Overview of FDA Regulation of Medical Devices (FDA 101)

Michelle Noonan
International Policy Analyst
Office of the Center Director
Center for Devices and Radiological Health
US Food and Drug Administration
michelle.noonan@fda.hhs.gov

Agenda

- FDA's mission and structure
- CDRH's mission and structure
- Medical device evaluation process
- Questions?

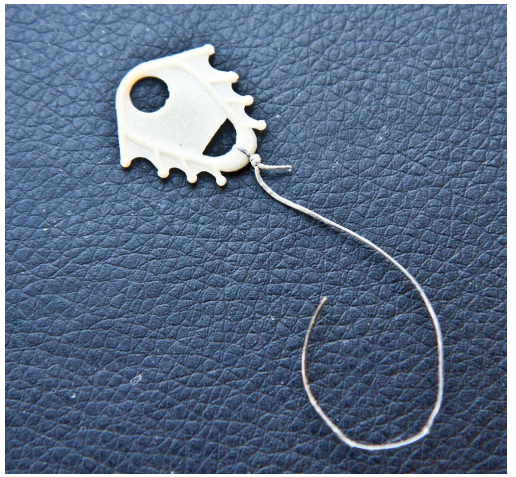
U.S. Food and Drug Administration's Mission

The Food and Drug Administration (FDA) is responsible for protecting the public health by ensuring the safety, efficacy, and security of human and veterinary drugs, biological products, and medical devices; and by ensuring the safety of our nation's food supply, cosmetics, and products that emit radiation. FDA also has responsibility for regulating the manufacturing, marketing, and distribution of tobacco products to protect the public health and to reduce tobacco use by minors.

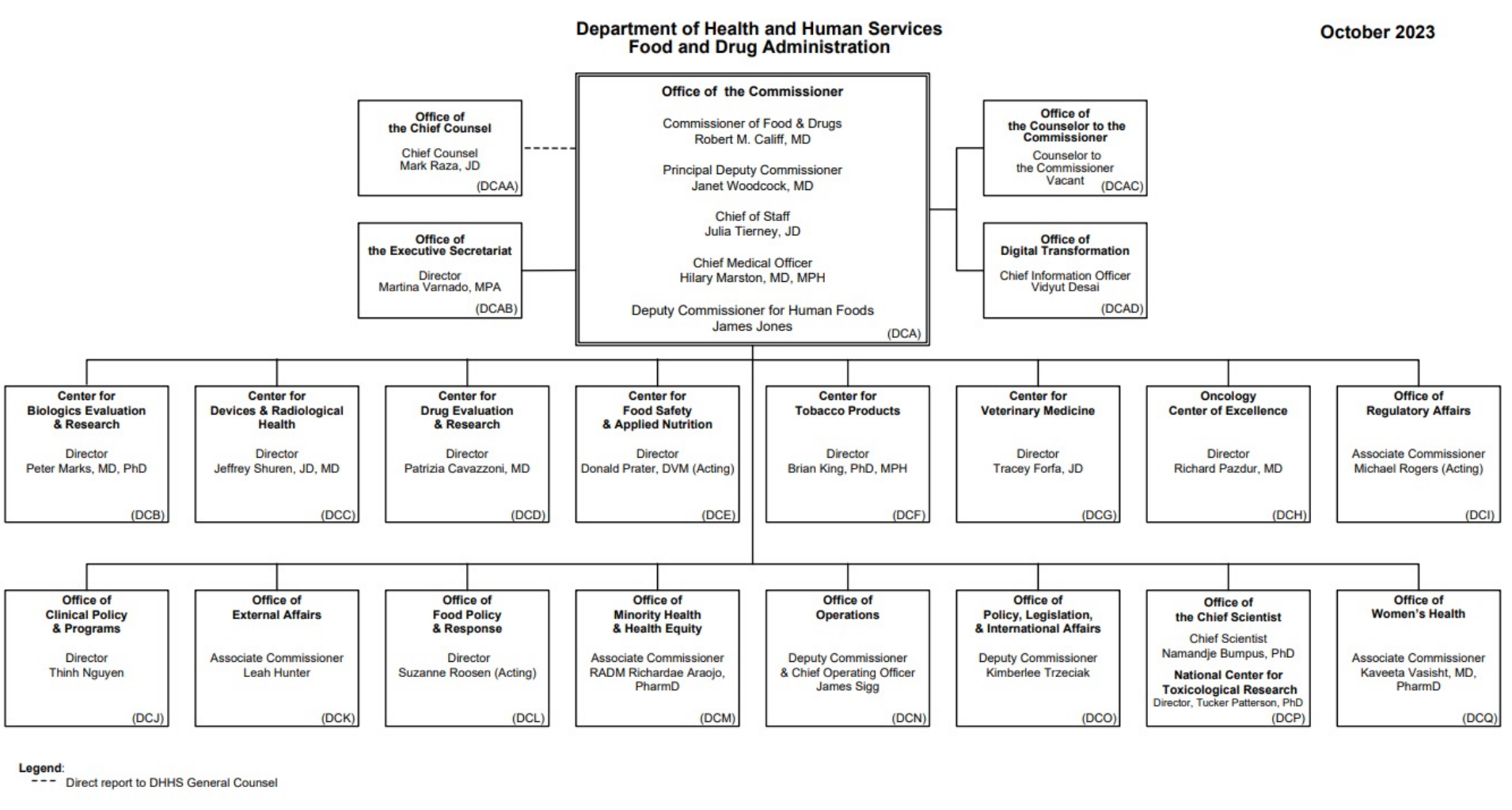
Why does the FDA exist?

