Designing Clinical Studies and Navigating the U.S. FDA Approval Process
Focus on Moving Neurological Devices and Brain Computer Interfaces to Patients

Author-Carlos Peña, PhD
Chief Regulatory Officer & Chief Quality Officer,
Jacobs Institute, USA
cpena@jacobsinstitute.org
CEO, Charlie Company, LLC
www.charliecompanyllc.org

A little background

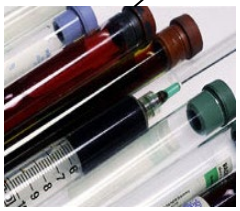
- **Entrepreneurship: Chief Regulatory Officer & Chief Quality Officer at The Jacobs Institute**
- **CEO: Lead a Regulatory Consulting Firm based outside Washington DC-Drugs, Biologics, Devices, and Combination Medical Product Areas**
- **Government: Past Director, FDA Office of Neurological and Physical Medicine Devices, at the FDA's Center for Devices and Radiological Health**
- Clinical Research: Principal Investigator for the first FDA Sponsored Pediatric Study on Neurological Devices
- Regulatory: Participant in the Medical Devices Innovation Consortium for Neurovascular Devices & EFS Studies (FDA, CMS, Industry Roundtable)
- Clinical Trials: Administrative Officer and Consultant for 10+ Early Feasibility Studies in Buffalo and counting…

Agenda

An Introduction to FDA Regulation
Neurological Device Clinical Trials
Closing Thoughts

Center for Food Safety & Applied Nutrition

Center for Drug Evaluation & Research



Center for Biologics Evaluation & Research

Center for Tobacco Products

Center for Devices & Radiological Health (CDRH)

Center for Veterinary Medicine

National Center for Toxicological Research

- **Patients 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.

Medical Device Definition

- 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 humans… or
  - "…intended to affect the structure or any function of the body … and which does not achieve any of its primary intended purposes through chemical action…."

A Risk Based Approach for Medical Devices since 1976

Increasing Risk

Classification determines extent of regulatory control (Risk Based)

Class I
low risk
- Generally exempt from premarket review
- In some cases require 510(k) / De Novo

Class II
Moderate/Controlled Risk
- Requires 510(k) to demonstrate substantial equivalence / De Novo if no classification exists

Class III
High Risk
- Requires PMA (Premarket approval)

General Controls [Electronic Establishment, Registration, Electronic Device Listing, Quality Systems, Labeling, Medical Device Reporting (MDR)]

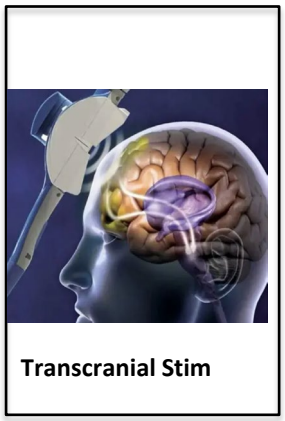
Performance standards
Special Controls [Controls to address safety and effectiveness]

Clinical performance data (to support a reasonable assurance of safety and effectiveness)

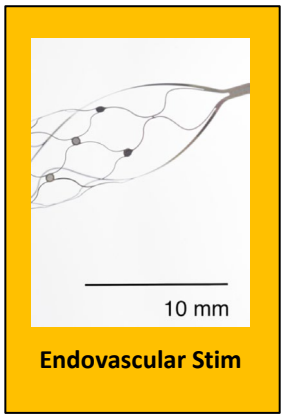
A Variety of Brain Computer Interfaces

From Non-Invasive to More Invasive

Surface Electrodes

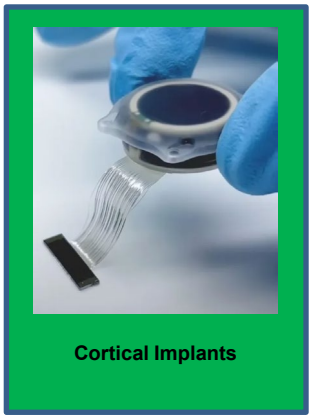


Transcranial Stim



Endovascular Stim

Deep Brain Stimulation



Cortical Implants

When is Clinical Data Needed?

