Research with Medical Devices

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Agenda

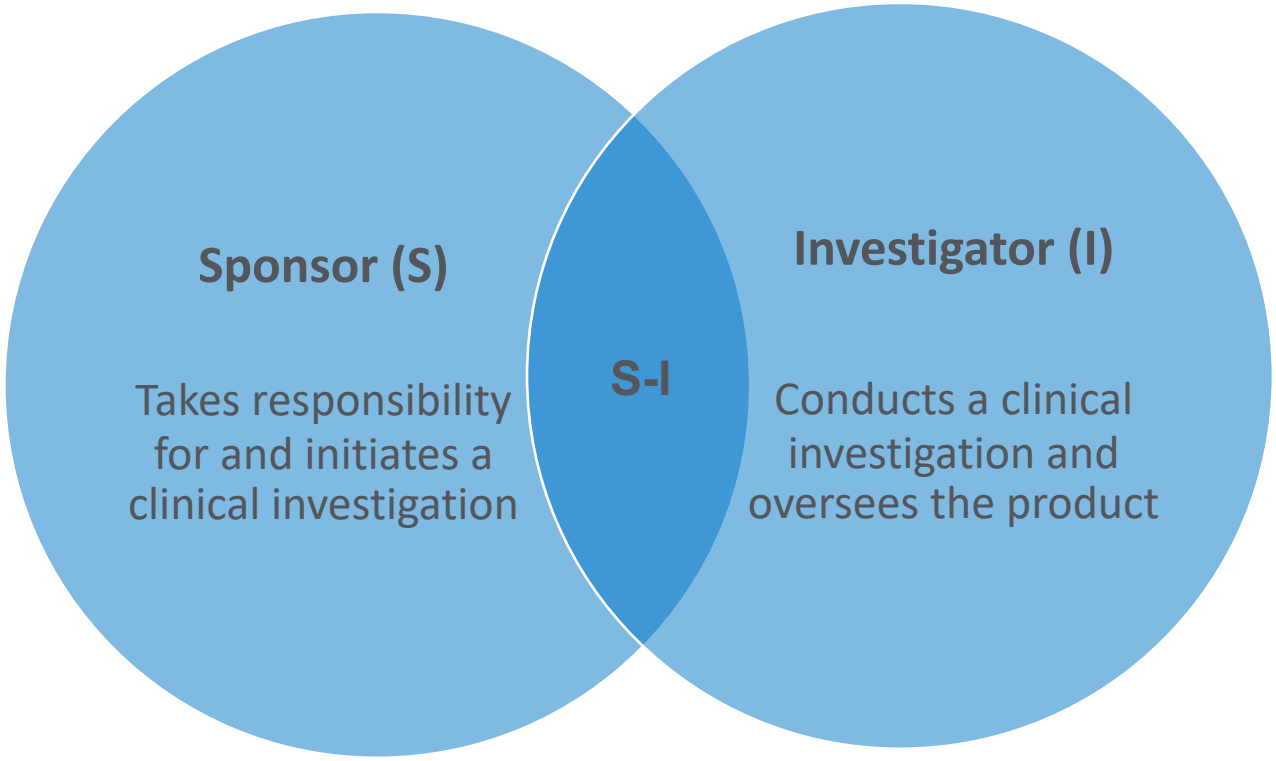
- Regulatory context for clinical investigations
- When an IDE is required
- Sponsor-Investigator Responsibilities
- Application process to FDA
- IRB Submission and Requirements

FDA Regulation

Food and Drug Administration (FDA) regulates the approval process and assures the safety, efficacy, and security of drugs, biological products, medical devices.

