



# Best Practices for Navigating the Pre-submission Process with FDA

Tim Marjenin

Chief, Neurostimulation Devices Branch  
Division of Neurological and Physical Medicine Devices  
Office of Device Evaluation  
Center for Devices and Radiological Health  
Food and Drug Administration

[timothy.marjenin@fda.hhs.gov](mailto:timothy.marjenin@fda.hhs.gov)



# Outline

- Organizational and Regulatory Overview
- Overview of the Pre-Submission Program
  - » Common Issues and Best Practices
- Other Available Resources and Programs



# Organizational Overview: CDRH

## CDRH OFFICES

Office of  
Management  
Operations

Office of  
Surveillance and  
Biometrics

Office of  
Compliance

Office of In Vitro  
Diagnostics and  
Radiological Health

Office of  
Science and  
Engineering  
Laboratories

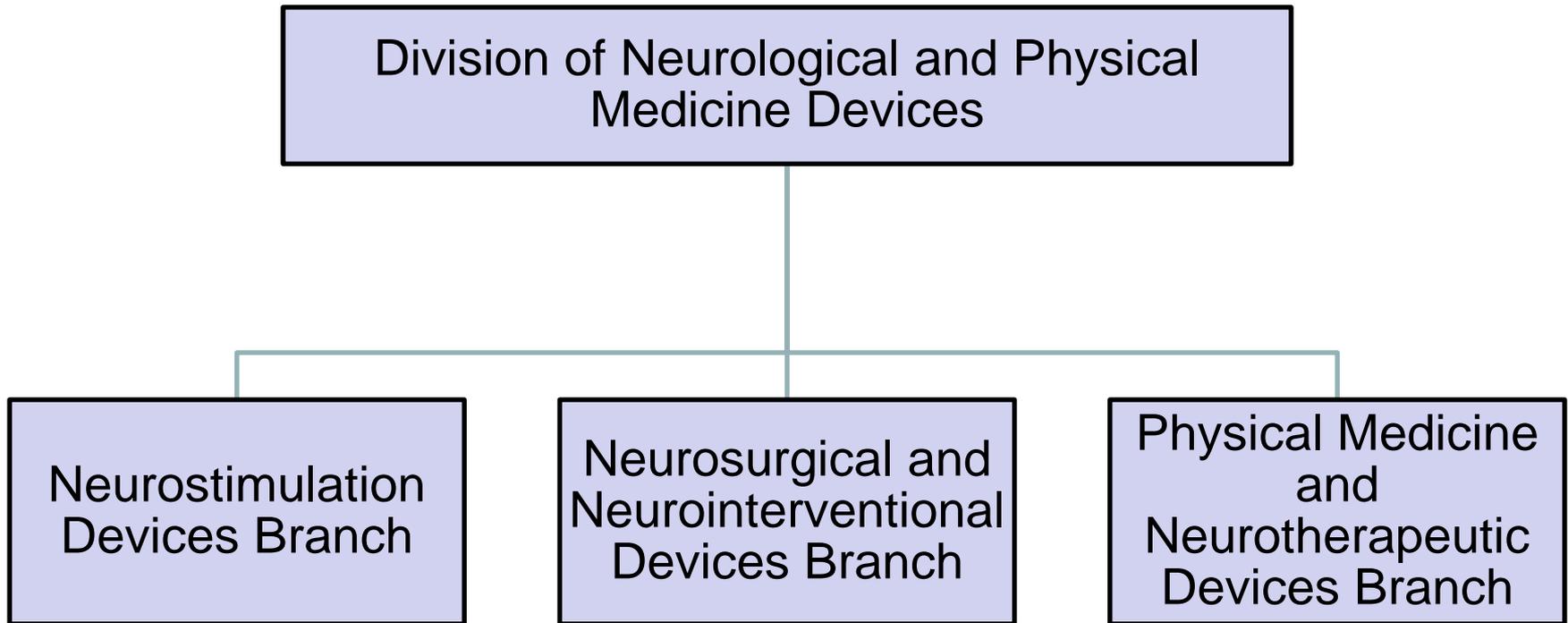
Office of Device  
Evaluation

Office of the  
Center Director

Office of  
Communication,  
Education, and  
Research



# Organizational Overview: ODE/DNPMD



# Neurostimulation Devices Branch

- Deep Brain Stimulation\*
- Spinal Cord Stimulation\*
- Vagus Nerve Stimulation
- External stimulation devices for pain and psychiatric disorders
- Non-EEG Neurodiagnostic devices

