

# **The Medical Device Review Process**

## **An FDA Staff Perspective**

**American Society of Neurorehabilitation**

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# Outline

- **Premarket Review of Medical Devices with Examples from Neurological Devices**
- **Regulation of Clinical Trials with an emphasis on Early Feasibility Studies**
- **Increasing Regulatory Transparency**
- **Engagement with Sponsors through the Q-Sub Process**
- **Points of Contact and Resources**



## CDRH Vision

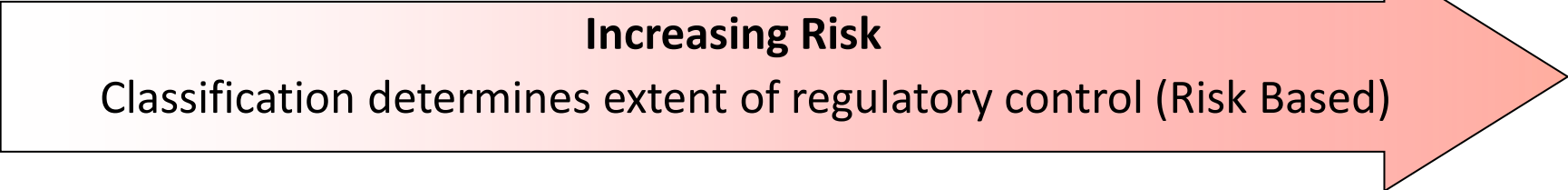
- Patients in the U.S. have access to high-quality, safe, and effective medical devices of public health importance first in the world.
- The U.S. is the world's leader in regulatory science, medical device innovation and manufacturing, and radiation-emitting product safety.
- U.S. post-market surveillance quickly identifies poorly performing devices, accurately characterizes real-world performance, and facilitates device approval or clearance.
- Devices are legally marketed in the U.S. and remain safe, effective, and of high-quality.
- Consumers, patients, their caregivers, and providers have access to understandable science-based information about medical devices and use this information to make health care decisions.

# What is a Medical Device?

- Definition of a medical device is specified in section 201(h) of the Federal Food, Drug and Cosmetic Act (21 U.S.C. 321) \*
- Section 201(h) states in part:
  - The term “device”...means an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is...”
  - “...intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man...” or
  - “...intended to affect the structure or any function of the body of man and which does not achieve any of its primary intended purposes through chemical action....”



# A Risk Based Approach for Medical Devices since 1976



**Class I**

- General Controls

*e.g., reflex hammers, tuning forks, manual prosthetic limbs*

**Class II**

- General controls
- Special controls

*e.g., EEG, EMG, TMS, FES, exoskeletons, nerve conduction, neurothrombectomy devices*

**Class III**

- General controls
- Premarket approval (PMA)

*e.g., deep brain stimulators, vagus nerve stimulators, implanted spinal cord stim*

**General Controls**

- Electronic Establishment Registration
- Electronic Device Listing
- Quality Systems
- Labeling
- Medical Device Reporting

**Special Controls (Addressing Risk)**

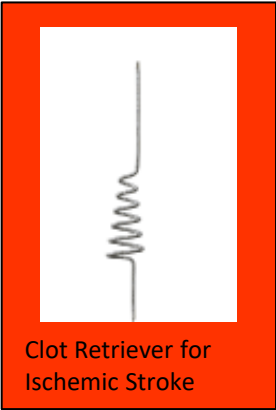
- Guidelines (e.g., Glove Manual)
- Mandatory Performance Standard
- Performance testing, such as biocompatibility, engineering, animal, etc.
- Special Labeling

# Classifications & Regulatory Pathways

- Class III: generally PMA (Premarket Approval)
- Class II: 510(k) (or premarket notification), if the intended use and technology are similar to something already classified
- De Novo: devices that aren't comparable enough to something on the market. This generates a new device classification regulation, and will typically (but not always) be Class II



