Navigating FDA:
Device (and Diagnostic) Development Requirements

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STTR Regional Technology Transfer Accelerator Hubs for IDeA States

OFFICE OF EXTRAMURAL RESEARCH | OFFICE OF THE DIRECTOR | NATIONAL INSTITUTES OF HEALTH

NIH SEED

Welcome

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Regulatory Specialist
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- Now
  - NIH Office of Extramural Research
    - SEED (Small Business Education & Entrepreneurial Development)
  - MITRE Corporation
    - Operating Federally Funded Research & Development Centers (FFRDC)
    - Not-for-Profit
- Before
  - FDA Center for Devices & Radiological Health (CDRH)
    - Division of Radiological Health
    - Division of Imaging Diagnostics & Software Reliability

Goal:
A basic understanding of premarket regulatory processes

- There are exceptions to much of the information that follows

CDRH PREMARKET PATHWAYS

National Institutes of Health
Office of Extramural Research

Disclaimer:
The content was developed by NIH SEED based on its collective experience working with the NIH innovator community. This information has been developed, for informational purposes, to address questions frequently asked by NIH awardees, and represents the experiences of the subject matter experts who contributed to its development.

There are three main regulatory pathways to get your device on the market:

Premarket Approval (PMA)	De Novo Classification	510(k) Premarket Notification
Novel Devices and/or High Risk	Novel Devices with Controllable Risk	Not-Novel Devices with Controllable Risk

Premarket Review at CDRH

For established device-types

Class	Risk	Review Pathway
III	High	Premarket "Approval" (PMA)
II	Medium	510(k) "Clearance"
I	Low	No Premarket Review

For first-of-their-kind device-types:

- PMA by default
- **De Novo** "granted" to pave the way for future 510(k)
  - Only an option if risk/benefit is controllable/suitable

For reference, in August + September 2020:

9 PMA (original)
6 De Novo
383 510(k) (traditional)

Summaries are available on CDRH public databases

The Destination of Each Path

FDA will determine based on your 510(k) if the device is Substantially Equivalent

FDA will determine based on your PMA if the device is Safe & Effective

FDA will determine based on your De Novo if the device is… we'll come back to De Novo

Intended Use and Indications For Use

- Intended Use
  - The general purpose of the device. Exactly what is it meant to do?
- Indications For Use (IFU)
  - The conditions or reason or situation for someone to use the device.

Name that device!

Intended Use	Indications for Use
Make images of internal structures of the body	Images are derived from nuclear magnetic resonance properties. Additional contrast agents may be used. When interpreted by trained physician, can be yield information to aid in diagnosis

Key Concepts for 510(k)

FDA will determine based on your 510(k) if the device is Substantially Equivalent to a Predicate Device