- FDA formed in 1906 mainly to combat:
  - Adulteration (Meat-packing)
  - Misbranding (Patent medicines)

- FDA authority subsequently increased to include:
  - Evaluation of drug safety prior to approval (1938)
    - Sulfanilamide
  - Evaluation of drug efficacy prior to approval (1962)
    - Thalidomide
  - Premarket approval of medical devices (1976)
    - Dalkon Shield
  - Manufacturing and marketing of tobacco products (2009)



U.S. FDA Organizational Structure

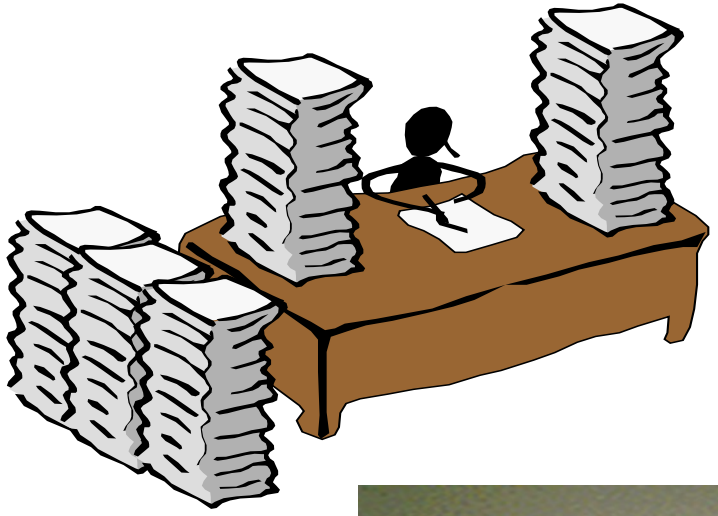


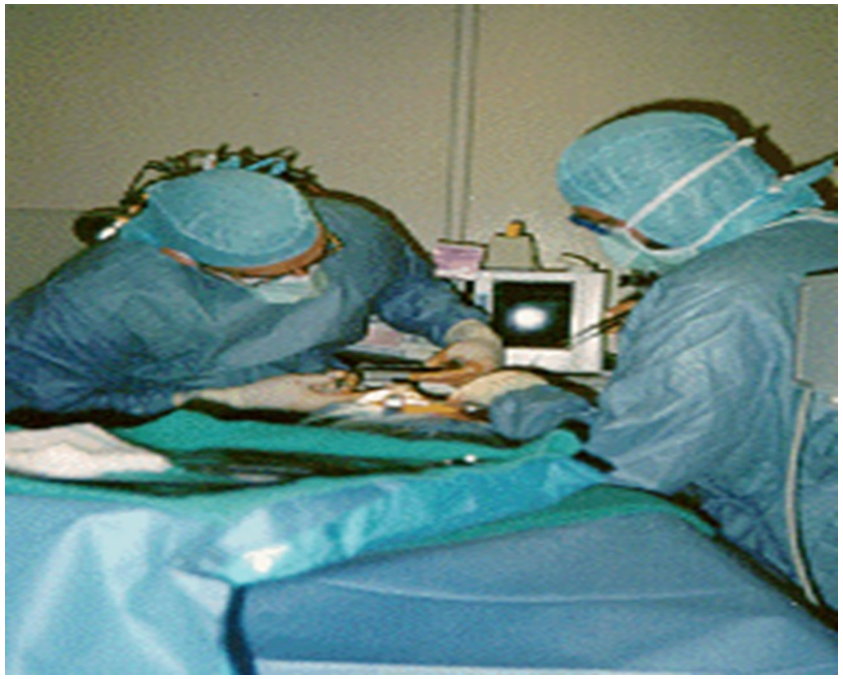
Main FDA Activities

- Product Review and Approval
- Approval of Clinical Studies
- Inspection of Manufacturing Facilities
- Post-Approval Monitoring
- Importing / Exporting
- Basic and Applied Scientific Research
- Education and Outreach

What does FDA not do that you thought we did?