# Examples from the Neurological and Rehabilitation Medical Devices Field





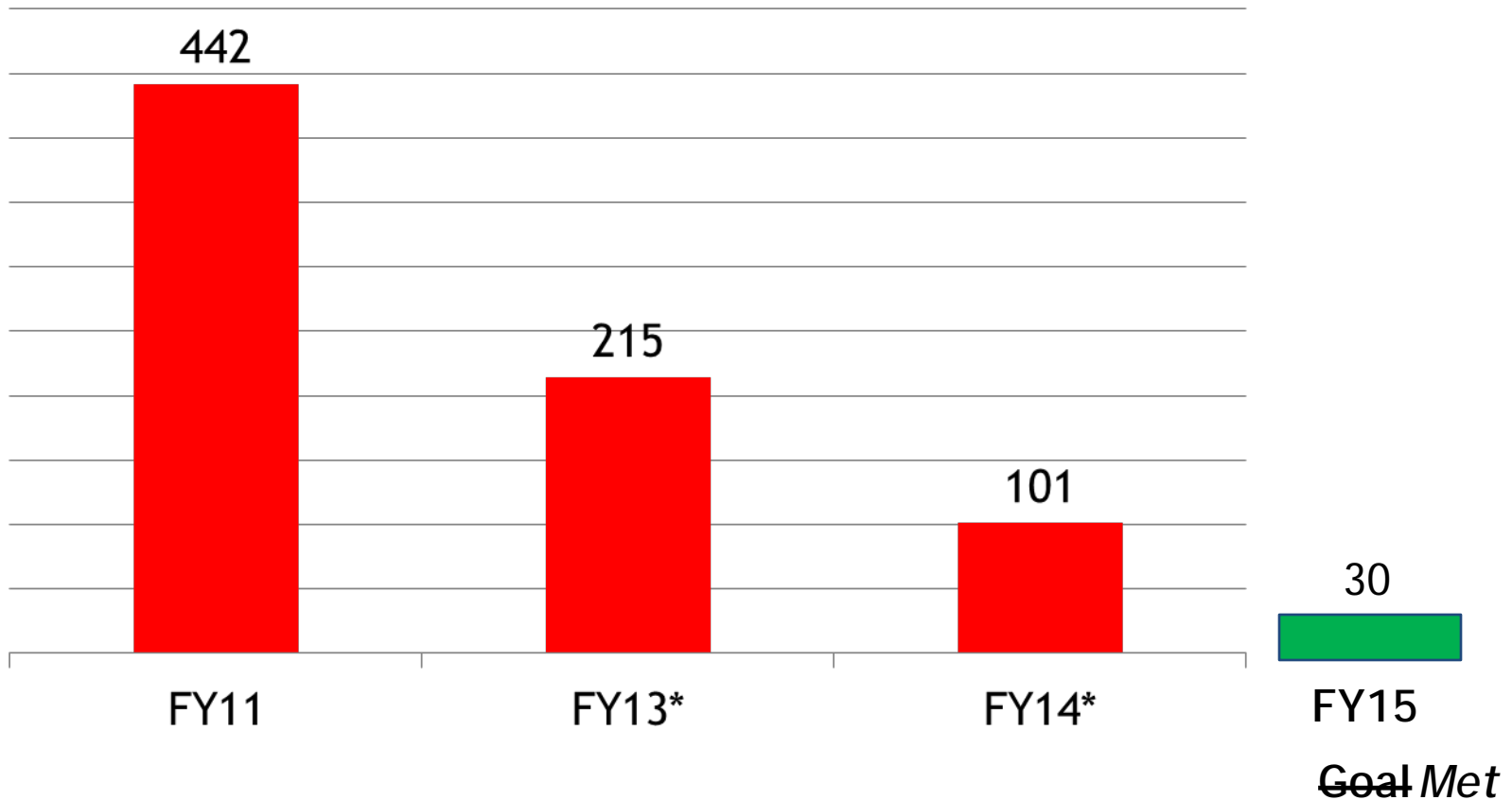
# Investigational Device Exemption (IDE)