- Center for Drug Evaluation and Research (CDER) – 21 CFR 312
- Center for Biologics Evaluation and Research (CBER) – 21 CFR 312
- Center for Devices and Radiological Health (CDRH) – 21 CFR 812

FDA Regulation



Medical Device Regulations

Food, Drug and Cosmetics (FD&C) Act (1938)

- FDA authorized to oversee safety of food, drug and cosmetics
- Title 21 CFR Parts 800 – 1299 cover regulations

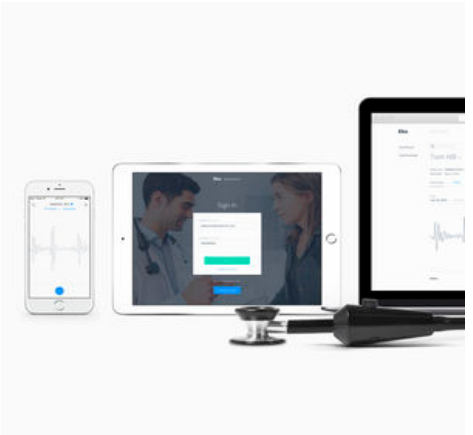
Medical Device Amendments (1976)

- Established device classifications based on risk
- Established Investigation Device Exemption (IDE)

Medical Devices

A medical device is an instrument, apparatus, implement, machine, software/application, contrivance, implant, *in vitro* reagent or a component part or accessory which is:

- Intended for diagnosis, cure or mitigation, treatment or prevention of a disease
- Intended to affect the **structure** or any **function** of the body
- Does not achieve its primary intended purposes by chemical or metabolic action.



Medical Device Classification

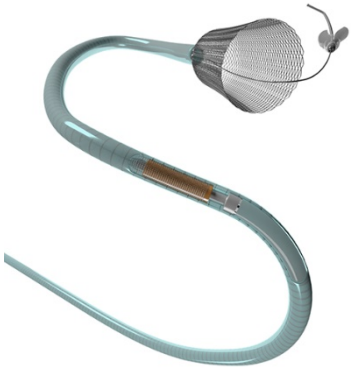
Class I	Class II	Class III
• Lowest risk • Generally exempt from 510(k) • Dental floss, medical scissors	• Intermediate risk • Usually need 510(k) • Power wheelchair, MRI	• Highest risk • Need Premarket Approval (PMA) • Heart valves, stents

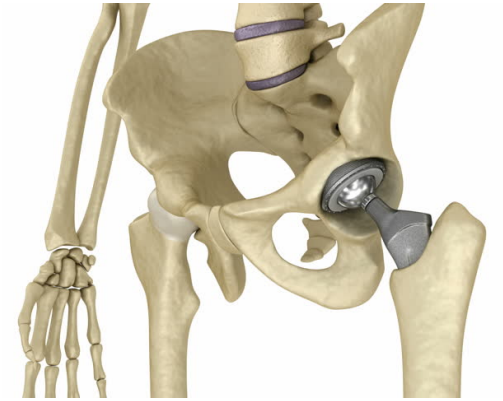
- **PMA** – Evaluates safety and effectiveness of Class III medical devices
- **510(k)** or Premarket notification (PMN) – Clearance for a device that is as safe and effective and substantially equivalent to a legally marketed device

What is a Significant Risk (SR) Device?

Presents a potential for **serious risk** to health, safety and welfare of a subject and is:

- an implant;
- necessary to support or sustain human life;
- of substantial importance in diagnosing, curing, mitigating, treating disease or preventing impairment of human health; **or**
- otherwise poses a risk.