- We don’t test new drugs, vaccines or medical devices -- manufacturers do. We evaluate the data.
- We don’t regulate medical procedures
- We don’t handle intellectual property – this is the job of the U.S. Patent and Trademark Office





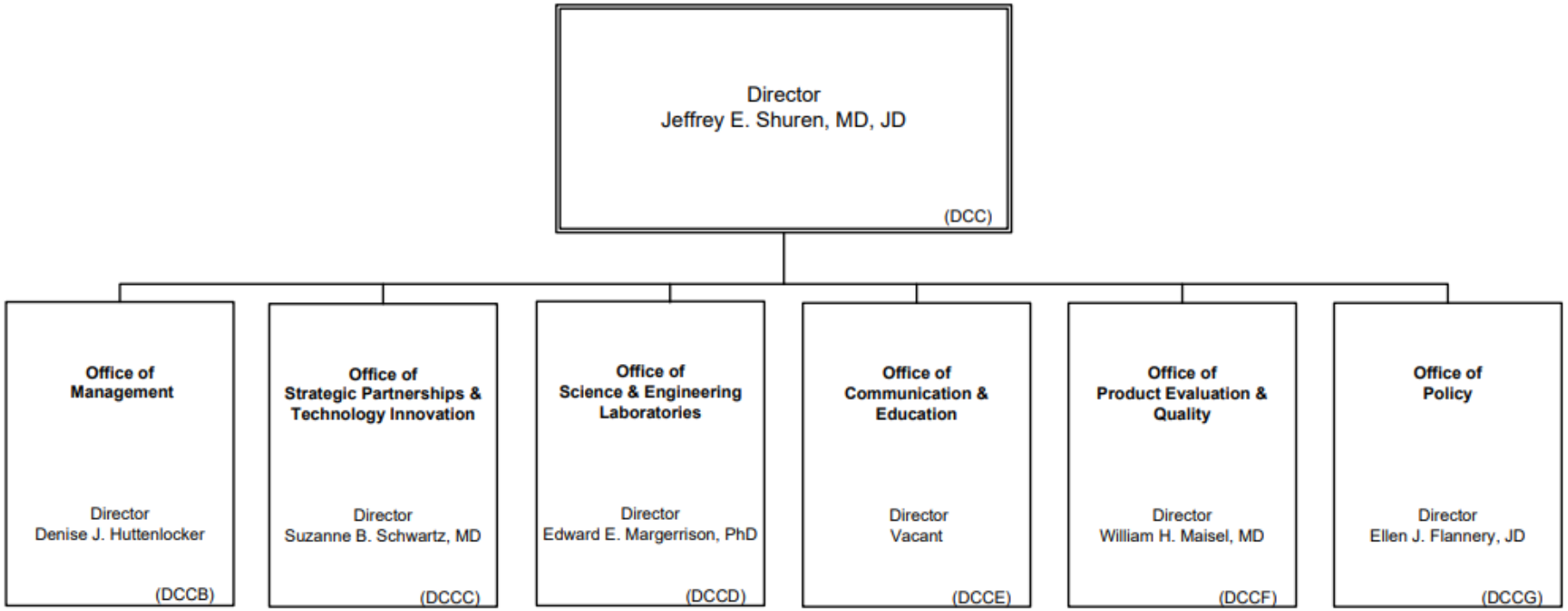
CDRH Mission

- Assure that patients and providers have timely and continued access to safe, effective, and high-quality medical devices and safe radiation-emitting products.
- Provide consumers, patients, their caregivers, and providers with understandable and accessible science-based information about the products we oversee.
- Facilitate medical device innovation by advancing regulatory science, providing industry with predictable, consistent, transparent, and efficient regulatory pathways, and assuring consumer confidence in devices marketed in the U.S.