- PMA: always needed
- De novo: typically needed, not always
- 510(k): generally not needed

You can request feedback on any protocols through the pre-submission process, preferably before starting the study

FDA Guidance-A Method to Communicate with Industry

Implanted Brain-Computer Interface (BCI) Devices for Patients with Paralysis or Amputation - Non-clinical Testing and Clinical Considerations

Guidance for Industry and Food and Drug Administration Staff

Document issued on May 20, 2021.

The draft of this document was issued on February 22, 2019.

Investigational Device Exemptions (IDEs) for Early Feasibility Medical Device Clinical Studies, Including Certain First in Human (FIH) Studies

Guidance for Industry and Food and Drug Administration Staff

Document issued on: October 1, 2013

The draft of this document was issued on November 10, 2011.

For questions regarding this document, contact CDRH's Andrew Farb, 301-769-6343, Andrew.Farb@fda.hhs.gov or Dorothy Abel, 301-796-6366, Dorothy.Abel@fda.hhs.gov, or CBER's Office of Communication, Outreach and Development at 1-800-835-4709 or 301-827-1800.

the IDE Submission
Investigational Device Exemption

- Early Feasibility Study
  - Small number of subjects (generally 15 subjects or less)
  - Device may be early in development, before final device design is set
  - Approval may be based on less nonclinical data than for a larger study
- Traditional Feasibility Study
  - Preliminary safety and effectiveness, 20-30 subjects, Near/Final device
- Pivotal Study
  - Designed to collect definitive evidence for a marketing submission

Take Home Messages

- **IDE Submissions are key to demonstrate device readiness**

Investigational Device Exemptions (IDEs) for Early Feasibility Medical Device Clinical Studies, Including Certain First in Human (FIH) Studies

---

Guidance for Industry and Food and Drug Administration Staff

Document issued on: October 1, 2013

The draft of this document was issued on November 10, 2011.

For questions regarding this document, contact CDRH's Andrew Farb, 301-769-6343, Andrew.Farb@fda.hhs.gov or Dorothy Abel, 301-796-6366, Dorothy.Abel@fda.hhs.gov, or CBER's Office of Communication, Outreach and Development at 1-800-835-4709 or 301-827-1800.

Direct Experience in Reducing FDA Review Timelines

Brain Computer Interfaces
Best Practices
Device Description

- A general overview of the whole system including module configurations
- Key component functions with relevant supporting information
- Complete description of every module
  If previously cleared or approved for another indication, the premarket submission number (such as 510(k) or PMA number) with a description of modifications to the cleared or approved devices should be provided.
- Description (for example, drawings, flow charts) of interactions between the various components, the user and patient, and the environment
- For a device that must be assembled or can be adjusted prior to use, an “exploded” view of the individual labeled components relative to each other
- If applicable: a brief description of the software
- If applicable: a complete description of radio frequency (RF) wireless technologies and supporting information
- Built in safety features
- For a device that applies electrical current to the muscle or nerves: provide the output stimulation characteristics
- Description of all devices intended to be used in conjunction with the implanted BCI device

Brain Computer Interfaces Best Practices

Human Factors

- **FDA recommends conducting usability evaluations early in the device design process and repeatedly throughout the device development and evaluation process.**
  - If your device is still under development and you intend to pursue an early feasibility study through an IDE, the early feasibility study could be conducted to obtain initial insights into human factors (for example, difficulties in comprehending procedural steps, insufficient training).
- Human factors validation and evaluation is typically not needed to support feasibility study approvals; however, human factors data may be needed to support your future marketing submission to the FDA.

Brain Computer Interfaces Best Practices

Clinical Performance Testing

Investigational Plan

- Purpose/Objective
- Study design
  - Randomization
  - Controls
  - Performance goals
  - Success criteria
  - Pooling of study populations

See FDA's Guidance for Industry, "E9 Statistical Principles for Clinical Trials" for more details on how to effectively incorporate and analyze multiple subject populations in a single study.