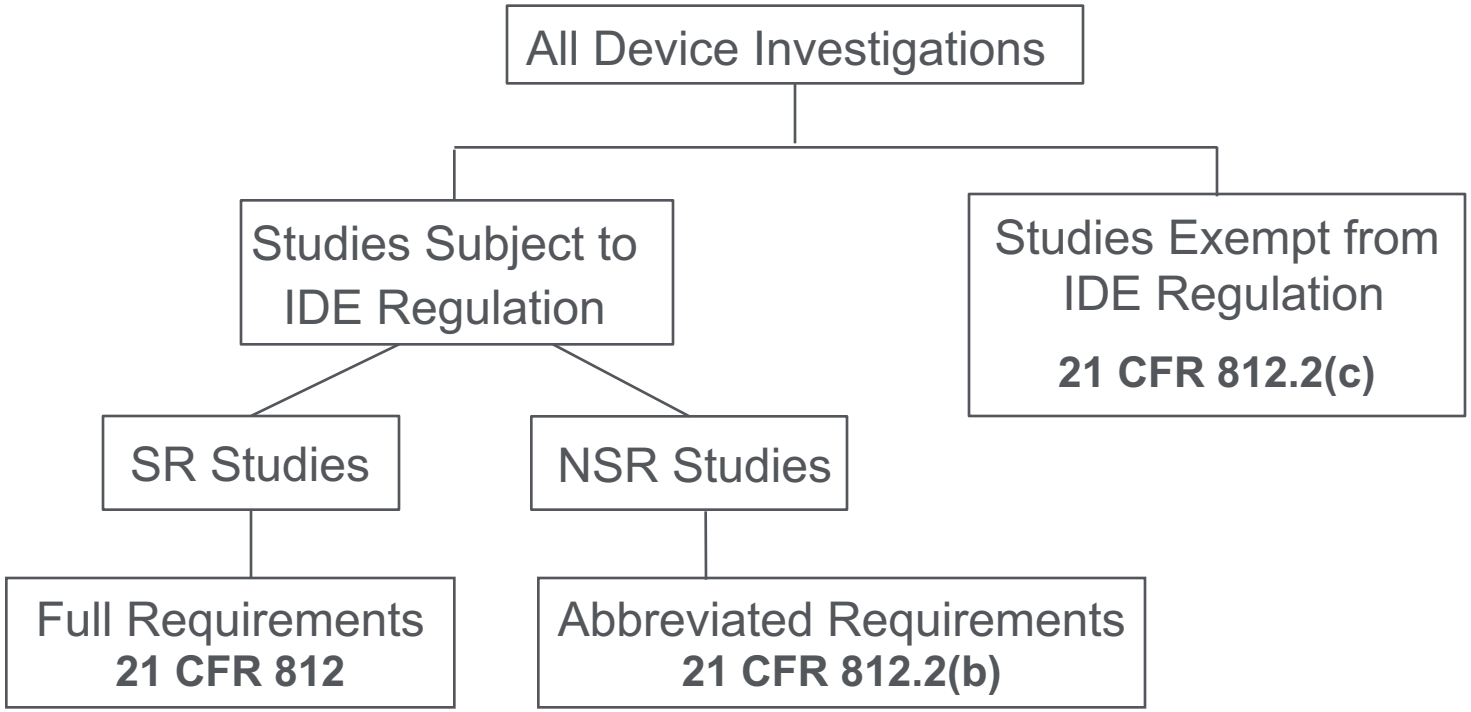
What is a Non-Significant Risk (NSR) Device?

Does not meet the definition of a significant risk device.

SR / NSR Determination

- Sponsors
  - Make the initial risk determination
  - Present the IRB with this information
- IRBs
  - Determine whether the device study involves a SR or NSR device
- FDA
  - Available to help
  - Final arbiter

Investigational Device Exemption (IDE)



Investigational Device Exemption (IDE)

- Permits clinical investigation of devices
- Allows for a device to be shipped lawfully
- All device studies must have an IDE or be exempt from IDE regulations.
- IRB serves as FDA surrogate for NSR investigations.
  - Initial and continuing review

IDE vs. Abbreviated IDE

IDE	Abbreviated IDE
• Significant risk (SR) studies	• Non-significant risk (NSR) studies
• FDA and IRB oversee the study	• IRB oversees the study
• Full requirements	• Abbreviated requirements: – Device labeling – IRB approval – Informed consent – Monitoring – Records and reports – Prohibitive promotion

IDE Exempt Investigations

Studies exempt from the IDE regulations include:

- Legally marketed devices used according to label
- Certain diagnostic devices
- Consumer preference testing, when not determining safety or effectiveness and does not put subjects at risk
- Veterinary devices or research on/with laboratory animals intended solely for veterinary use
- Custom devices (21 CFR 812.3(b))

21 CFR 812.2(c)

In Vitro Diagnostic (IVD) Devices

- Include reagents, instruments, or systems intended for use in diagnosis of disease or conditions
- Considered significant risk (SR) if the use affects the therapeutic type or strategy subjects may be exposed to or includes **invasive** sampling
- Sponsors must have an IDE approved by FDA if a trial includes a SR investigational IVD.
  - Novel IVD
  - IVD legally marketed in US for different intended use
  - Legally marketed IVD that has been significantly modified
  - Applies even if there is no intent to commercialize the IVD