- Pertains to devices that have not been approved or cleared for marketing OR that are being tested for a new indication
- IDE allows an investigational device to be used in a clinical study in the US in order to collect safety and/or effectiveness data necessary to support a marketing application (e.g., 510(k), PMA, or HDE)
- May be Approved, Approved with Conditions, or Disapproved depending on adequacy of information submitted to support preliminary safety of subject
- Sponsors/investigators may submit a Presub to obtain preliminary feedback from the FDA (e.g., risk determination, feedback on proposed study design, etc.)



# Reducing FDA Review Timelines

Median Days to Full IDE Study Approval



# What is an Early Feasibility Study?

## IDE - Investigational Device Exemption

- An IDE submission allows an investigational device to be used in a clinical study in order to collect safety and effectiveness data

## EFS IDE - A standard IDE except...

- Small number of subjects (< 10) in the clinical investigation
- Device is generally early in development
- Device iterations are expected
- Limited non-clinical data may be available
- Enhanced clinical mitigations may be required

**EFS is an informal designation**

# How can an EFS benefit you?

## **Permits A More Efficient Pathway to US Commercialization**

- FDA feedback early in product development may help you improve your development strategy and reduce unnecessary testing
- Data collection in the US patient population may be easier to leverage to support later studies or marketing applications

## **Enables collection of high quality clinical data for:**

- Optimizing device design or operator technique
- Refining the intended use population
- Refining nonclinical test plans
- Developing subsequent clinical study protocols

# Increasing Regulatory Transparency

## **NEW Targeted Guidance for Sponsors (and Developers & Innovators)**

- Presubmission Guidance
- IDEs for Early Feasibility Clinical Studies Guidance Document
- Design Considerations for Pivotal Clinical Investigations
- Expedited Access for Premarket Approval Medical Devices Intended for Unmet Medical Need for Life Threatening or Irreversibly Debilitating Diseases or Conditions
- **Clinical Considerations for IDEs for Neurological Devices Targeting Disease Progression and Clinical Outcomes**

# Benefit Risk Considerations

Several considerations when evaluating Benefits and Risks:

- What are the **probable benefits**? Type, magnitude, duration, etc.
- What are the **probable risks**? Type, severity, probability, duration, etc.
- **Additional Factors**, such as:
  - Uncertainty
  - Patient tolerance for risk and perspective on benefit
  - Alternative therapies and their risk profiles

GUIDANCE: Factors to Consider When Making Benefit-Risk Determinations in Medical Device Premarket Approvals and De Novo Classifications

<http://www.fda.gov/RegulatoryInformation/Guidances/ucm267829.htm>

# Focus on Patients

- Patient use and patient preference
  - Incorporating into decision making and establishing appropriate benefit and risk
- Partnering with patients
  - Outreach to patient groups
- Advance use of patient reported outcomes
  - How to identify where gaps are
  - How to validate new measures

GUIDANCE: Patient Preference Information in PMA, HDE and de novo submission

<http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm446680.pdf>

# Mobile Medical Applications

- FDA has made efforts to:
  - Provide clarity and predictability for manufacturers of mobile medical apps
  - Provide information on FDA's current thinking
- FDA has developed team to specifically address questions related to Digital Health ([digitalhealth@fda.hhs.gov](mailto:digitalhealth@fda.hhs.gov))

GUIDANCE: Mobile Medical Applications: Guidance for Industry and FDA  
<https://www.fda.gov/downloads/MedicalDevices/.../UCM263366.pdf>

# General Wellness Products

FDA has provided guidance for general wellness products that present a very low risk to users' safety and are for:

- “An intended use that relates to a maintaining or encouraging a general state of health or a healthy activity, or
- “An intended use claim that associates the role of healthy lifestyle with helping to reduce the risk or impact of certain chronic diseases or conditions and where it is well understood and accepted that healthy lifestyle choices may play an important role in health outcomes for the disease or condition.”