Predicate

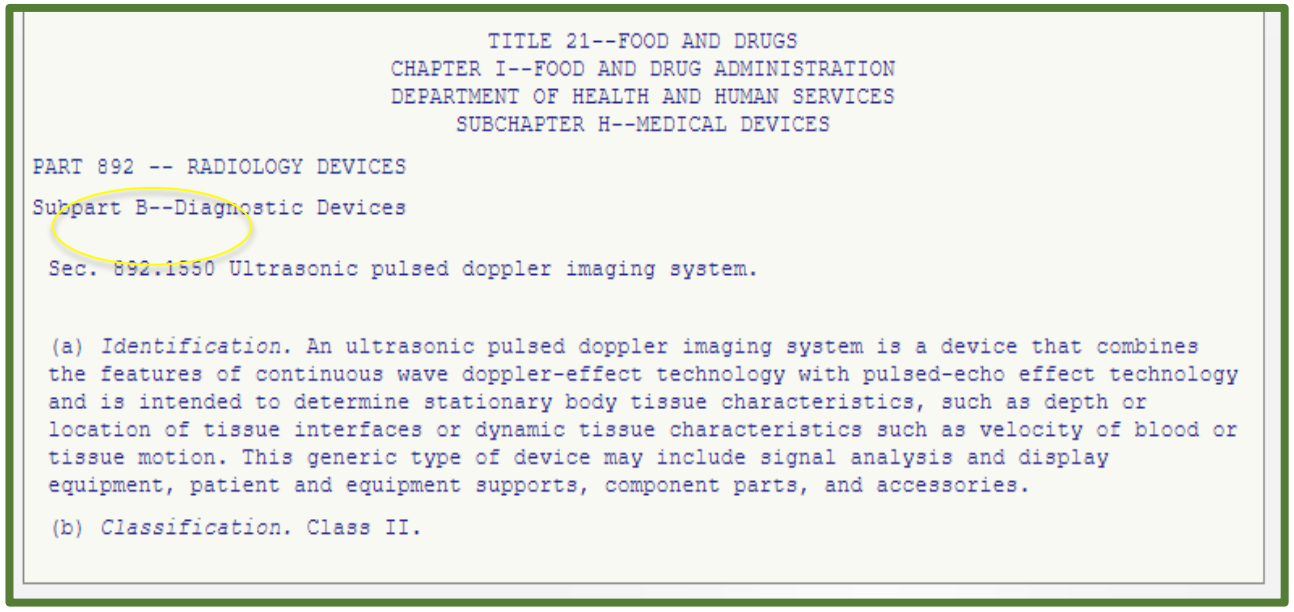
- Existing device, already has 510(k) clearance (or De Novo)
- Same device-type (regulation/classification) as yours

Substantial Equivalence (SE)

- Same **intended use** as the **predicate**
  - May or may not have different *IFU*
- And where there are technical differences...
  data shows your device is as safe and effective as the **predicate**

FDA Databases

- Intended Use
  - Check the corresponding regulation & product classification
  - e.g., 21 CFR 892.1550
- Indications For Use (IFU)
  - Check the publicly available summaries for cleared/approved technologies
  - e.g., K202406



TITLE 21--FOOD AND DRUGS
CHAPTER I--FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES
SUBCHAPTER H--MEDICAL DEVICES