Contents of FDA Application

	IDE Application
FDA Forms	Sponsor information Investigator Agreements (IA) Form FDA 3674
Study Design	Protocol with monitoring plan and risk analysis
Product Information	Device design (diagram of all parts recommended)
Nonclinical Information	Nonclinical laboratory and animal data
Clinical Information (if any)	Report of Prior Investigations (RPI)
Labels	Device label
Attachments	Device manual with manufacturer's information
Format	1 original and 2 electronic copies (eCopy)

FDA IDE Application Approval Process

	IDE Application
Timeline for FDA response	30 calendar days from receipt of application
FDA Determination	• IDE issued (SR) • NSR determination • IDE exempt
Outcomes	• Approval • Approval with conditions • Disapproval • Conversion to Pre-submission track

Common Deficiencies

	IDE Applications
Background and Rationale	• Report of prior publications • Rationale for animal selection and design
Investigational plan	• Study design and objectives • Risks • Monitoring plan
Product information	• Device information • Validation testing • Manufacturing controls

Case Study 1

Dr. H wants to investigate the use of a catheter to detect atrial signals in individuals with atrial fibrillation. The catheter is FDA approved for use in right atrial procedures to assist in the diagnosis of complex arrhythmias, but Dr. H wants to measure signals in the left atrium.

Case Study 2

Dr. R wants to investigate a diagnostic assay and its ability in determining potential therapies for individuals with lung cancer. The assay allows for cultures of tumor cells to be grown in microwells in order to test a range of drugs on the cultured tumor cells. The assay is intended to validate candidate agents that are most effective in targeting the lung cancer cells.

IND/IDE Assistance Program (IAP)

- Collaboration with the IRB
- Regulatory assistance for Sponsor-Investigator trials
  - IND/IDE determination
  - FDA submissions
  - Protocol development
  - Monitoring plans
  - FDA inspections
- Education and training
  - Understanding obligations
  - S-I training and CRC training

Contact Us

Clinical Trials Office (CTO)