GUIDANCE: General Wellness: Policy for Low Risk Devices

<https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm429674.pdf>



# Using Real World Data

- Real world evidence is collected routinely
- FDA is exploring ways real world data can be used to support regulatory decision making
- Need to ensure that data is of sufficient quality

GUIDANCE: Leveraging Real World Evidence in Premarket Submissions  
Guidance

<https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm513027.pdf>

# Pre-Submissions

- An opportunity to obtain **FDA feedback** prior to IDE or marketing submission
- Meeting (optional) within 75 days after submission
- Written feedback 5 days in advance of meeting
- Obtain feedback on proposed clinical and/or non-clinical test protocols and proposed regulatory paths

GUIDANCE: Requests for Feedback on Medical Device Submissions: The Pre-Submission Program and Meetings with Food and Drug Administration Staff  
<http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm311176.pdf>

# Why Engage As Early As You Can?

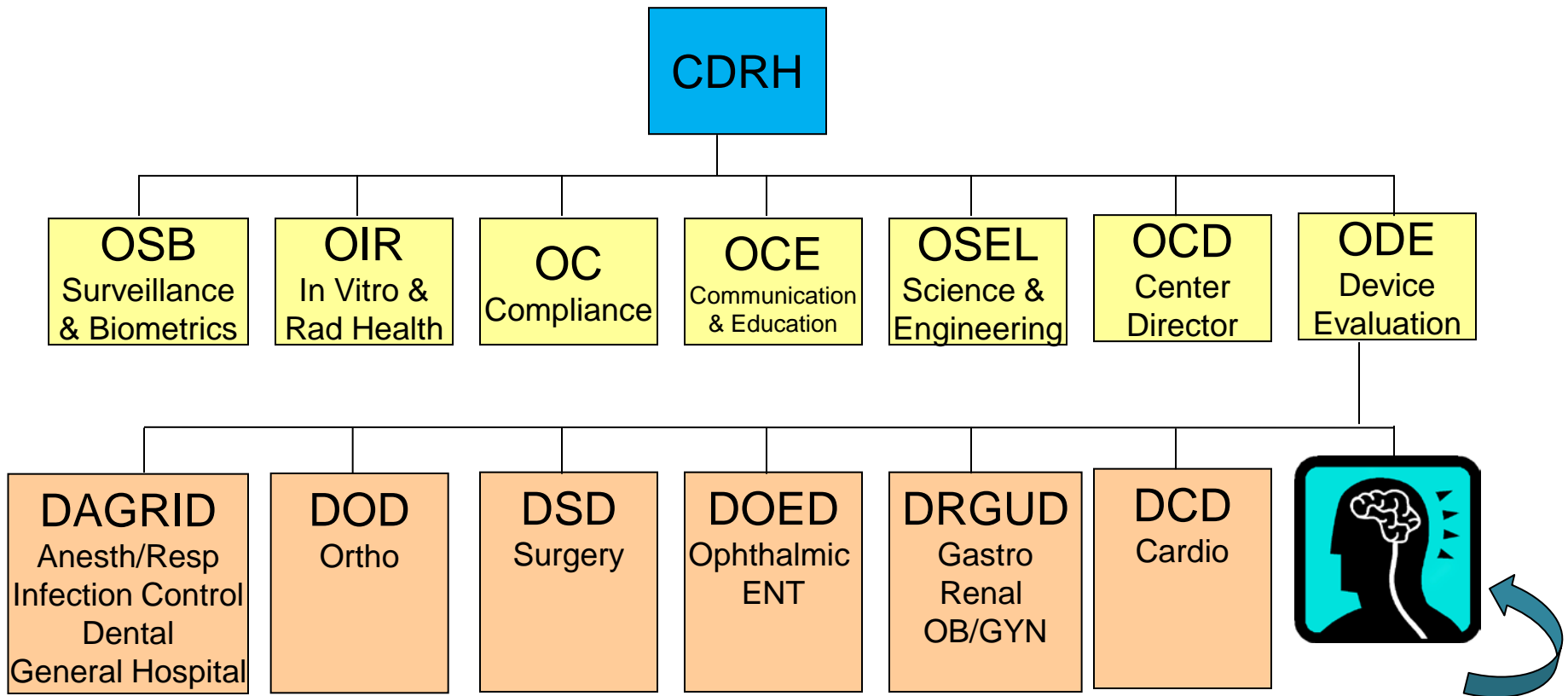
- Pre-submission interactions allow potential issues to be identified earlier, and we can work through them with you as appropriate
  - This is particularly useful if there are concerns related to novel technology or testing
- If needed, you can submit a supplement to get additional feedback



