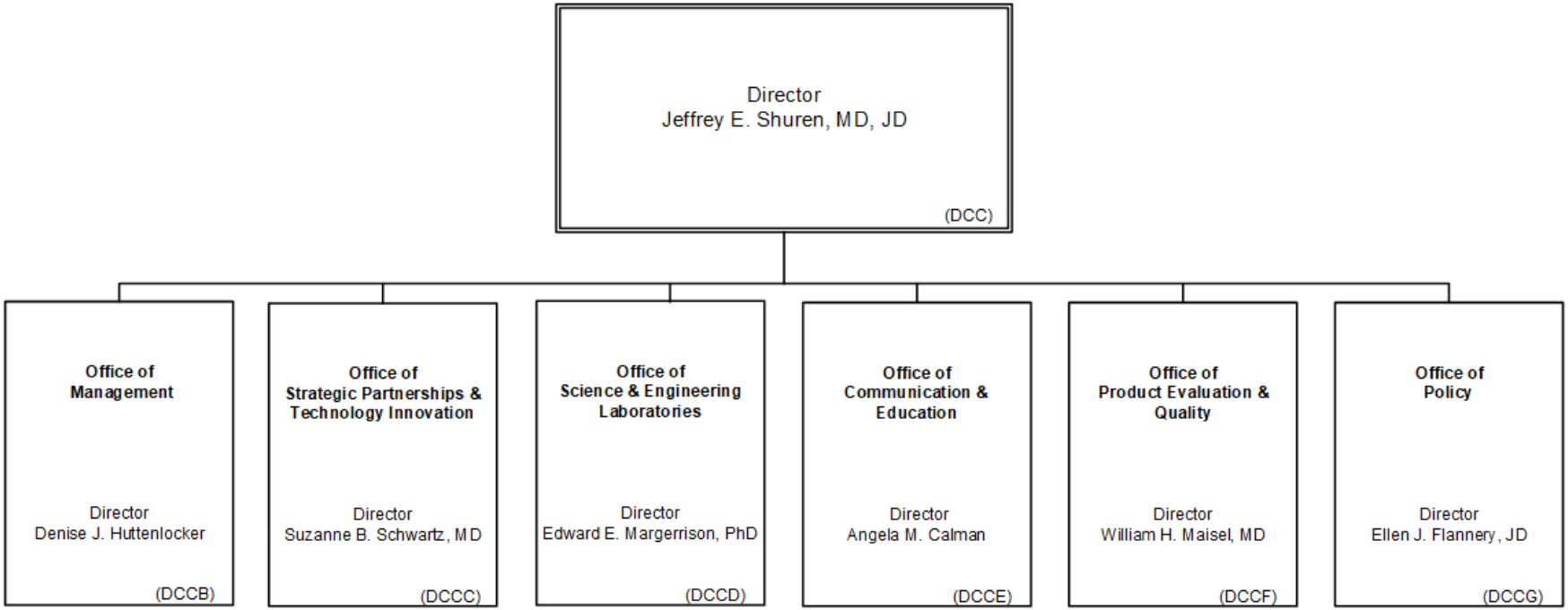
**November 1, 2021**




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 Management Directory by Organization

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**CDRH Offices**

Office of the Center Director

Office of Communication and Education

Office of Management

Office of Policy

Office of Product Evaluation and Quality

Office of Science and Engineering Laboratories

Office of Strategic Partnerships and Technology Innovation

*This information is current as of October 09, 2021*

## Office of the Center Director

| | | |
|---|---|---|
| **Center Director** | Jeffrey Shuren, M.D., J.D. | 301-796-5900 |
| Deputy Center Director for Science | Douglas Kelly, M.D. | 301-796-5900 |
| Deputy Center Director for Policy | Ellen Flannery, J.D. | 301-796-5900 |
| Associate Director for Scientific and Regulatory Programs | Elizabeth Hillebrenner | 301-796-5900 |
| Associate Director for International Affairs | Melissa Torres | 301-796-5576 |
| Associate Director for Strategic Communications | Nicole Ellis | 301-796-5900 |
| **Quality Management Staff** | | |
| Staff Director and Associate Director for Quality Management | Nancy Collazo-Braier, Ph.D. | 301-796-5676 |
| Assistant Director for Quality Management Systems | Olga Claudio, Ph.D. | 301-796-7601 |
| Assistant Director for Process Improvement | Cathy Oliveri | 301-796-5549 |

