SPONSOR-INVESTIGATOR IDE TRAINING MODULE 1:

Investigational Device Exemptions

IND/IDE Support Program

May 22, 2024

Children's Hospital of Philadelphia®

OVERVIEW

- Introduction to Devices
- Introduction to Sponsorship
- Regulatory Requirements of an IDE Application
- IDE Determinations: What to expect from the FDA?

INTRODUCTION TO DEVICES

MEDICAL DEVICE: DEFINITION

- An instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is…
  - Recognized in National Formulary and United States Pharmacopeia (USP)
  - Intended for use in diagnosis, cure, mitigation, treatment, or prevention of disease or condition, **or**
  - Intended to affect the structure or any function of the body, and does not achieve primary purposes through chemical action within or on the body and is not dependent upon being metabolized

MEDICAL DEVICES: CLASSIFICATION

- FDA places all medical devices into one of three regulatory classes, based on risk.
- Devices in all three classes are subject to general controls which require, in part, that companies:
  - Register their establishments and list the medical devices they market with FDA
  - Manufacture their devices in accordance with Good Manufacturing Practices
  - Label their devices in accordance with labeling regulations

MEDICAL DEVICE CLASSES

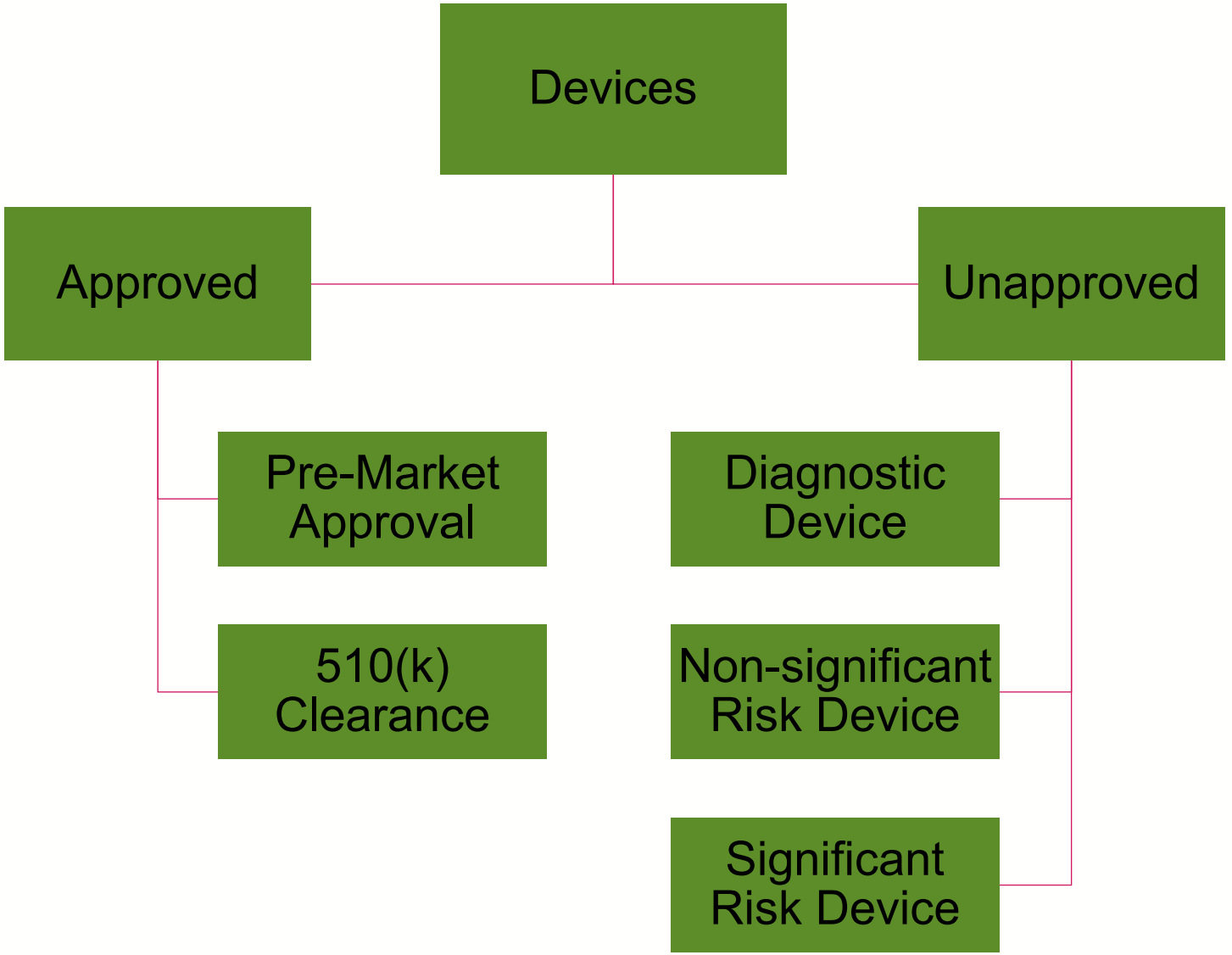
Device Classification	What type of controls are required?	Examples
Class I	• Requires only general controls • Lowest potential for harm and simpler in design than Class II and III devices	• elastic bandages • examination gloves • hand-held surgical instruments
Class II	• General controls are not sufficient to assure the device is safe and effective • Subject to special controls identified by the FDA, which may include special labeling requirements, performance standards and post-market surveillance	• powered wheelchairs • infusion pumps • surgical drapes
Class III	• There is not sufficient information that general or special controls are enough to assure the device is safe and effective	• replacement heart valves • silicone gel-filled breast implants • implanted cerebellar stimulators