Experience in Supporting Public Access to Neurological Medical Devices

From **Bench to Market**


Clot Retriever for Ischemic Stroke


MRI Technologies


Cognitive Function following concussion


Prosthetic Arm


Bifurcation Stent Designs


Microcatheters for the neurovasculature

Valid Scientific Clinical Trial Evidence* (Business Decision Options)

- Prospective Double Blind, Randomized, Sham-Controlled study
- Prospective Single Blind, Randomized, Sham-Controlled study
- Prospective Open Label Single arm study, with concurrent active control
- Prospective Open Label Single arm study, with retrospective control
- Prospective Open Label Single arm study (+ Lit Review)
- Registry
- Case Series
- Retrospective Review of a Clinical Trial / Chart Review
- Published literature

** Does not include additional considerations such as traditional vs. novel endpoints, number(s) of sites, number(s) of investigators, on-label vs. off-label concomitant treatments, US vs. OUS, standards of care, etc.*

The Pre-Submission Process

Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program

---

Guidance for Industry and Food and Drug Administration Staff

FREE

Document issued on June 2, 2023.

Document originally issued on May 7, 2019.

This document supersedes Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program issued January 6, 2021.

Pre-submissions

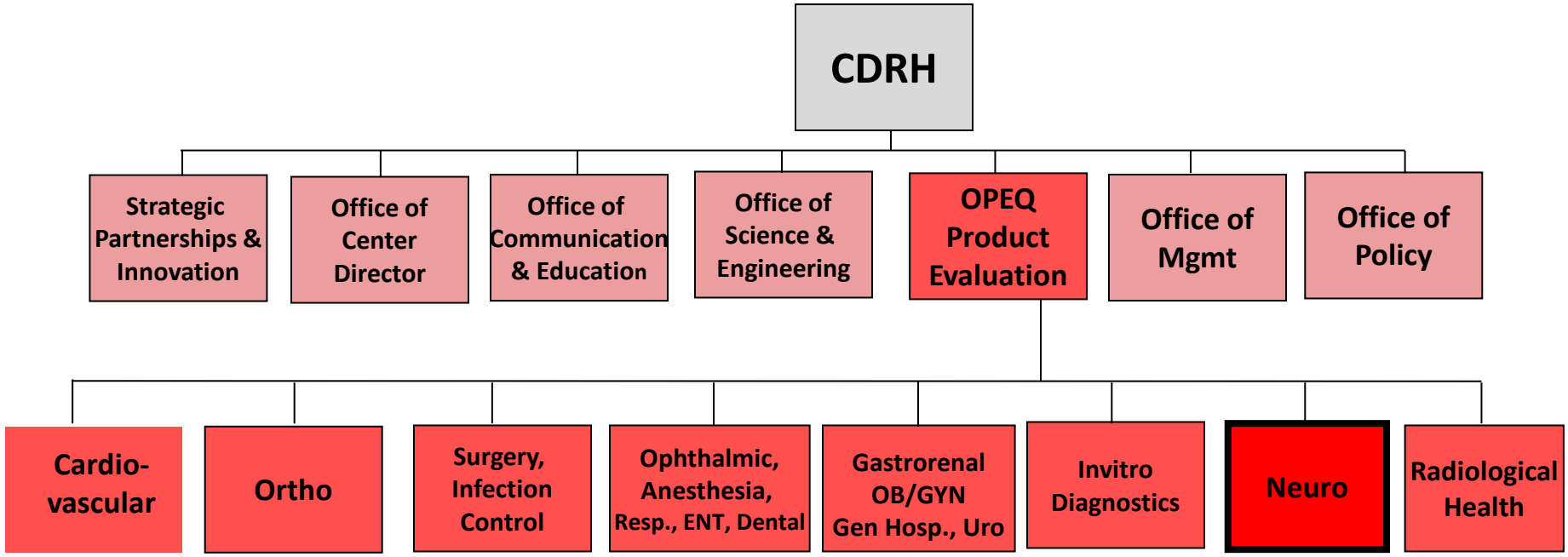
What is it:	**An opportunity to ask questions about a clinical trial design, non-clinical animal study, regulatory pathway, or other questions related to a planned IDE or marketing application prior to submission**
What you get:	**Written feedback in 70 days or 5 days in advance of meeting (whichever sooner)** **Meeting (optional) within 75 days after submission receipt**
What it is not:	**Pre-submissions are NOT intended for "pre-review" of data** **The purpose of any discussion during the meeting is to clarify our feedback, not to respond in real-time to new information or proposals.**