## Office of Communication and Education

## Office of Management

## Office of Policy

## Office of Product Evaluation and Quality

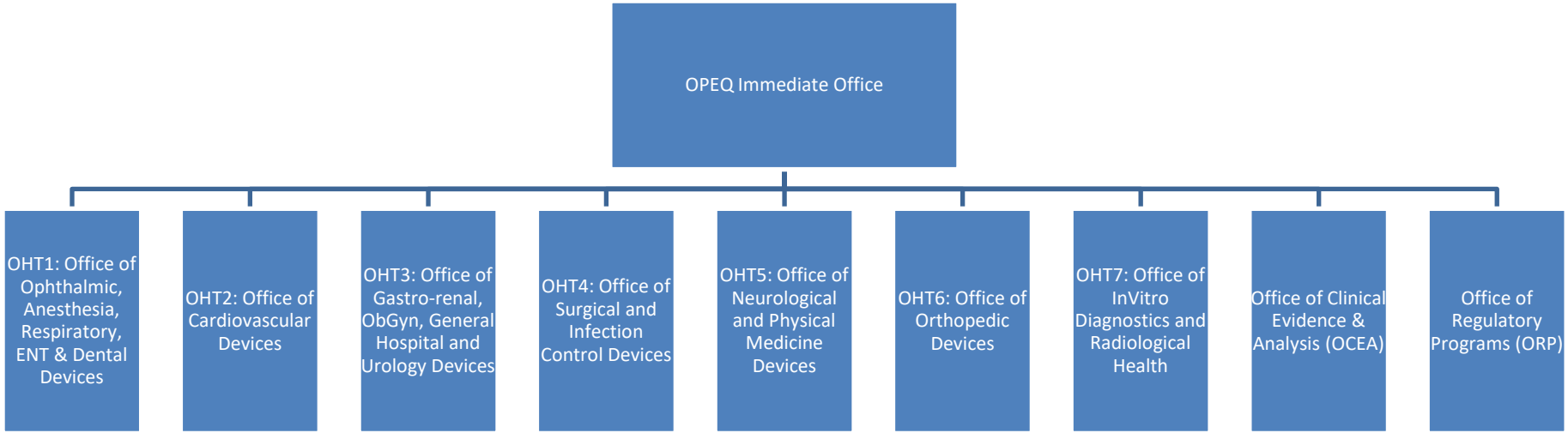
## Office of Science and Engineering Laboratories