IS THE DEVICE AN INVESTIGATIONAL DEVICE?

Investigational device: a device, including a transitional device, that is the object of an investigation.
Investigation: a clinical investigation or research study involving one or more subjects to determine the safety or effectiveness of a device.

Medical Device	Investigational Device
• MRI Scanner • Blood Pressure Cuff • Optical coherence tomography (to visualize retina) • Echocardiography • ECG	• Unapproved MRI sequences • Contact lenses • Unapproved stent

DEVICE CATEGORIZATION



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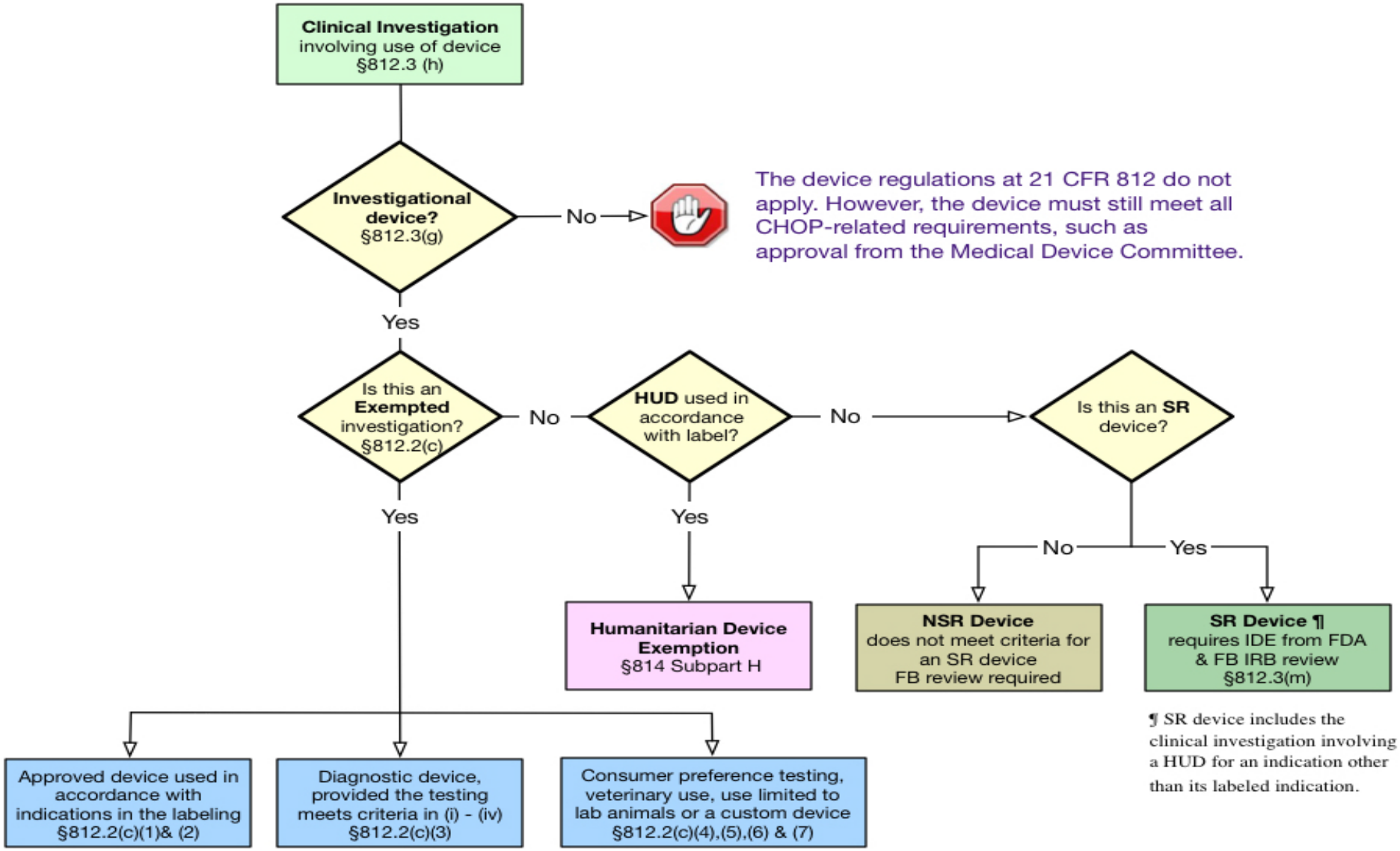
APPROVED DEVICES