Center for Devices and Radiological Health (CDRH)

May 2023

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



Day-to-Day Activities at CDRH

- Review medical device and combination product applications
- Evaluate scientific data (engineering tests, lab results, clinical data, etc.)
- Meet with industry and clinical representatives
- Formulate regulatory and scientific policies
- Attend and present at scientific meetings
- Visit manufacturing and clinical study sites

Is My Product a Medical Device?

What is a Medical 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:

(2) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease in man, or (3) intended to affect the structure or any function of the body of man, and which does not achieve its primary intended purposes through chemical action within or on the body of man and which is not dependent upon being metabolized for the achievement of its primary intended purposes.

Section 201, Food Drug and Cosmetic Act

Let's Break It Down – Medical Device Definition

1. Is an article, an item, such as, not limited to:
   - Instrument
   - Machine
   - Implement
   - Implant
   - Apparatus
   - In vitro reagent

Let's Break It Down – Medical Device Definition

2. Intended for use:
   - in diagnosis of disease or other conditions
   - or in the cure, mitigation, treatment, or prevention of disease
   - or intended to affect the structure or any function of the body

Let's Break It Down – Medical Device Definition

3. Does NOT achieve its primary intended purposes through chemical action or dependent on being metabolized

- Note: Software can be a medical device
  - Certain software functions are excluded pursuant to Section 520(o) of Federal Food, Drug and Cosmetic Act

Safe and Effective Medical Devices

- Safety
  - There is reasonable assurance that a device is safe when it can be determined based on valid scientific evidence that the probable benefits to health from use of the device for its intended uses and conditions of use, when accompanied by adequate directions and warnings against unsafe use, outweigh the probable risks. 21 CFR 860.7(d)(1)
- Effectiveness
  - There is reasonable assurance that a device is effective when it can be determined, based upon valid scientific evidence, that in a significant portion of the target population, the use of the device for its intended uses and conditions of use, when accompanied by adequate directions for use and warnings against unsafe use, will provide clinically significant results. 21 CFR 860.7(e)(1)

Bringing a Medical Device to Market in the U.S.

- **Step One**
  - **Classify your device and understand applicable regulatory controls**
- Step Two
  - Select and prepare the correct premarket submission
- Step Three
  - Send your premarket submission to the FDA and interact with FDA staff during review
- Step Four
  - Comply with applicable regulatory controls including the establishment registration and device listing

Medical Device Classification

- Device classification depends on the intended use of the device and also upon the indications for use.
- Device classification is also risk based – the risk the device poses to the patient and/or the user is another factor in the class the device is assigned.
  - Class I = lowest risk
  - Class III = greatest risk
- Classification determines the extent of regulatory controls on your device.

“Intended Use” and “Indications for Use”

Intended Use	Indications for use
• General purpose of device or its function. • Per device label • Includes indications for use. • **What** the device is used for	• Describes **disease or condition** the device will diagnose, treat, prevent, cure or mitigate • Includes description of **patient population** for which device is intended. • **Where, when, and how** the device will be used

Medical Device Classification

- 1700 generic groups of devices
- Classified within 16 medical specialties
  - 21 CFR 862-892

862 = Chemistry/Toxicology
864 = Hematology/Pathology
866 = Immunology/Microbiology
868 = Anesthesiology
870 = Cardiovascular
872 = Dental
874 = Ear, Nose and Throat
876 = Gastro/Urology
878 = General Plastic Surgery
880 = General Hospital
882 = Neurological
884 = Obstetrical/Gynecological
886 = Ophthalmic
888 = Orthopedic
890 = Physical Medicine
892 = Radiology