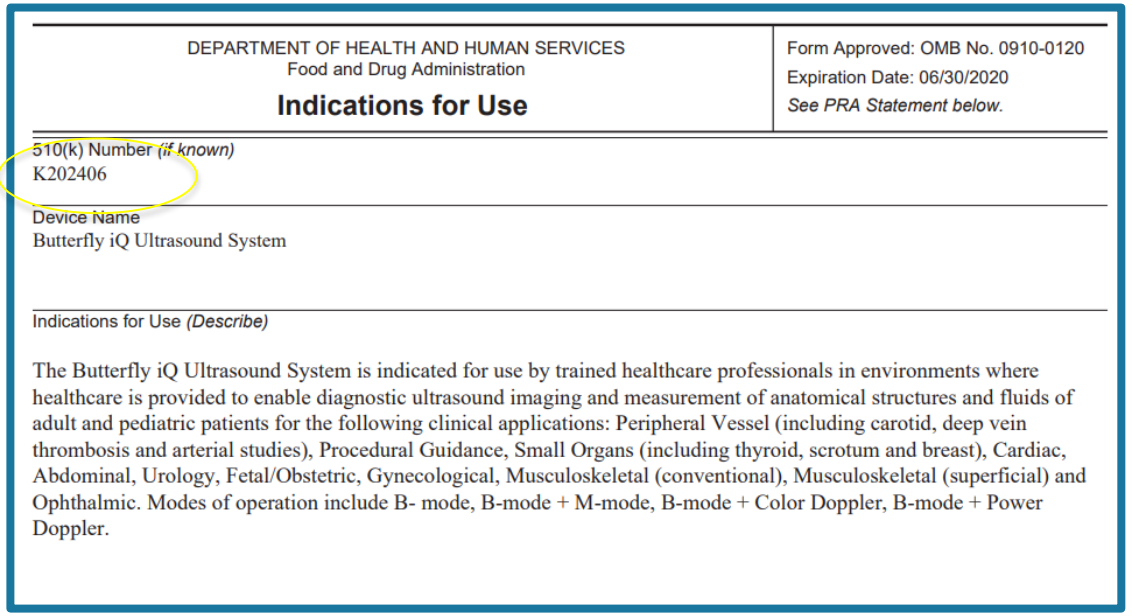
PART 892 -- RADIOLOGY DEVICES

Subpart B--Diagnostic Devices

Sec. 892.1550 Ultrasonic pulsed doppler imaging system.

(a) *Identification.* An ultrasonic pulsed doppler imaging system is a device that combines the features of continuous wave doppler-effect technology with pulsed-echo effect technology and is intended to determine stationary body tissue characteristics, such as depth or location of tissue interfaces or dynamic tissue characteristics such as velocity of blood or tissue motion. This generic type of device may include signal analysis and display equipment, patient and equipment supports, component parts, and accessories.

(b) *Classification.* Class II.



DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
K202406

Device Name
Butterfly iQ Ultrasound System

Indications for Use *(Describe)*

The Butterfly iQ Ultrasound System is indicated for use by trained healthcare professionals in environments where healthcare is provided to enable diagnostic ultrasound imaging and measurement of anatomical structures and fluids of adult and pediatric patients for the following clinical applications: Peripheral Vessel (including carotid, deep vein thrombosis and arterial studies), Procedural Guidance, Small Organs (including thyroid, scrotum and breast), Cardiac, Abdominal, Urology, Fetal/Obstetric, Gynecological, Musculoskeletal (conventional), Musculoskeletal (superficial) and Ophthalmic. Modes of operation include B- mode, B-mode + M-mode, B-mode + Color Doppler, B-mode + Power Doppler.

Key Concepts for PMA

FDA will determine based on your PMA if the device is **Safe and Effective**

Safe an Effective

- High probable benefit versus likelihood of injury or illness
- High reliability
- In context of Intended Use & Indications For Use & “Other Relevant Factors”
  - 21 CFR 860.7

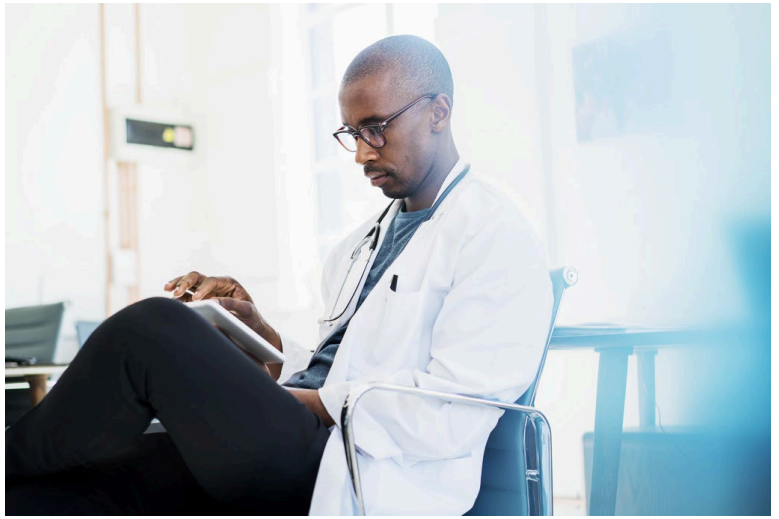
The Safety and Efficacy is typically demonstrated via clinical investigations

Oversight of Clinical Investigations

FDA authorizes the clinical *study* of a **Significant Risk** device before it begins
This is called an Investigational Device Exemption (IDE)

Significant Risk (SR) device is an investigational device that

1. Is an implant
2. Supports or sustains human life
3. Is of substantial clinical importance
4. Otherwise presents serious risk to safety/welfare