- Pre-Market Approval (PMA):
  - FDA determines that there is sufficient valid scientific evidence to provide reasonable assurance that the device is safe and effective for its intended use(s).

- 510(k) Clearance:
  - FDA agrees the new device is substantially equivalent to a legally marketed device for which premarket approval is not required
  - This type of clearance does not frequently require clinical data

IRB REGULATORY PATHWAY FOR DEVICES



¶ SR device includes the clinical investigation involving a HUD for an indication other than its labeled indication.

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EXEMPT STUDIES: NO IDE NEEDED

The device study does not need an IDE when the device is:

- Commercially available and is used according to the FDA labeling
- A diagnostic device, such as a glucometer
- Being tested for consumer preference, for a modification, or for a combination of devices (and the study is not looking at safety or effectiveness, and not putting subjects at risk)
- A veterinary device, or the research is conducted on/with laboratory animals
- A custom device, which is a device that is manufactured for a specific patient.

***21 CFR 812.2 (c);* 812.3(b)**

NON-SIGNIFICANT RISK DEVICE STUDIES

- If the study is using a non-significant (NSR) risk device, there is no IDE submission to the FDA
- The study is submitted for IRB review using an abbreviated IDE pathway
- The IRB serves as the FDA's surrogate for review, approval, and continuing review of the NSR device studies
- The study is still under FDA regulations (for example, labeling requirements)
- An NSR device study may start at the institution as soon as the IRB reviews and approves the study

SIGNIFICANT RISK DEVICE STUDIES

- If the study is using a significant risk (SR) device, there must be both FDA and IRB approval prior to starting

- A SR device is an investigational device that:
  - Is an implant and presents a potential for serious risk to the health, safety, or welfare of a subject;
  - Is for use in the support or sustaining of human life and presents a potential for serious risk to the health, safety, or welfare of a subject;
  - Is used for 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.

21 CFR 812.3 (m)

WHO MAKES THE RISK DETERMINATION?

- The IDE sponsor makes initial determination
- The IRB reviews the sponsor's determination. Information provided by the sponsor includes device description, prior investigations, investigational plan, subject selection, risk assessment and rationale used in making an SR or NSR determination
- If the IRB disagrees with a sponsor's NSR assessment, the IRB must inform the clinical investigator, and where appropriate, the sponsor.
- If the IRB cannot confirm that it is a non-significant risk device, the sponsor submits the study to the FDA, and they provide the final determination if the device is a significant risk or a non-significant risk device.

21 CFR 812.66

IDE Determination Checklist can be found in supplement

STUDY RISK DETERMINATION INQUIRIES TO FDA

- Sponsor submits “Study Risk Determination” Q-Submission
- FDA issues letter indicating if study is
  - Basic physiological research
  - Exempt
  - SR or NSR

The Pre-submission Program and Meetings with FDA Staff: http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM311176.pdf

WHAT IS AN IDE?

- An IDE is a regulatory submission that permits clinical investigation of devices.
- When the IDE is approved, this approval allows a device to be shipped lawfully for the purpose of conducting studies of the device. Without this approval, the device would be required to meet a performance standard or have pre-market approval to be shipped lawfully.