Regulations and Product Codes Example

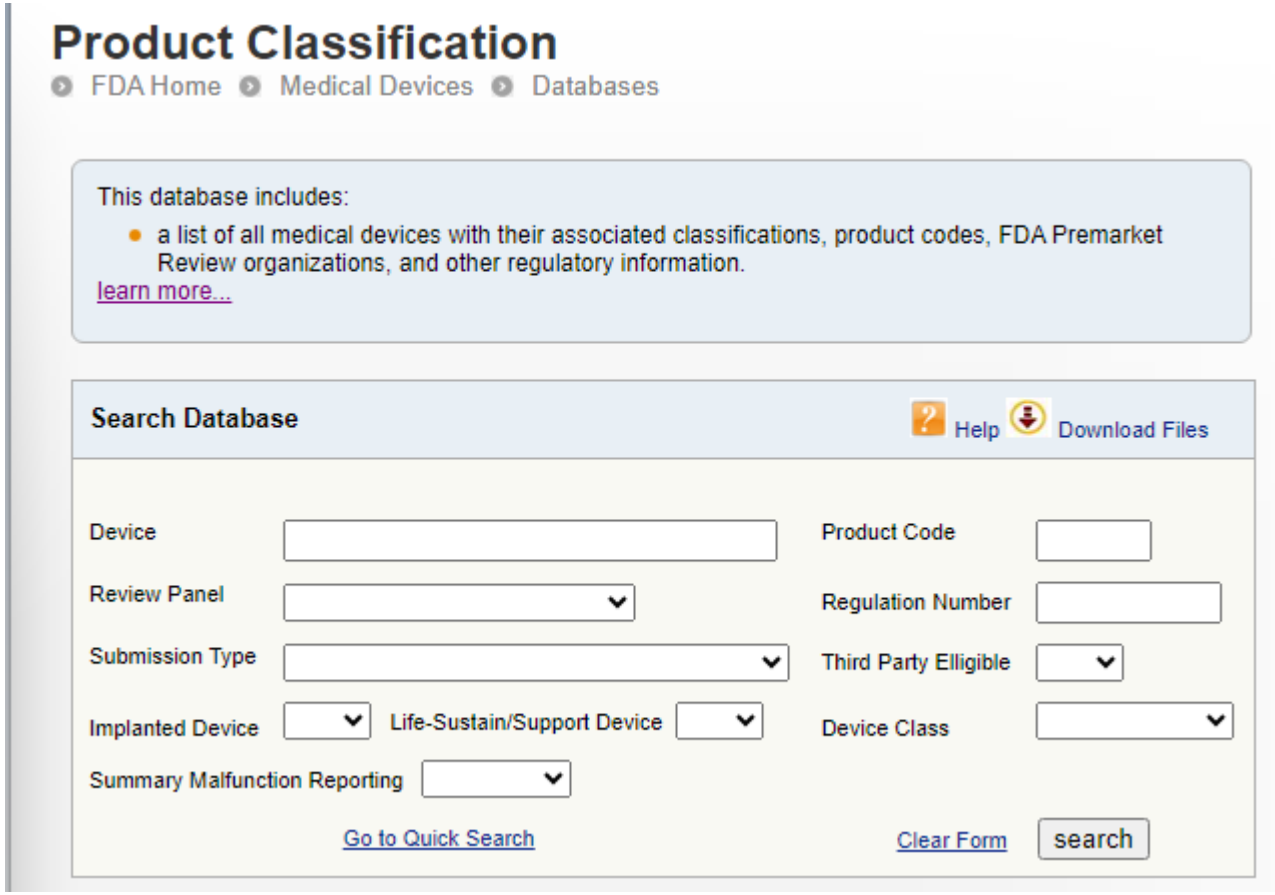
Regulation Number: 21 CFR 880.5780

- (a) Medical support stocking to ***prevent the pooling of blood in the legs***.
  - Class II and requires 510(k).
  - **Product code** DWL.

- (b) Medical support stocking for ***general medical purposes***.
  - Class I and is exempt from 510(k).
  - **Product code** FLL.