\*For uses other than for restoring function



# Neurosurgical and Neurointerventional Devices Branch

- Neurothrombectomy Devices
- Flow Diverter Devices
- Cerebrovascular Aneurysm Coils
- CSF Shunts
- Other Cerebrovascular Guidewires and Catheters
- Cranial Materials and Other Sealants



# **Physical Medicine and Neurotherapeutic Devices Branch**

- Brain-Computer Interface Devices
- Powered Exoskeletons
- Functional Electrical Stimulation Devices
- Electromyography Devices
- EEG-based Neurodiagnostic Devices



# Device Classifications (21 CFR 860.3)

- Based on the level of regulatory control needed to provide a “reasonable assurance of safety and effectiveness”
  - » Class I: subject to only the general controls authorized by the FD&C Act (e.g., toothbrushes)
  - » Class II: general controls alone are insufficient to provide reasonable assurance of its safety and effectiveness, and there is sufficient information to establish special controls (e.g., transcranial magnetic stimulation)
  - » Class III: general controls alone are insufficient, and not enough information to establish special controls (e.g., deep brain stimulation)



# Regulatory Marketing Submissions

- 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 regulation, and will typically (but not always) be Class II

# Humanitarian Device Exemption (HDE)

- Is considered a marketing application, and is similar to a PMA
- As defined in 21 CFR 814 Subpart H, the purpose of the applicable section of the statute (FD&C Act) is “to encourage the discovery and use of devices intended to benefit patients in the treatment or diagnosis of diseases or conditions that affect or are manifested in fewer than 4,000 individuals in the United States per year.”



# **Overview of the Pre-Submission Program**

# Pre-Submission 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/medicaldevice/s/deviceregulationandguidance/guidancedocuments/ucm311176.pdf>
- While the guidance covers multiple types of interactions, today we will focus on the “Pre-Submission”



# Timeframe for Review

- Per the guidance, FDA strives to hold a meeting (if requested) within 75-90 days of acknowledged receipt
  - » If you request a meeting, we will provide written feedback about 3 days in advance of the scheduled date of the meeting
- You should generally plan to meet with us or receive written feedback 75-90 days after receipt, due to workload considerations of review staff
- Make sure you budget your time accordingly

# 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

# Common Issue: eCopy

- Make sure you comply with the eCopy guidance
  - » <http://www.fda.gov/ucm/groups/fdagov-public/@fdagov-meddev-gen/documents/document/ucm313794.pdf>
- Your submission will NOT be officially logged in, the review clock will not start, and nothing else will happen until we receive a valid eCopy
- Questions: [cdRH-eCopyinfo@fda.hhs.gov](mailto:cdRH-eCopyinfo@fda.hhs.gov)



# Submission Contents

- Cover Letter
- Background information, which can include:
  - » Device description
  - » Bench/animal testing protocols
  - » Clinical study protocols
- Specific Questions

# Common Issue: Not Enough Information Provided Upfront

- An analysis of a number of Investigational Device Exemption (IDE) letters showed that the area generating the most questions was “Device Description”:
  - » What the device is and does
  - » Instructions for use
  - » Hazard Analysis
- We encounter similar issues across other submission types



## **How This Impacts the Review Process**

Without enough information to understand the device, CDRH ends up asking a lot of questions. Providing complete responses to our questions takes time, and extends the overall length of the review.