An Institutional Review Board (IRB) monitors and reviews throughout the study

- Nonsignificant Risk (NSR) device investigations
- The dialog on clinical study and risk **starts with the IRB**

De Novo

FDA will determine based on your De Novo if
- Probable benefits outweigh probable risks
- and Regulatory Controls provide reasonable assurance of safety and efficacy

General controls
- Standard pre- and post-market requirements
- For example, 510(k)

Special controls
- *Device specific* requirements
- For example, performance standards or specific labeling

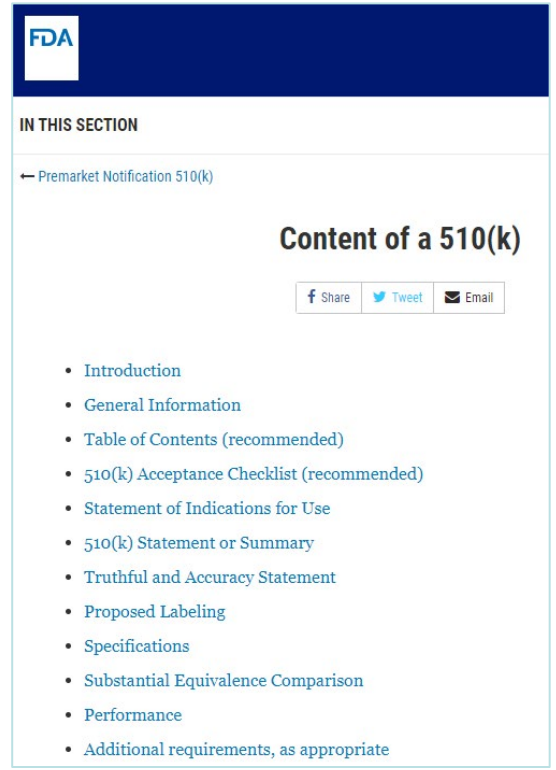
De Novo submissions apply only to first-of-their-kind devices
- FDA classifies the device as Class II or Class I
- Can be used as predicate for future 510(k)

Your Premarket Submissions and Documents

- Your submission is your argument to FDA that your device is ready to market

- The argument will be supported by:
  - Technical/clinical description of device
  - Detailed comparison of similarities and differences (if applicable)
  - Performance data
  - Draft labeling
    - User manual
    - Promotional language
  - Any other documents to make your case!

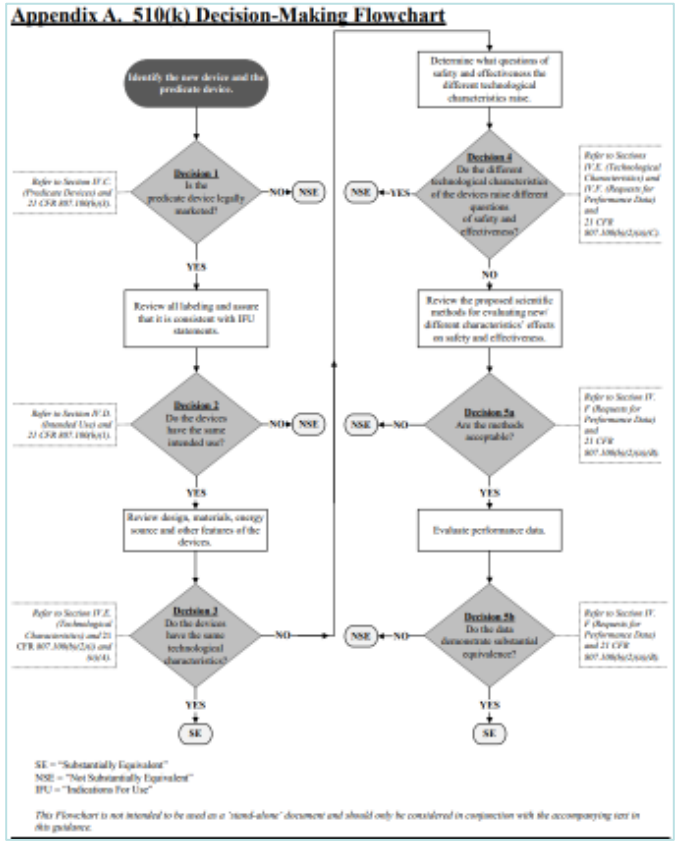
- Expected content is detailed on FDA's website
  - 510k, PMA, De Novo, IDE