## Office of Strategic Partnerships and Technology Innovation

**Content current as of:**
10/26/2021

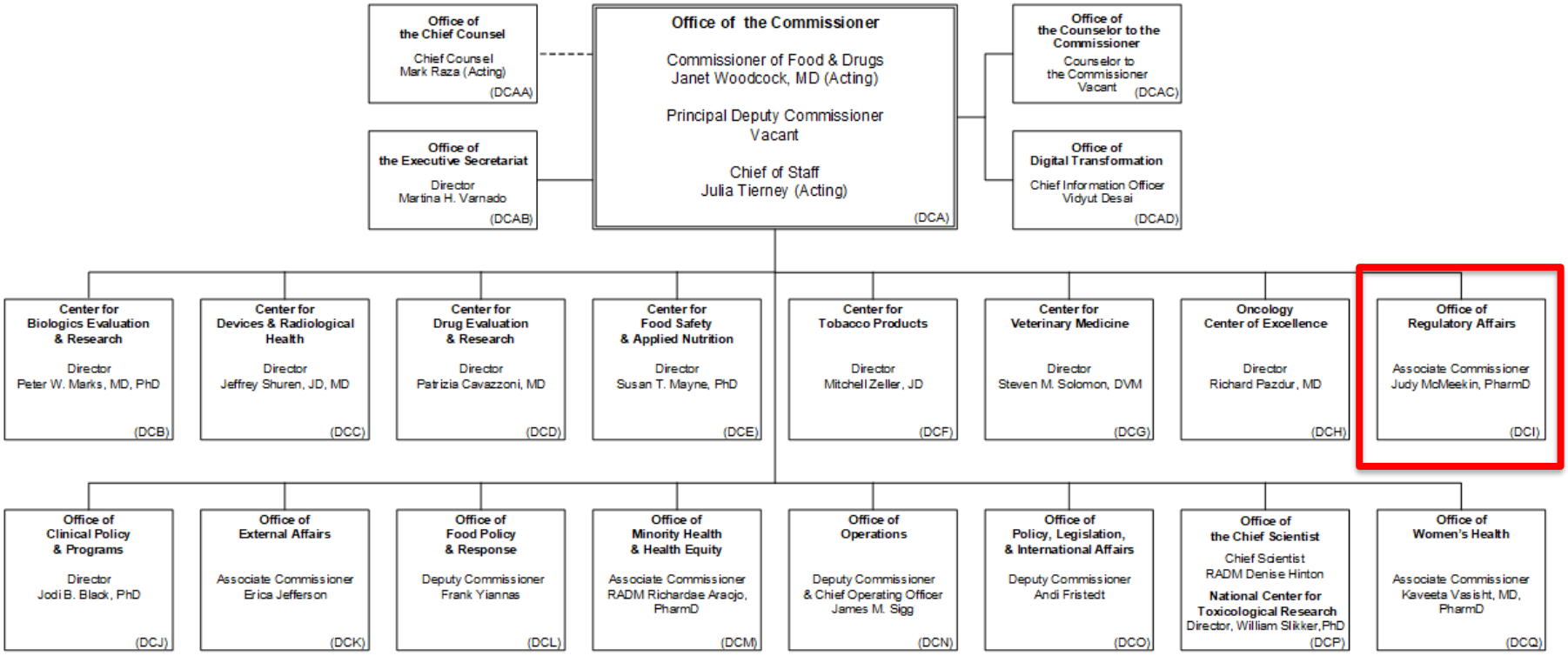
**Topic(s)**
Administration

# Office of Product Evaluation and Quality – “Super Office”



**Department of Health and Human Services**
**Food and Drug Administration**

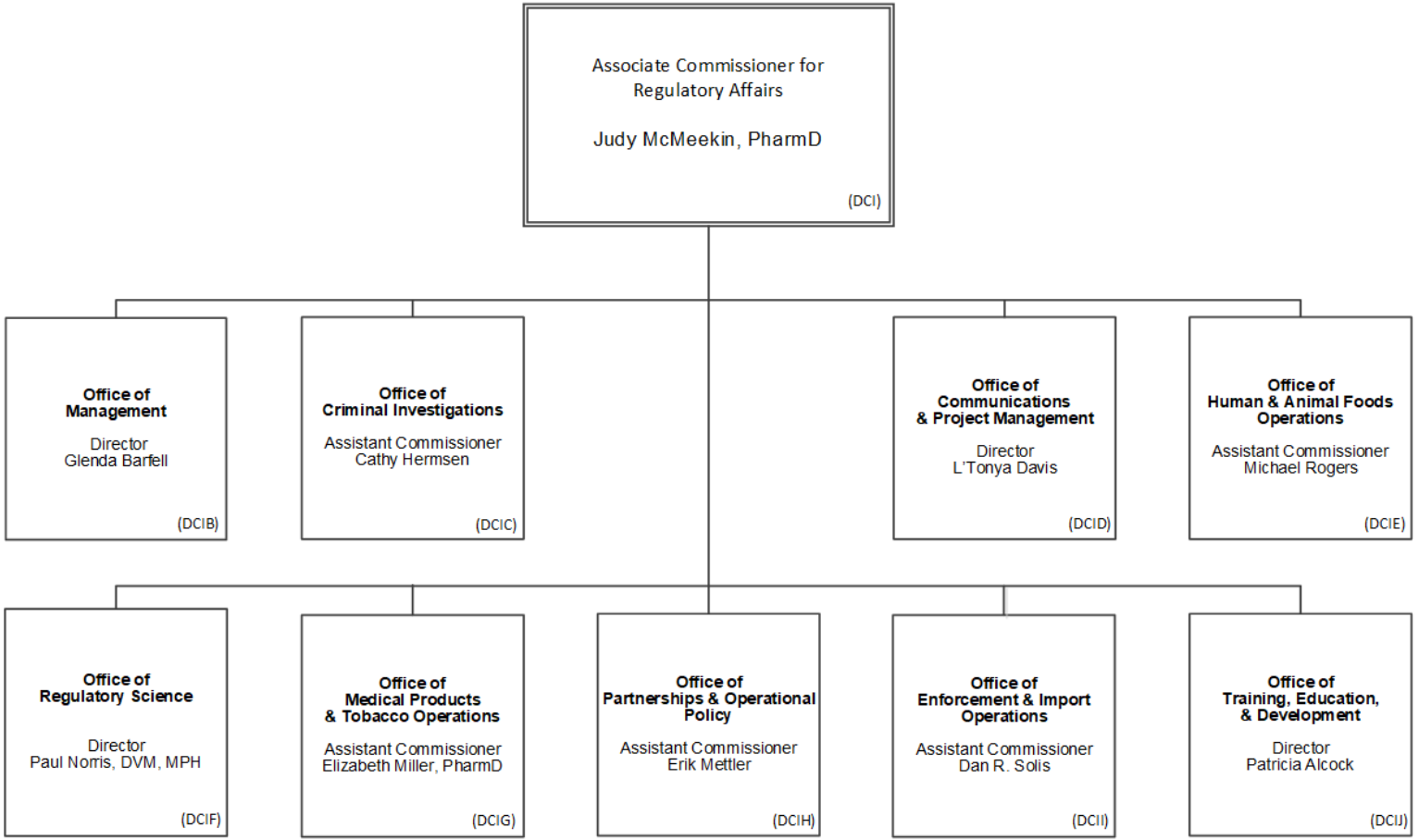
**November 1, 2021**




Legend:
- - - Direct report to DHHS General Counsel

June 2021

# Department of Health and Human Services
# Food and Drug Administration
# Office of Regulatory Affairs



# Department of Justice

- FDA, on its own, can take administrative action, such as warning letters, untitled letters, mandatory recalls, administrative detention of devices, disqualification of clinical investigators

- When seeking judicial action, FDA recommends cases to DOJ for enforcement
  - Criminal prosecutions, seizures, injunctions, inspection/search warrants
  - Handled by the Office of Consumer Protections Branch and local United States Attorneys

- FDA Office of the Chief Counsel (OCC) prepares referrals to DOJ. OCC attorneys serve as subject matter experts, draft memoranda, help develop case strategy, conduct negotiations, prepare and respond to discovery, etc.

# Relationships with States

- FDA and states work closely together
  - Sharing of FDA's non-public information
  - State jurisdiction differs from FDA's jurisdiction
  - Delineate each party's responsibilities through Memorandum of Understanding (MOU)
- States have their own FDCA
  - Roughly 42 states adopted the Uniform State FDCA, based on the Federal FDCA
  - Differences remain:
    - A few states only adopted part of the Uniform FDCA; a few states instead adopted the 1906 Pure Food and Drugs Act
    - Fewer than half the states automatically incorporate federal amendments
    - States can pass additional food and drug laws

# Recommendations for Interacting with FDA

- Do your homework
  - Which office to contact: OC, CDRH, CDER; In CDRH, which office, division, branch?
  - Whom to contact: staff level, deputy director, director?; email or phone?
  - Anonymous or identify client
  - Understand regulatory issues
  - Depth of detail

- Offer recommendation

- Former FDA employees

# Questions?

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