Product Classification Database

- https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPCD/classification.cfm



Classification System Risk Categorization

- Class I – Low Risk
  - *General Controls*
- Class II – Moderate Risk
  - *General Controls and*
  - *Special Controls*
- Class III – High Risk
  - *General Controls and*
  - *Premarket Approval*

General Controls

- Regulatory requirements applicable to all devices (unless exempted) outlined in the Food, Drug, and Cosmetic Act and include, for example:

Control	Regulation (21 CFR Part)	Brief Description
Labeling	801	provide information for users
Medical Device Reporting	803	report device-related injuries and deaths
Establishment Registration	807	register business with FDA
Device Listing	807	identify devices
Quality System	820	ensure safe, effective finished devices
Adulteration	FD&C Act 501	contaminated, filthy, putrid, or decomposed substances or intention of committing fraud
Misbranding	FD&C Act 502	provide false or misleading labeling

Special Controls

- Applied when general controls are insufficient
- Usually device specific and include:
  - Performance Standards
  - Postmarket Surveillance
  - Patient Registries
  - Special Labeling Requirements
  - Premarket Data Requirements
  - Guidelines

Class I Medical Devices

- Level of device risk may be sufficiently managed by least amount of regulatory control
  - General Controls
- Typically no premarket submission required
- Device Examples
  - adhesive bandage, I.V. stand, sunglasses

Class II Medical Devices

- General and Special Controls (special labeling, mandatory performance standard, guidelines, etc.)
- Typically requires a 510(k) submission
- Device Examples:
  - syringe, surgical mask, powered wheelchair

Class III Medical Devices

- Insufficient information exists to assure safety and effectiveness solely through general or special controls
- Typically requires a Premarket Approval (PMA) application or Humanitarian Device Exemption (HDE) application
- Devices that support or sustain human life
- Device Examples
  - heart valves, implantable neuromuscular stimulator, coronary stent

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Submission Types

- Premarket Notification [510(k)]
- Premarket Approval (PMA)
- Humanitarian Device Exemption (HDE)
- Investigational Device Exemption (IDE)

Premarket Notification 510(k)

- Marketing Clearance Process
- Comparison of the proposed device to one or more similar legally marketed devices in the US
- Demonstration that the device to be marketed is at least as safe and effective (substantially equivalent (SE)) to a legally marketed device in US
- A 510(k) is required when:
  - Marketing for the first time
  - Making a significant change to an existing device (January 10, 1997 – “Deciding When to Submit a 510(k) for a Change to an Existing Device”)
- https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm

Classification of New Devices

- “New” means that the device has not previously been classified
- By default, these devices are classified into Class III and require PMA approval, regardless of risk
- Regulatory burden may exceed what is necessary
- Potential Option: *de novo*

Classification of New Devices – *de novo*

- *de novo* is a classification process for new novel devices whose type has not previously been classified which:
  - utilizes a risk-based strategy
  - is used to classify the devices into Class I or II
- After *de novo* is granted
  - New Device is Legally Marketed
    - Subject to post-market requirements applicable to that device and class (including general controls, special controls as applicable)
  - New Device Establishes New Classification
    - The subject device is eligible to serve as a predicate for new medical devices, where appropriate [510(k) process]
    - New "device type" along with classification, regulation, class (either Class I or II), necessary controls and product code
  - FDA publishes order announcing new classification, controls
- https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/denovo.cfm

Premarket Approval (PMA)

- Only applies to Class III devices (high risk)
- Based on a determination that the application contains sufficient valid scientific evidence to assure that the device is safe and effective for its intended use(s).
- Device is approved **not** determined to be substantially equivalent "SE"
- Typically includes clinical data from clinical trials
- https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm

Humanitarian Device Exemption (HDE)

- Only applies to Class III devices (high risk)
- For devices intended to treat or diagnose a disease or condition that affects or is manifested in fewer than 4,000 individuals in the US per year
- Similar to PMA, but do not have to demonstrate effectiveness
- Demonstrates safety and probable benefit
- https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfHDE/hde.cfm

Investigational Device Exemption (IDE) – Clinical Trials

- Allows an investigational (unapproved) device to be used in human subjects as a part of a clinical study in order to collect safety and effectiveness data

- Must be approved by CDRH prior to initiating the clinical study

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Code of Federal Regulations (CFR) Citations

- **21 CFR Part 807**
  - Establishment Registration and Listing
  - Premarket Notification [510(k)]
- **21 CFR Part 814:** Premarket Approval (PMA)
- **21 CFR Part 812:** Investigational Device Exemptions
- **21 CFR Parts 801, 809, 812, 820**
  - Medical Device Labeling
- **21 CFR Part 820:** Quality System Regulation
- **21 CFR Part 821:** Tracking Requirements
- **21 CFR Part 803:** Medical Device Reporting

