IND-IDE
for Sponsor Investigators

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With color commentary from Rob Silbergleit, MD

Disclosures

- Khatri
  - Dept received funds from Genentech (PRISMS) and Lumosa (consultation, DSMB) Johnson & Johnson shortly (ENDO LOW IIS Grant)
  - Personal consultation to Biogen (DSMB), Greenwich, PTC therapeutics, and medicolegal cases
- Silbergleit
  - None

IND vs IDE FDA Definitions

- An IND, or **investigational new drug application**, is a request for authorization from the FDA to administer an investigational drug or biological product to humans.
  - Center for Drug Evaluation and Research (CDER)
- An IDE, or **investigational device exemption**, allows an investigational device to be used in a clinical study to collect safety and effectiveness data required to support a premarket approval (PMA) application or a premarket notification [510(k)] submission to the FDA.
  - Center for Devices and Radiological Health (CDRH)

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What is a Sponsor? YOU

- Sponsor is an individual, company, academic institution, or other organization that takes responsibility for and initiates a clinical investigation.
  - The sponsor is not the “funding organization” by FDA definitions.

When IND Needed?

- Sponsor/Investigator intends to conduct a clinical study with an **investigational drug**

- Sponsor/Investigator intends to conduct a study with an **approved drug, but…**
  - New indication/population
  - New dosage form or range not covered in the current package insert (i..e, label)

IND Exemption Criteria

- Approved and:
  - Not intended to support a new indication;
  - Not intended to support a change in advertising;
  - Does not involve a factor that increases risk of use;
  - Conducted in compliance with IRB and Informed Consent requirements;
  - Complies with the requirements for promotion and charging of investigational drugs.

Components of IND application

- Final Protocol
- Final Informed Consent Document
- Draft Case Report Forms
- PI CV (signed and current)
- Investigator's Brochure
- Labeling information (if approved drug)
- Letter of Authorization (LOA) to cross-reference a company's product (for off-label use)
- Relevant reference articles

IND Application Organization

- Cover Sheet
- Forms (1571, 1572, 3674)
- Table of Contents
- Introductory statement and General Investigational Plan
- Investigator Brochure (IB)
- Study Protocol and Informed Consent
- *Chemistry, Manufacture, and Control Information (via LOA)*
- *Pharmacology and Toxicology Information (via LOA)*
- *Previous Human Experience (via LOA)*
- Additional Information (draft CRFs, hard-copy reference articles)

IND Approval

- The FDA review team has 30 days to review the original IND submission.
- FDA responds to IND applications in one of two ways:
  - Approval to begin clinical trials.
  - Clinical hold to delay or stop the investigation. FDA can place a clinical hold for specific reasons, including:
    - Participants are exposed to unreasonable or significant risk.
    - Investigators are not qualified.
    - Materials for the volunteer participants are misleading.
    - The IND application does not include enough information about the trial's risks.

Sponsor Responsibilities

Submission	Timing
***Amendment* - New protocol**	**After IRB approval**
***Amendment* - Changed protocol**	**At time of change**
***Amendment* - New investigator**	**Within 30 days of being added**
***Amendment* - Information**	**At time of occurrence**
IND safety report (Serious and unexpected suspected adverse reaction, findings from other studies, findings from animal or in vitro testing, increased rate of occurrence of serious suspected adverse reactions)	**Within 15 calendar days of receiving notification**
IND safety report (Unexpected fatal or life-threatening suspected adverse reaction)	**Within 7 calendar days of receiving notification**
Annual report	**Within 60 days of anniversary of IND**
Withdrawal of IND	**At time of withdrawal**
Discontinuation of investigation	**Within 5 working days of discontinuance**
Financial disclosure report	**At time of change**