At the heart of FDA? People

Current Medical Device Review Offices at FDA

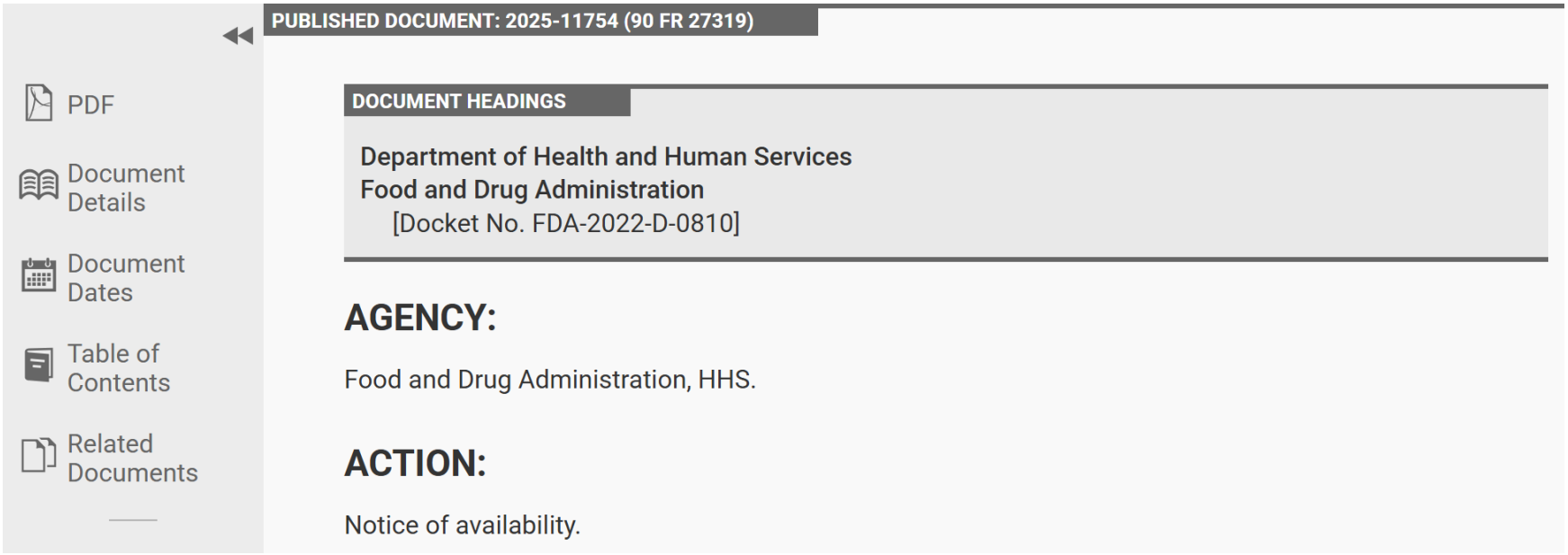
Center for Devices and Radiological Health (CDRH) Organization

Pathway for Cardiovascular and Neurological Regulatory Submissions



Conducting Remote Regulatory Assessments-Questions and Answers; Guidance for Industry; Availability

A Notice by the Food and Drug Administration on 06/26/2025



Take Home Message-Assist FDA in its mission to protect public health, oversee regulated industry, and help ensure regulated products comply with FDA requirements.

Closing Remarks

FDA-It's *always* about the Patients
Contact FDA early in the process
FDA relationships are Key

Resources

- Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program (https://www.fda.gov/regulatory-information/search-fda-guidance-documents/requests-feedback-and-meetings-medical-device-submissions-q-submission-program)

- Listing of IDE-related Guidance Documents (https://www.fda.gov/medical-devices/investigational-device-exemption-ide/ide-guidance)

FDA Regulation of Neurological and Physical Medicine Devices: Access to Safe and Effective Neurotechnologies for All Americans

https://www.cell.com/neuron/pdf/S0896-6273(16)30786-3.pdf