154 Haven Avenue, 3rd Floor

New York, NY 10032

Website: https://research.columbia.edu/content/clinical-trials-office

IND/IDE Assistance Program (IAP): INDHelp@columbia.edu

Telephone: (212) 342-2763 / (212) 342-1643

IRB Submission Requirements

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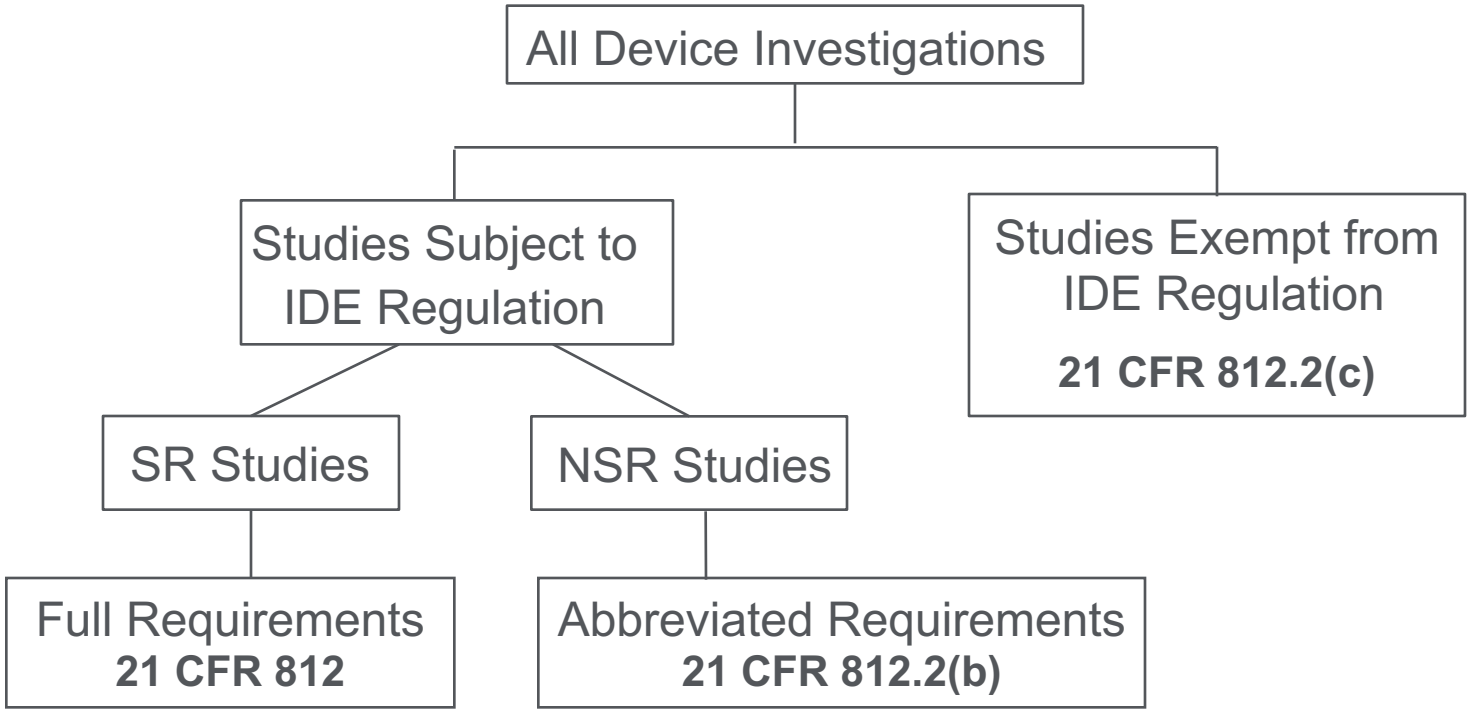
IRB Review of Medical Device Research

- FDA regulations apply when a protocol evaluates the safety or effectiveness of a medical device in subjects, healthy controls or on human specimens
  - FDA Informed Consent Regulations (21 CFR 50)
  - FDA IRB regulations (21 CFR 56)
  - FDA Device Regulations (21 CFR 812)

Regulatory Pathway for IRB Review:



Protocols Exempt from IDE Regulation

- The use of the device meets one of the criteria at 21 CFR 812.2 (c)
- Must still comply with 21 CFR 50 & 56
- If FDA determined that the study is exempt from 21 CFR 812.2 (c) and documentation of this determination is available, the IRB will confirm the determination made by the FDA.
- If not, the IRB will make the determination that the investigation meets one of the IDE exemptions listed at 21 CFR 812.2.(c).

Rascal Pages: Medical Device (Exemption)

- Mark “Yes” to Medical Devices on the Procedures page in Rascal
- Complete the Medical Device page
  - Describe device
  - Address questions related to FDA status
  - Select the applicable category of exemption
  - Attach evaluation by Sponsor or FDA, if available
- Consent document should include reference to FDA in Confidentiality section
- IDE exempt trials could still be inspected in response to a problem or issue with the device.

Rascal Pages: Medical Device (Exemption)

*Is the device *FDA-approved* and used in accordance with its labeling?

( ) Yes (•) No

An Investigational Device Exemption (IDE) may be required.

*Select Category:

(•) Not FDA-approved ( ) FDA-approved but not being used in accordance with labeling

*Provide plans for storage, control and accounting of the device:

*Is an FDA-issued Investigational Device Exemption (IDE) required?

(•) No. The criteria for exemption from the IDE requirements are met.

( ) Yes. This is a Significant Risk Device.

( ) No. This is a Nonsignificant Risk device (21 CFR 812.2(b)).

*Select the applicable category of exemption for this device:

( ) 21 CFR 812.2(c)(3) criteria met - The device is a diagnostic device and the sponsor complies with applicable requirements in 21 CFR 809.10(c). In addition, the testing: (i) Is noninvasive; (ii) Does not require an invasive sampling procedure that presents significant risk; (iii) Does not by design or intention introduce energy into a subject; and (iv) Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure.