21 CFR 812.1

TYPES OF STUDIES

Types of studies	
Feasibility Study	• Capture preliminary safety and effectiveness data • Typically in a small number of subjects (typically to inform a pivotal study)
Early Feasibility Study	• Small number of subjects • Device may be early in development, before final device design • Approval may be based on less nonclinical data than would be needed to support the initiation of a larger clinical study on a more final device design
Pivotal Study	• Designed to collect definitive evidence of safety and effectiveness for a specified intended use of a device • Typically in a statistically justified number of subjects

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

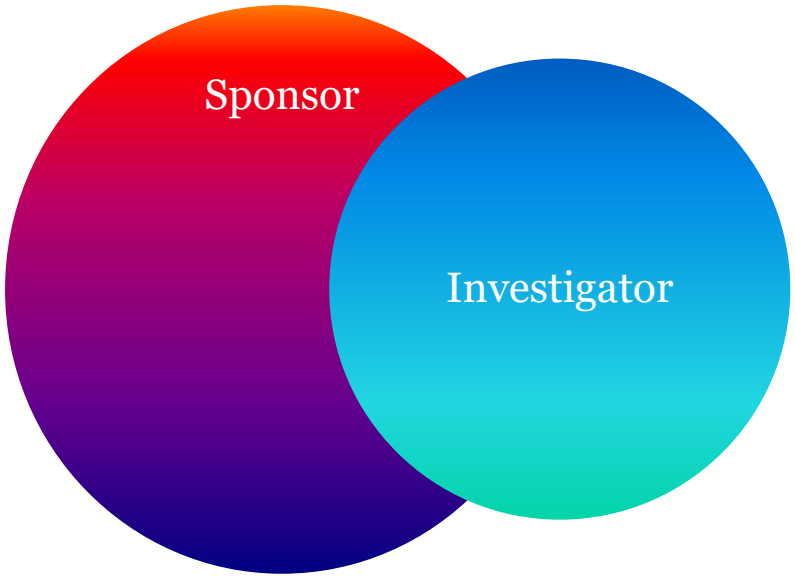
INTRODUCTION TO IDE SPONSORSHIP

KEY ROLES

- Sponsor:
  - Initiates the clinical investigation
- Investigator:
  - Conducts the clinical investigation
- Sponsor-investigator:
  - An individual who both initiates and conducts the clinical investigation. The obligations of a sponsor-investigator include those of an investigator and those of a sponsor

SPONSOR AND INVESTIGATOR RESPONSIBILITIES

Sponsor and Investigator
Separated Responsibility



Sponsor-Investigator
Compounded Responsibility

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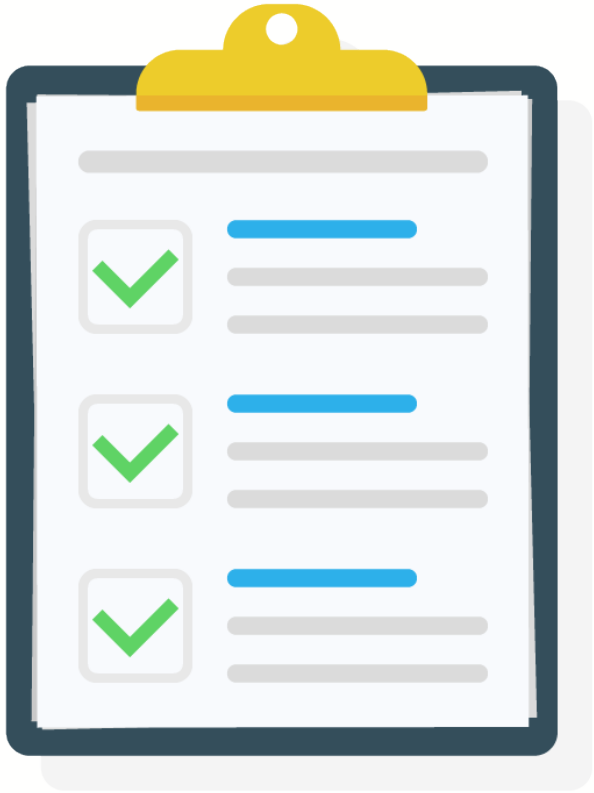
IDE APPLICATION

BEFORE YOU START AN IDE APPLICATION

- A well written protocol, using a CHOP IRB approved template and has been reviewed by the IND/IDE SRC.
- An informed consent document, using a CHOP IRB approved template
- Manufacturers Brochure and/or Instructions For Use for all devices to be used in the study
- 510(k) or PMA Status



THE IDE APPLICATION: OVERVIEW

- Name and address of sponsor
- Report of prior investigations and investigational plan
- Manufacturing, processing, packing, and storage of device
- Investigator agreement
- List of the name, address, and chairperson of each IRB
- Participating institutions
- Charge for device
- Environmental assessment
- Labeling
- Subject materials including informed consent
- Additional information requested by FDA

21 CFR 812.20

Please see additional information regarding IDE Application content in supplement

TYPES OF FDA SUBMISSIONS AFTER APPROVAL

- Supplements
  - Change in protocol
  - Change in device
- Reports
  - Annual progress report
  - Unanticipated adverse device effects
  - Follow up completion report
  - Updated list of investigators (every 6 months)
  - Final report
- Amendment – Change, response to any of above

Reference: CFR 812.35, 812.150

IDE DETERMINATIONS: WHAT TO EXPECT FROM THE FDA?