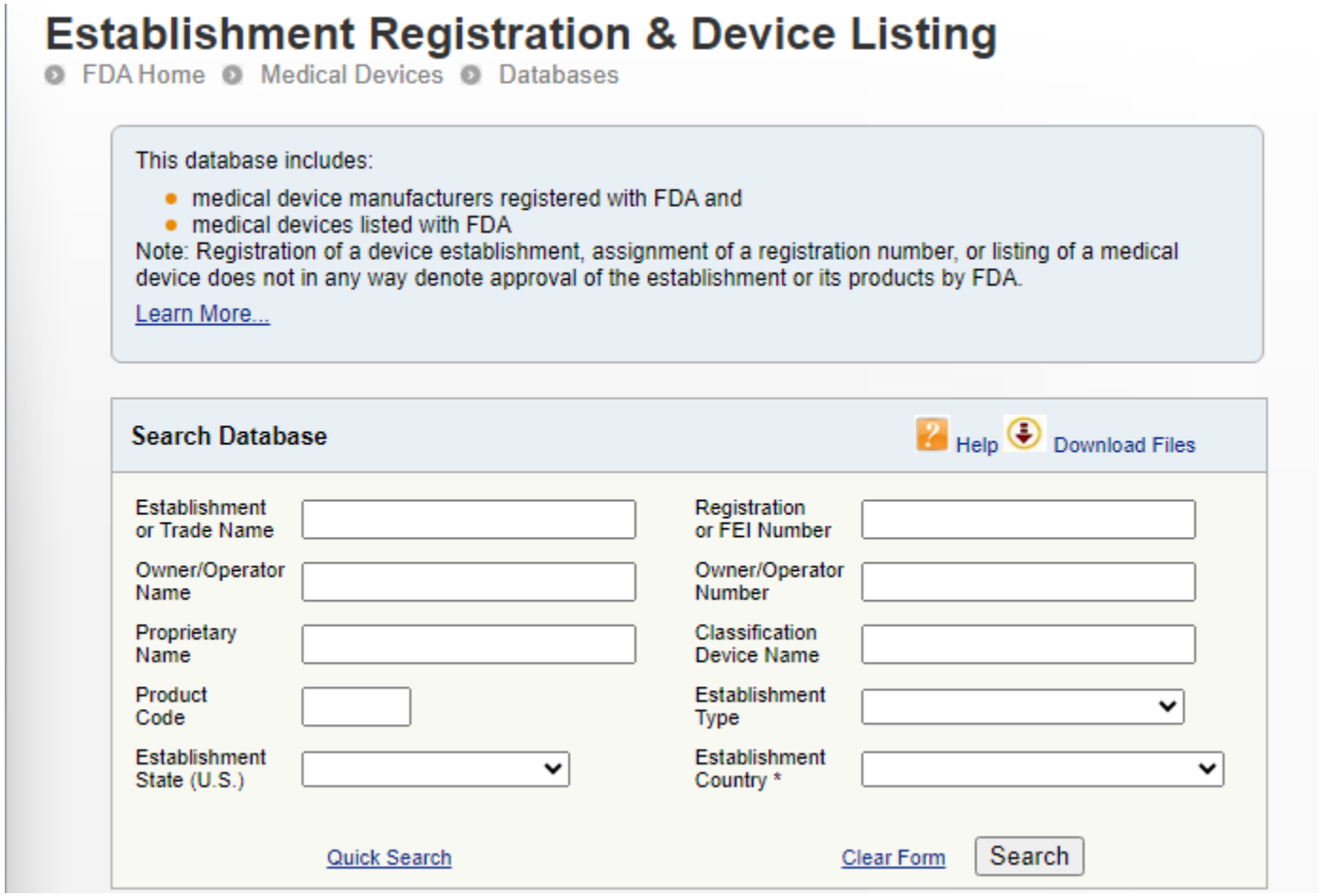
CFR Online at: CFR - Code of Federal Regulations Title 21 (fda.gov)

Establishment Registration & Medical Device Listing 21 CFR 807

- Electronic Registration of Medical Device Establishments
  - Notification of U.S. Agent for “Foreign” Establishments
- Electronic Medical Device Listing
- Annual Registration Fee (no waivers)