( ) 21 CFR 812.2(c)(4) criteria met - A device undergoing consumer preference testing, testing of a modification, or testing of a combination of two or more devices in commercial distribution, and the testing is not for the purpose of determining safety or effectiveness and does not put subjects at risk.

( ) 21 CFR 812.2(c)(7) criteria met - A custom device as defined in 812.3(b), unless the device is being used to determine safety or effectiveness for commercial distribution.

Protocols Subject to IDE Regulation

- IRB may receive protocols with a valid FDA approved IDE application or documentation that the protocol is subject to abbreviated IDE requirements
- In other circumstances, the convened IRB must assess use of the device in the protocol and document their device determination
  - Significant Risk Device
  - Non-Significant Risk Device

Sponsors are responsible for making the initial risk determination

Rascal Pages: Medical Device

- Mark “Yes” to Medical Devices on the Procedures page in Rascal
- Complete the Medical Device page
  - Describe device
  - Address questions related to FDA status
  - Select the whether the device is a Significant Risk Device or a Non-Significant Risk Device and complete fields that are generated
  - If Sponsor has assessed the device to be Non-Significant Risk, describe justification in “device description” on Medical Device page or refer IRB to Sponsor’s justification
  - Attach evaluation by Sponsor or FDA if available

Rascal Pages: Medical Device

*Is the device *FDA-approved* and used in accordance with its labeling?
◯ Yes ◉ No

An Investigational Device Exemption (IDE) may be required.

*Select Category:
◯ Not FDA-approved ◯ FDA-approved but not being used in accordance with labeling

*Is an FDA-issued Investigational Device Exemption (IDE) required?
◯ No. The criteria for exemption from the IDE requirements are met.
◉ Yes. This is a Significant Risk Device.
◯ No. This is a Nonsignificant Risk device (21 CFR 812.2(b)).

*Select the current status of the IDE:
◯ IDE number assigned (include all numbers and letters) ◯ IDE pending ◯ IDE application not yet submitted

*IDE holder name:
0 / 100

*IDE holder address:

*IDE holder contact info:

*Select type of IDE holder:
◯ Columbia University Faculty
◯ Industry, e.g., pharmaceutical company or device manufacturer
◯ Federal Agency
◯ Non-profit organization
◯ Other

Submission Requirements: Medical Devices

- Device manual, if industry-sponsored;
- Documentation of current FDA status;
- Completion of Rascal Device Page
- Data and safety monitoring plan (DSMP);
- Device management plan;
- Clinical Investigator Agreement; and
- Centers for Medicare and Medicaid Services (CMS) coverage decision.

Submission Requirements: Medical Devices

- If the study constitutes S-I research, additional consideration must be given as to **how compliance with FDA requirements will be maintained**
- **Form of Notice** by CU Faculty IDE Holder letter that documents the Department Chair and the S-I both have provided commitment that adequate resources will be provided that will permit the conduct of the study in compliance with FDA regulatory requirements
- **Completion of TC0096**: FDA Requirements of Sponsor-Investigator Studies

Significant Risk Device

- IRB evaluates seriousness of harm that may result from use of the device in protocol related tests and procedures in addition to the harm that may be caused by the device alone
- If SR: The Sponsor (which could be the PI) must submit an IDE application to the FDA and obtain the agency's approval of the study
- IRB will not approve the submission but will require re-review by the convened IRB

Non-Significant Risk Device

- Study may start as soon as the IRB reviews and approves the study and without prior approval by the FDA.
- IRB serves as the FDA's surrogate for review, approval and continuing review of the device study.
- FDA considers an NSR device study to have an approved IDE after IRB approval and when sponsors meet the **abbreviated requirements at 21 CFR 812.2(b)**.

Consultation

- When in doubt regarding the risk category for a medical device, contact the HRPO and CTO (IND/IDE Assistance Program (IAP)).

Contact Us

Human Research Protection Office (HRPO)

154 Haven Avenue, 1st Floor

New York, NY 10032

Walk-in Consultations: Tuesdays, 10-11 am

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