FDA REVIEW OF THE APPLICATION

- FDA sends the sponsor an acknowledgement with IDE number:
  - GYYxxxxx (e.g. G230001 where the first two digits after G are the year)
- IDE sent to appropriate review division based on the intended use of the device
- Lead reviewer assembles team of experts to review the application and make a decision within 30 days
- FDA issues a decision letter to the sponsor

FDA DECISIONS

- Approval
- Approval with conditions
- Staged Approval
- Disapproval

APPROVAL

- FDA does not have remaining questions that must be addressed prior to enrollment of the approved number of subjects
- Study is approved for a specified number of enrolled subjects and investigational centers
- Study may be initiated upon IRB approval

APPROVAL WITH CONDITIONS

- FDA has determined that, despite some outstanding issues, the information provided in the IDE application is sufficient to allow the study to move forward once IRB approval is obtained.

- The sponsor is not required to resolve these issues prior to starting enrolling on the study, with the exception of certain issues related to the informed consent document (which must be corrected prior to enrollment)

- Sponsor is required to respond to the FDA regarding these issues within 45 days of the FDA's decision letter.

APPROVAL WITH CONDITIONS (CONT.)

- Examples of Conditions:
  - Requests for additional information, data or changes that relate to protecting subjects in the study
  - Late stage follow-up procedures and assessments that relate to the care of study subjects but, because they occur late in the study, will likely be addressed prior to subjects reaching that point in the study

STAGED APPROVAL

- If the study received staged approval, the risk-benefit profile of the study is favorable enough to justify a portion of subjects to be enrolled.
- This type of approval allows a study that might otherwise be disapproved to begin, while at the same time mitigating risk to subjects by limiting how many are exposed to the device.
- The sponsor would be allowed to expand enrollment once an IDE supplement which contains the necessary additional information is submitted to FDA and found to be acceptable.

DISAPPROVAL

- If the FDA disapproves the study, the sponsor will need to submit an amendment to the IDE to respond to the study issues/deficiencies identified in FDA's letter
- The study may not begin until the sponsor receives a letter from the FDA granting approval or approval with conditions

OTHER ELEMENTS OF FDA DECISION LETTERS: STUDY DESIGN CONSIDERATIONS

- Study design considerations are recommendations (not requirements) to help achieve study goals

- Examples include issues related to:
  - Primary and major secondary endpoints
  - Randomization, control, and blinding
  - Follow-up duration and assessments
  - Statistical analysis plan

OTHER ELEMENTS OF FDA DECISION LETTERS: FUTURE CONSIDERATIONS

- Future considerations are intended to provide helpful advice to sponsors regarding important elements of a future marketing application that the IDE may not specifically address

- Examples:
  - Known limitations of the IDE clinical investigation with regard to supporting certain claims or indications
  - Specific non-clinical testing that, while not necessary to support approval of the IDE, will be needed to support the marketing application

WHO TO CONTACT

- IND-IDE Support Office (INDIDE@chop.edu)
- Dr. Greg Podsakoff, Director, Clinical Trials Research (podsakoff@chop.edu)
- Mark Wentworth, IND/IDE Specialist (wentworthm@chop.edu
- IRB Office (IRBoffice@chop.edu

REFERENCES

- FDA Information Sheet Guidance For IRBs, Clinical Investigators, and Sponsors; Frequently Asked Questions About Medical Devices, 2006
- FDA Information Sheet Guidance For IRBs, Clinical Investigators, and Sponsors; Significant Risk and Nonsignificant Risk Medical Device Studies, 2006
- FDA Guidance on IDE Policies and Procedures, 1998
- FDA Guidance on Decisions for Investigational Device Exemption Clinical Investigations, 2014
- 21 CFR 812,
- 21 CFR 50, 56,
- 45 CFR 46
- 21 CFR 812
- 21 CFR 50, 56
- 45 CFR 46
- FDA Presentations
  - (http://www.fda.gov/Training/CDRHLearn/)
- FDA Medical Devices Website
  - http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionIDE/default.htm

Gregory M Podsakoff, M.D.

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