# Investing in Review-A New Division at FDA

## Center for Devices and Radiological Health (CDRH) Organization

### Pathway for Neurological and Physical Medicine Regulatory Submissions



## Division of Neurological and Physical Medicine Devices

# Division of Neurological and Physical Medicine Devices

## Neurodiagnostic and Neurosurgical Devices

- Cranial Materials & Other Sealants
- EEG & Non-EEG Diagnostic Devices
- Neurocognitive Diagnostic Devices
- Surgical Instruments & Tools
- Stereotactic Systems
- Dural Sealants

## Neurointerventional Devices

- Embolization Coils
- Flow Diverters
- Guidewires & Catheters for the Neurovasculature
- Neuro-thrombectomy Devices
- Neurovascular & Cerebral Interventional Devices
- Cerebrospinal Fluid Shunts

## Neurostimulation Devices Neurology Branch

- Stimulation Devices for Movement Disorders, Epilepsy, Alzheimer's Disease, Headache, and Traumatic Brain Injury
- Devices may include cortical stimulation devices and deep brain stimulation devices

## Neurostimulation Devices Psychiatry Branch

- Stimulation Devices for Major Depression, Obsessive Compulsive Disorder, and Post Traumatic Stress Disorder
- Stimulation for Pain Conditions
- Devices may include cranial electrical stimulation devices, electroconvulsive therapy, and transcranial magnetic stimulation devices

## Physical Medicine & Rehabilitation Devices

- Brain Computer Interfaces
- Diathermy
- Functional Electrical Stimulators
- Iontophoresis Devices
- Massagers/Vibrators
- Orthoses, Exoskeletons
- Powered Muscle Stimulators
- Rehabilitation Equipment
- Wheelchairs, Walkers

# Points of Contact

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# Resources

- Early Feasibility Study (EFS) Guidance  
<https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm279103>
- Pre-Submission Guidance  
<https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm311176.pdf>
- IDE Submission Information  
<http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionIDE/ucm046706.htm#regele>
- Design Controls Guidance  
<http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070627.htm>
- Electronic Submissions Guidance  
<https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm313794.pdf>
- EFS CDRH Learn Modules  
[http://www.accessdata.fda.gov/cdrh\\_docs/presentations/EFS/story.html](http://www.accessdata.fda.gov/cdrh_docs/presentations/EFS/story.html)
- 510(k) Guidance  
<https://www.fda.gov/downloads/MedicalDevices/.../UCM284443.pdf>

# Resources

- Expedited Access Pathway Guidance  
<https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM393978.pdf>
- Benefit Risk Guidance for PMA and De Novo Submissions  
<https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm517504.pdf>
- Benefit Risk Guidance for IDE Submissions  
<https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm451440.pdf>
- Patient Preference Information in Premarket Submissions Guidance  
<https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm446680.pdf>
- Leveraging Real World Evidence in Premarket Submissions Guidance  
<https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm513027.pdf>
- Design Considerations for Pivotal Clinical Investigations Guidance  
<https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM373766.pdf>



# It's About the Patients



## Thank You

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