Starting Points

Become familiar with your path early on in development

- Use the public database to get summaries of similar products
  - What standards did they use?
  - What performance data did they include?
  - Which CDRH office reviewed it?
  - Start to compare and contrast
- Find relevant guidance documents
  - For example, the 510(k) flowchart
- Utilize your resources
  - IDeA Networks
  - NIH SEED
  - Academic Institutions



Pre-Submission Meetings with CDRH

- Pre-Submission Meetings (aka Q-Subs)
  - Serve a variety of purposes including
    - General questions ahead of an anticipated 510(k)/PMA/De Novo
    - Study risk determinations ahead of a potential IDE
    - Breakthrough device designation requests
    - Meetings held for an ongoing application
  - Free!
    - Formal detailed feedback from FDA experts within three months
    - Written, teleconference, or in-person

- One of these is a good Pre-Submission question:

How should we design our bench testing validation plan?	Does FDA agree that the bench testing plan, as we described, sufficiently quantifies the accuracy and precision?

Quick Notes on Diagnostics and Digital Health

Diagnostics

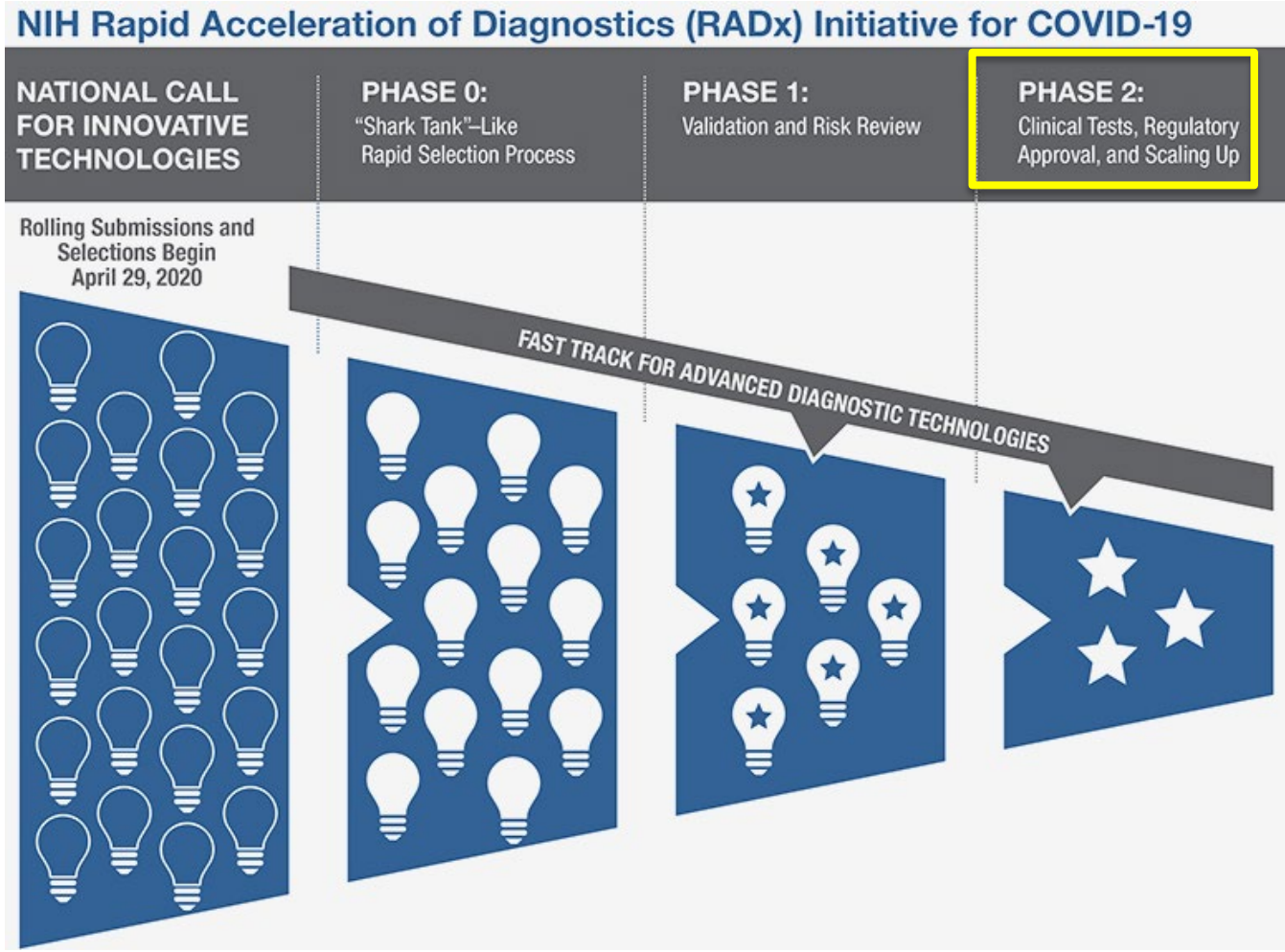
- *In vitro* (test tube) diagnostics are medical devices (that may also be biologics)
  - They are subject to the same regulatory procedures as other devices