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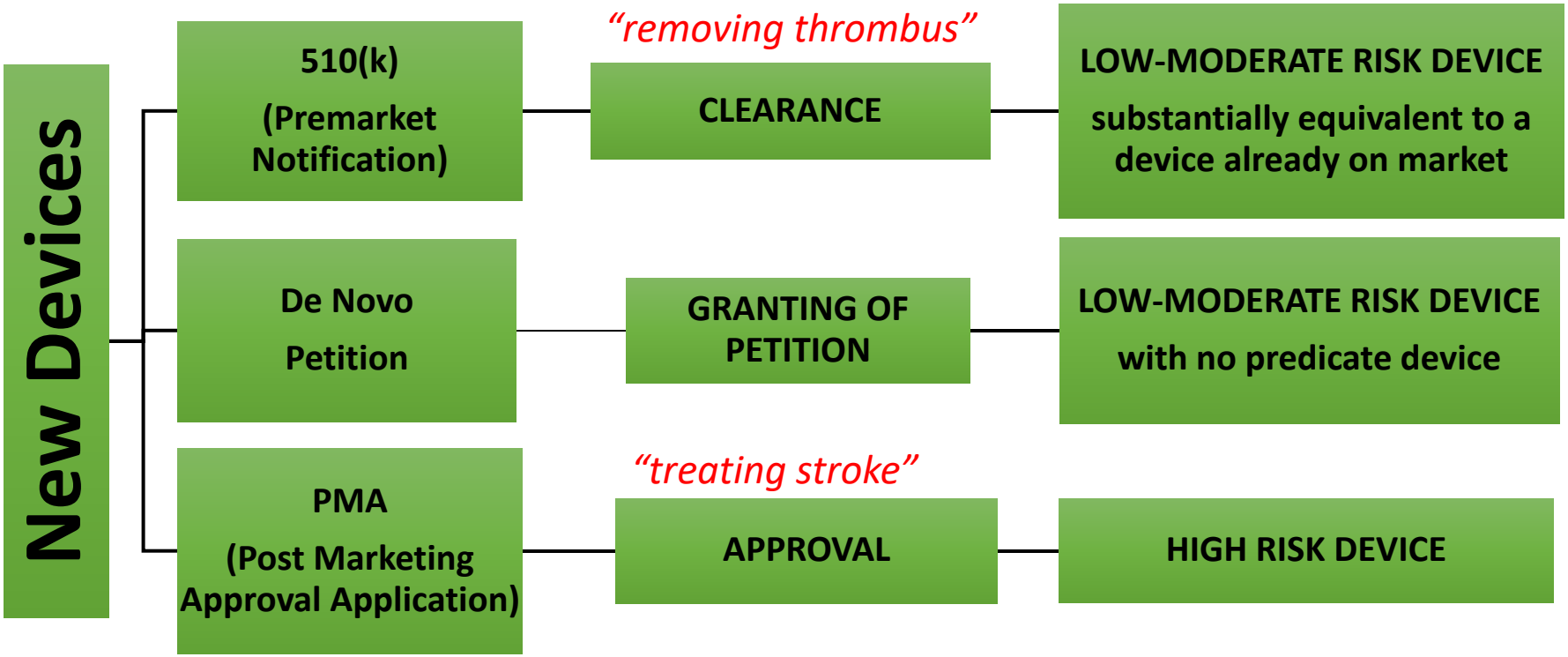
FDA Device Process



- **MERCI Retriever predicate**=Concentric Retriever (foreign body retrieval)
- **Concentric Retriever predicate**=Endovascular Snare, Amplatz Goose Neck Microsnare
- **Prior predicate devices….**

Becker and Brott, Stroke, 2005; Fargen, JNIS. 2012

IDEs

- **All significant risk** devices
- No preprinted forms for an IDE application
- Demonstrate
  - Risks to human subjects are outweighed by the anticipated benefits to subjects
  - Importance of the knowledge to be gained
  - Investigation is scientifically sound
  - Reason to believe device's proposed use will be effective

What is a significant risk (SR) device?

- Is intended as an **implant** and presents a potential for serious risk to the health, safety, or welfare of a subject;
- Is purported or represented to be for use **supporting or sustaining human life** and presents a potential for serious risk to the health, safety, or welfare of a subject;
- Is for a use of **substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health** and presents a potential for serious risk to the health, safety, or welfare of a subject; or
- **Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.**

Who decides SR?

- **Sponsors** are responsible for making the initial risk determination and presenting it to the IRB.
- Modify the determination if the **IRB** disagrees with the sponsor
- **FDA** is also available to help sponsor and IRB
  - FDA is the final arbiter
  - If FDA has already made the SR or NSR determination, this determination is final

IDE Exemption Criteria

- Used in accordance with indications/labeling
- Non-invasive diagnostic
- Consumer preference testing
- Solely for veterinary use
- Research on or with lab animals

IDE Application

- Name and address of the sponsor
- Complete report of prior investigations of the device
- Investigational Plan, including monitoring procedures
- Description of the methods, facilities, and controls used for the manufacture, processing, packing, storage of the device
- Investigational agreement
- Investigator names, institutions, and CVs
- IRB information
- Amount being charged for the device and explanation why the sale does not constitute commercialization
- Labels
- Informed Consent
- Additional information