Registration & Listing Database

- https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfRL/rl.cfm



Quality System (QS) Regulation

- 21 CFR 820 states that manufacturers must establish and following quality systems to help ensure their products consistently meet applicable requirements and specifications
- Applies to finished device manufacturers who intend to commercially distribute medical devices
- Covers the design and manufacture of medical devices sold in the U.S.
- Similar to ISO 13485
- Standard for audit of device establishment

Proposed Rule: Quality System Regulation Amendment

- On February 23, 2022, FDA published a proposed regulation to amend the device current good manufacturing practice requirements of the QS Regulation to incorporate the international standard specific for medical device quality management systems set by the International Organization for Standardization (ISO), ISO 13485:2016 Medical devices – Quality management systems – Requirements for regulatory purposes.
- This action, if finalized, would harmonize quality management system requirements for FDA-regulated devices with requirements used by many other regulatory authorities around the world.

Medical Device Tracking

- 21 CFR Part 821
- Manufacturers are required to track certain devices from their manufacture through the distribution chain when they receive an order from the FDA to do so.
- Purpose is to ensure devices can be located promptly in commercial distribution
- Information may be used to facilitate notifications and recalls ordered by FDA in the case of serious risks to health presented by the devices

Medical Device Tracking

- The types of devices subject to a tracking order may include any Class II or Class III device:
  - the failure of which would be reasonably likely to have serious adverse health consequences;
  - which is intended to be implanted in the human body for more than one year; or
  - which is intended to be a life sustaining or life supporting device used outside a device user facility.
- Examples of devices with mandatory tracking requirements include silicone breast implants, defibrillators, heart valves, and pacemakers

522 Postmarket Surveillance Studies

- Section 522 of the FD&C Act gives FDA the authority to requirement a manufacturer to conduct postmarket surveillance of a class II or class III device that meets any of these criteria:
  - Its failure would be reasonably likely to have serious adverse health consequences.
  - It is expected to have significant use in pediatric populations.
  - It is intended to be implanted in the body for more than one year.
  - It is intended to be a life-sustaining or life-supporting device used outside a device user facility.

Medical Device Reporting (MDR) 21 CFR 803 "Adverse Event Reporting"

- Mechanism for FDA to identify and monitor adverse events involving medical devices
- August 14, 2015 – eMDR mandatory for manufacturers only

- **Events:** Death, Serious Injury, and Malfunction
- **Reported by:** Manufacturer, User Facility, and Importers of medical devices

Electronic Export Certificate Issuance

- Export certificates are often required by importing countries as one of the requirements to market a medical device. FDA does not require export certificates to export human medical devices/products that can be legally marketed in the U.S.

- U.S. Food and Drug Administration's (FDA) Center for Devices and Radiological Health (CDRH)
  - What: Transitioning to an electronic version of all export documents
  - When: January 2, 2024

- The electronic certificates (e-certificates) for human medical devices/products will be issued as a downloadable PDF through the CDRH Export Certification Application and Tracking System (CECATS).

Electronic Export Certificate Issuance

- **Old process**
  - Starting January 2, 2024, Exports Certificates and documents will no longer be:
    - Printed on security paper
    - Mailed
- **Unchanged process**
    - Still requested in CDRH Export Certificate Application and Tracking System (CECATS)
- **New Process**
  - If granted after review by FDA:
    - Requester receives an email with instructions
    - One time access to print or save a PDF within 45 days
- **To validate:**
  - Access the FDA Export Certificate Validator (FECV) website
    - Enter certificate number
  - FDA will add a unique Quick Response (QR) code to the e-certificate

Industry Education Resources

1. **CDRH Learn – Multi-Media Industry Education**
   - over 80 modules
   - videos, audio recordings, power point presentations, software-based “how to” modules
   - mobile-friendly: access CDRH Learn on your portable devices

   http://www.fda.gov/Training/CDRHLearn

2. **Device Advice – Text-Based Education**
   - comprehensive regulatory information on premarket and postmarket topics

   http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance

3. **Division of Industry and Consumer Education (DICE)**
   - Contact DICE if you have a question
   - Email: **DICE@fda.hhs.gov**
   - Phone: 1(800) 638-2014 or (301) 796-7100 (Hours: 9 am-12:30 pm; 1 pm-4:30pm EST)
   - Web: **http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/ContactUs--DivisionofIndustryandConsumerEducation/default.htm**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