# What You Can Do

- Remember, **YOU** as the applicant know the most about your submission, not FDA
- The more you can explain your thought processes when you submit a pre-submission, the more we can focus on the substance and give you better feedback

# Understand the Existing Landscape

- Search for and review applicable guidance documents and standards (if there are any), such as:
  - » Biocompatibility, if you are not using an approved device (ISO 10993)
  - » “Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices”
- Explain the relationship of what you’re proposing compared to what’s been done in the past



# Guidance Documents

Search:

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

### Filter Results

**Product**  
Medical Devices

**Date Issued**

**FDA Organization**  
Center for Devices and Radiological Health (CD...)

**Document Type**  
Guidance Documents

**Subject**

- 510(k)
- Acidified/Low-Acid
- Administrative Detention
- Administrative / Procedural
- Adverse Event Reporting



# Recognized Standards

Search:

<https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfstandards/Search.cfm>

### Search Database ? Help

Standards Organization

Standard Designation Number   
*Note: numbers only, e.g., 14971, 60601-1*

Standards Title or Keywords  (30 chars. max)  
*Note: do not include standard designation number*

Specialty Task Group Area

[Product Classification](#) Product Code  Regulation Number (e.g., 888.1111)   
*e.g., for vertical standard searches*

Type of Standard   
*(use ctrl button with mouse click to select up to 3 types, e.g., Horizontal, National, Materials Specification)*

FR List Publication Date  to

Sort By

[Quick Search](#) [Clear Form](#)

# Best Practices: Background Information

- It's ok to err on the side of including what you think may be more information than we would need
  - » Make sure it's organized and easy to follow
- If you cite literature articles, please provide copies in the submission
- There is such a thing as too much information:
  - » Circuit diagrams
  - » Lines of software code
  - » A copy of your entire grant

# Best Practices: Background Information

- Avoid assumptions:
  - » Unless there is an applicable guidance, standard, or other regulatory precedent you can cite, identify the most appropriate approach for **YOUR** needs and justify it
  - » Example: not every animal study needs to use a non-human primate model. Some other model and protocol may be better suited to your particular situation

## Common Issue: “Specific” Questions

- Not providing your own proposal for us to review:
  - » “What animal model should we use?”
  - » “How large should the sample size be?”
  
- Wanting FDA to review data:
  - » “Does FDA have any comments on the nonclinical test results?”

# Best Practices: Specific Questions

- The questions should build on the background information you have provided
  - » Good question: “What concerns do you have with our proposed animal model?”
  - » Good question: “Are the proposed sample size calculation method and related elements of the statistical analysis plan appropriate for the proposed clinical study?”



# Other Available Resources and Programs

[www.fda.gov/MedicalDevices](http://www.fda.gov/MedicalDevices)

- CDRH Learn
- Device Advice
- CDRHNew



# Device Advice

- Comprehensive regulatory assistance
  - » Overview of and access to all regulations
  - » Medical device databases for clearances, approvals, and more
  - » “How-to’s” for what to include in the various submission types

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



## CDRH Learn

“CDRH Learn is an innovative multimedia catalog of online educational modules intended to provide information about medical device laws, regulations, and policies that is comprehensive, interactive, and easily accessible.”

This can be helpful if you're new to FDA regulatory processes.

<http://www.fda.gov/Training/CDRHLearn/default.htm>



# CDRHNew

- Updates on guidance documents, approved devices, and other regulatory actions
- Email and RSS subscriptions

<http://www.fda.gov/MedicalDevices/NewsEvents/News/default.htm>

## Not Sure Who to Talk to?

- For simple, basic questions (particularly administrative), start with a branch chief
  - » NSDB: Tim Marjenin (me)
  - » NNDB: Dr. Lin Zheng  
([xiaolin.xheng@fda.hhs.gov](mailto:xiaolin.xheng@fda.hhs.gov))
  - » PNDB: Dr. Vivek Pinto  
([vivek.pinto@fda.hhs.gov](mailto:vivek.pinto@fda.hhs.gov))
- If your question is more detailed and specific, we will likely tell you that it is more appropriately addressed as part of the pre-sub itself



# Thank You!

## Contact Information:

Tim Marjenin

Branch Chief

Neurostimulation Devices Branch

Division of Neurological and Physical Medicine Devices

[timothy.marjenin@fda.hhs.gov](mailto:timothy.marjenin@fda.hhs.gov)