- Additional standards and requirements for lab test manufacturers apply
  - As established in the Clinical Laboratory Improvement Amendments (CLIA)
  - You may seek a CLIA waiver after your premarket clearance/approval
    - Or alongside your 510(k)
    - Goal: demonstrate that the test is *"accurate as to render the likelihood of erroneous results by the user negligible"*
    - With a CLIA waiver – more labs are certified to utilize the lower risk test

Example: EUA for COVID-19 Diagnostics

- Recent emphasis and urgency on Emergency Use Authorization (EUA)
  - 280+ authorized diagnostic tests
- Fast response from FDA
  - Guidance, fact sheets, and templates
  - Tests that receive EUA can be marketed during the ongoing emergency
    - Without need for 510(k) or PMA

- NIH has worked closely with FDA to accelerate emergency diagnostics:
  RADx "Shark Tank" has funded 22 companies with a total $476.4 million
- RADx projects increasing test capacity by **2.7 million tests PER DAY** by end of December.



Software and Digital Health

- Many medical devices contain software
  - FDA guidance on how software design & validation should be documented
- In some cases, software is a medical device
  - Examples
    - Radiological image processing software tools
    - Smartphone apps that utilize external sensors

    → Regulated medical device

    - Video games to motivate physical therapy at home
    - Medication tracking tools

    → Medical device under *enforcement discretion*

    - Access to patient health records
    - Electronic medical dictionaries

    → Not a medical device
  - FDA guidance with more examples
- Software & Digital Health is a rapidly changing regulatory space
  - Federal Trade Commission – Interactive Tool

"Can you help me determine whether the FDA would consider my digital health product to be an actively regulated product?"

Yes – per **FDA website**, email DigitalHealth@fda.hhs.gov

Recap and Final Thoughts

Your premarket “arguments” to FDA

- 510(k): substantial equivalence
- De Novo: new product; paving the way for future 510(k)
- PMA: new/high-risk product; safety & efficacy via clinical studies

Your resources

- FDA public databases and guidance documents
- NIH SBIR/STTR support
- CDRH Division of Industry & Consumer Education (DICE)

Your first steps

- Use your resources and create a strategy for your technology and intended use
- Strongly consider a pre-submission meeting
- Engage early – FDA feedback benefits your technology and your business

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