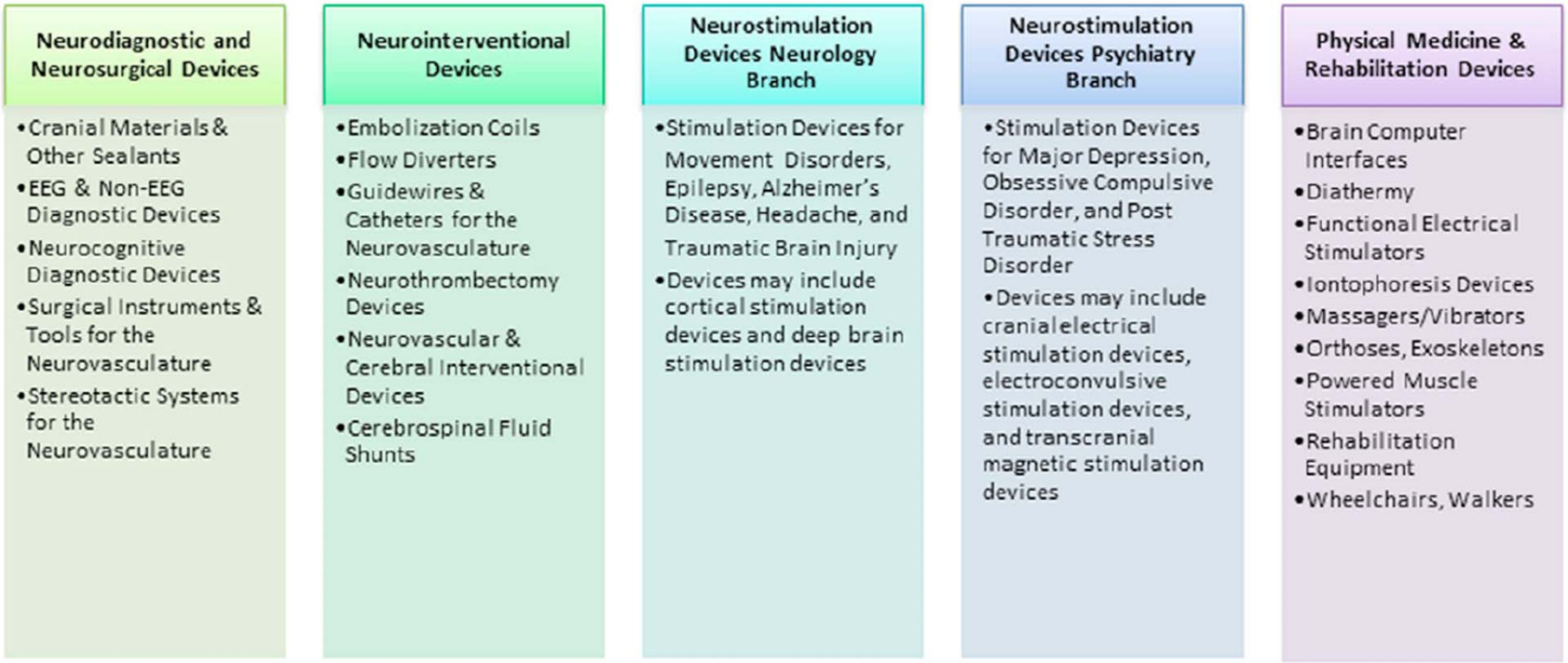


Figure 3. Organization of the Division of Neurological and Physical Medicine Devices and Types of Devices Reviewed in Each Branch

The Division of Neurological and Physical Medicine Devices (DNPMD) is comprised of five branches: the Neurodiagnostics and Neurosurgical Devices Branch (NDNB), the Neurointerventional Devices Branch (NIDB), the Neurostimulation Devices Neurology Branch (NSDN), the Neurostimulation Devices Psychiatry Branch (NSDP), and the Physical Medicine and Rehabilitation Devices Branch (PMDB). Representative neurological and physical medicine devices regulated by CDRH across these five branches are also shown.

Anderson et al, Neuron, 2016

Sponsor IDE Responsibilities

Submission	Timing
***Supplement*- New protocol**	**After IRB approval**
***Supplement*- Changed protocol**	**At time of change**
***Supplement* - New investigator**	**Within 30 days of being added**
***Supplement* - Information**	**At time of occurrence**
Unanticipated Adverse Device Effects	**Within 10 working days of receiving notification**
Recalls and Device Disposition	**Within 30 days**
Progress/Annual report	**At regular intervals (at least yearly)**
Withdrawal of IRB or FDA approval	**Within 5 working days of receipt of notice**
Completion or Termination of investigation – Final Report	**Within 30 days**
http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionIDE/ucm046717.htm	

References

- FDA websites
- MICHR IND/IDE Assistance Program (MIAP)