# Introduction to Investigational Device Exemption (IDE)

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# Outline of Presentation

- What is an IDE
- The purpose of an IDE submission
- What an IDE does and does not permit
- When one should seek an IDE
- Significant and Non-Significant Risk (examples)
- General process and requirements of an IDE application

# Investigational Device Exemption

- An IDE is a **regulatory submission** that permits clinical investigation of devices/IVDs
- IVD tests: any combination of equipments, instruments, reagents, software, procedures, algorithms used in clinical trials outside their cleared/approved intended uses are investigational devices
- This investigation is **exempt** from some regulatory requirements
- The term “IDE” stems from this description in 21 Code of Federal Regulations (CFR) 812.1:

  *“An approved investigational device exemption (IDE) permits a device that otherwise would be required to comply with a performance standard or to have premarket approval to be shipped lawfully for the purpose of conducting investigations of that device.”*

# Approved IDEs are Exempt from Regulations Pertaining to:

- Misbranding
- Registration
- Pre-Market Notification [510(k)]
- Pre-Market Approvals (PMAs)
- Performance standards
- Good Manufacturing Practices (GMPs) **except Design Controls**
- Color additive requirements
- Banned devices
- Restricted device requirements

**21 CFR 812.1**

# Approved IDEs are not Exempt from Regulations Pertaining to:

- Adulteration
- Labeling
- Prohibition of: promotion and/or marketing, commercialization, prolonging the investigation, representing the device as safe and effective
- Import/export requirements

**FD&C Act, Section 501; 21 CFR 812.5, 812.7, 812.18**

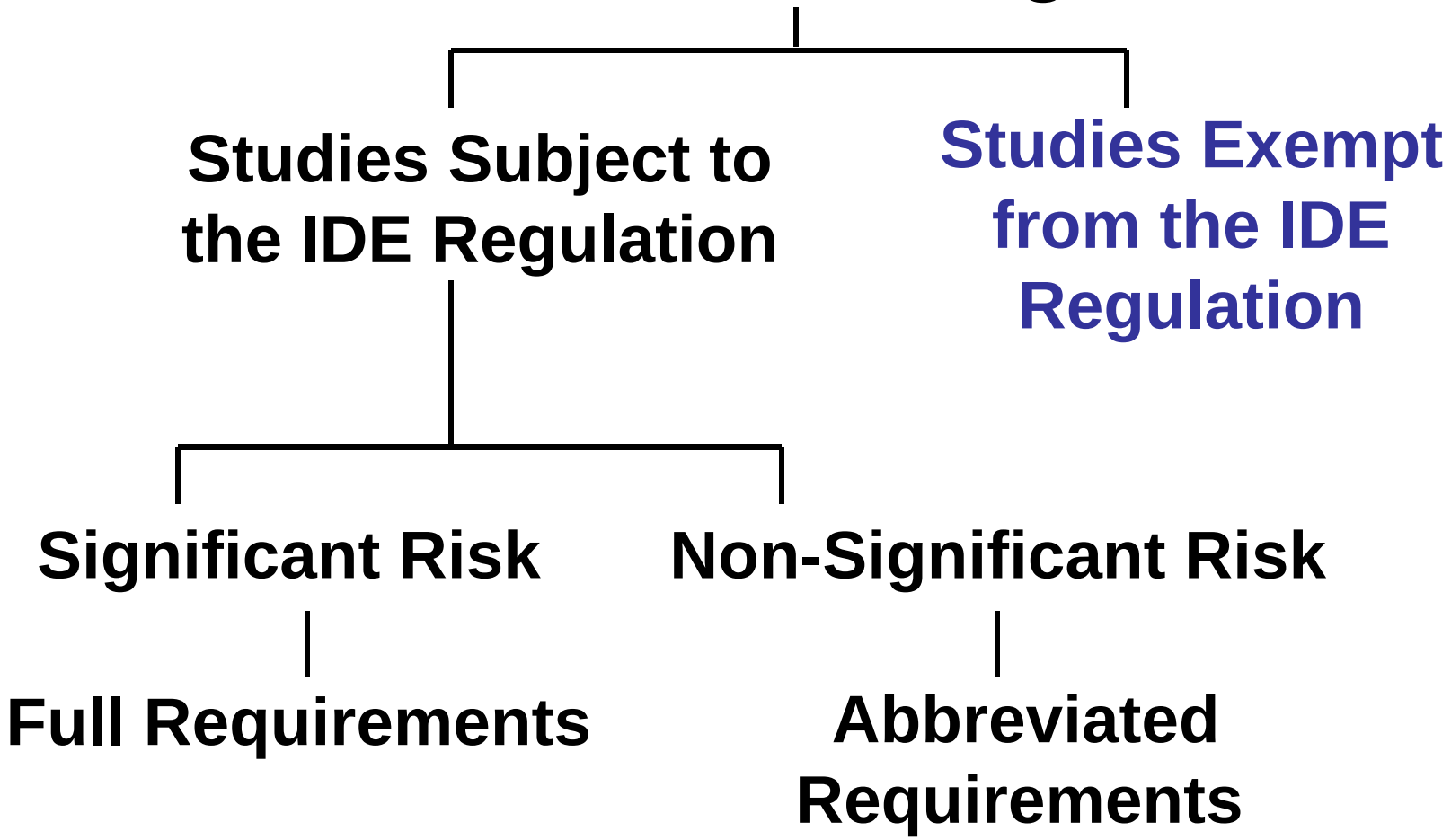
# Purpose of an IDE

An approved Investigational Device Exemption allows:

- an investigational device to be used in a **clinical study** in order to collect **safety and effectiveness data** required to support a Premarket Approval (PMA) application, a Premarket Notification [510(k)] submission to FDA, or a Humanitarian Device Exemption (HDE)

- a device to be **shipped lawfully** for the purpose of conducting investigations

# All Device Investigations

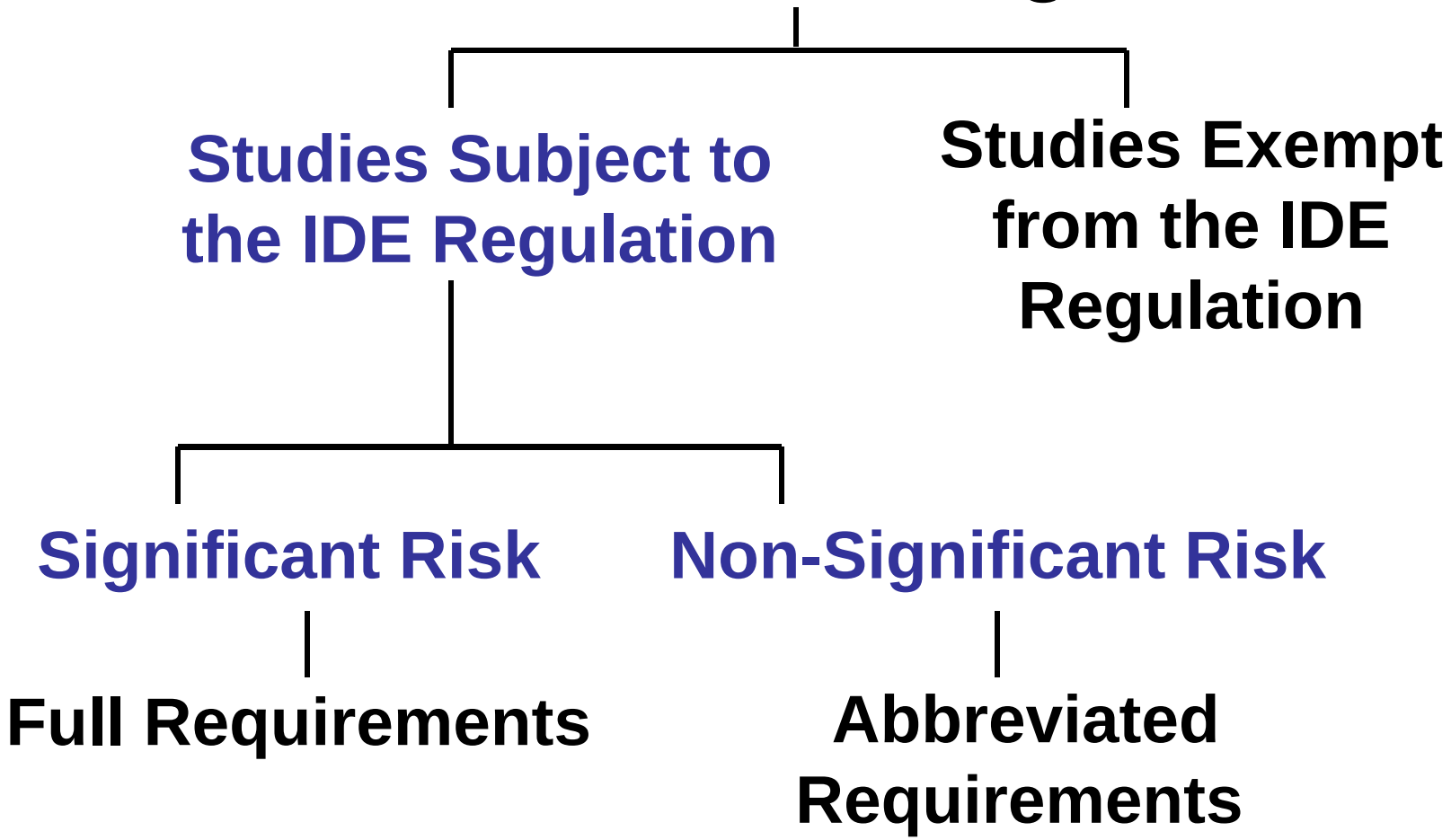


# IDE Exempt Investigations

Studies exempt from the IDE regulation include a diagnostic device that is:

- Non-invasive
- Does not require an invasive sampling procedure that present significant risk
- Does not by design or intention introduce energy into a subject
- Is not used as a diagnostic procedure without confirmation by another medically established diagnostic product or procedure

# All Device Investigations



# If not Exempt from Device Regulation, then…

- Need to assess whether proposed study of device is considered **Significant Risk (SR),** or **Non-significant Risk (NSR)**
- IRBs can and do make this assessment most of the time
- If IRBs or sponsors need assistance in making or request that FDA make risk determinations, FDA's determination is final

# All Device Investigations

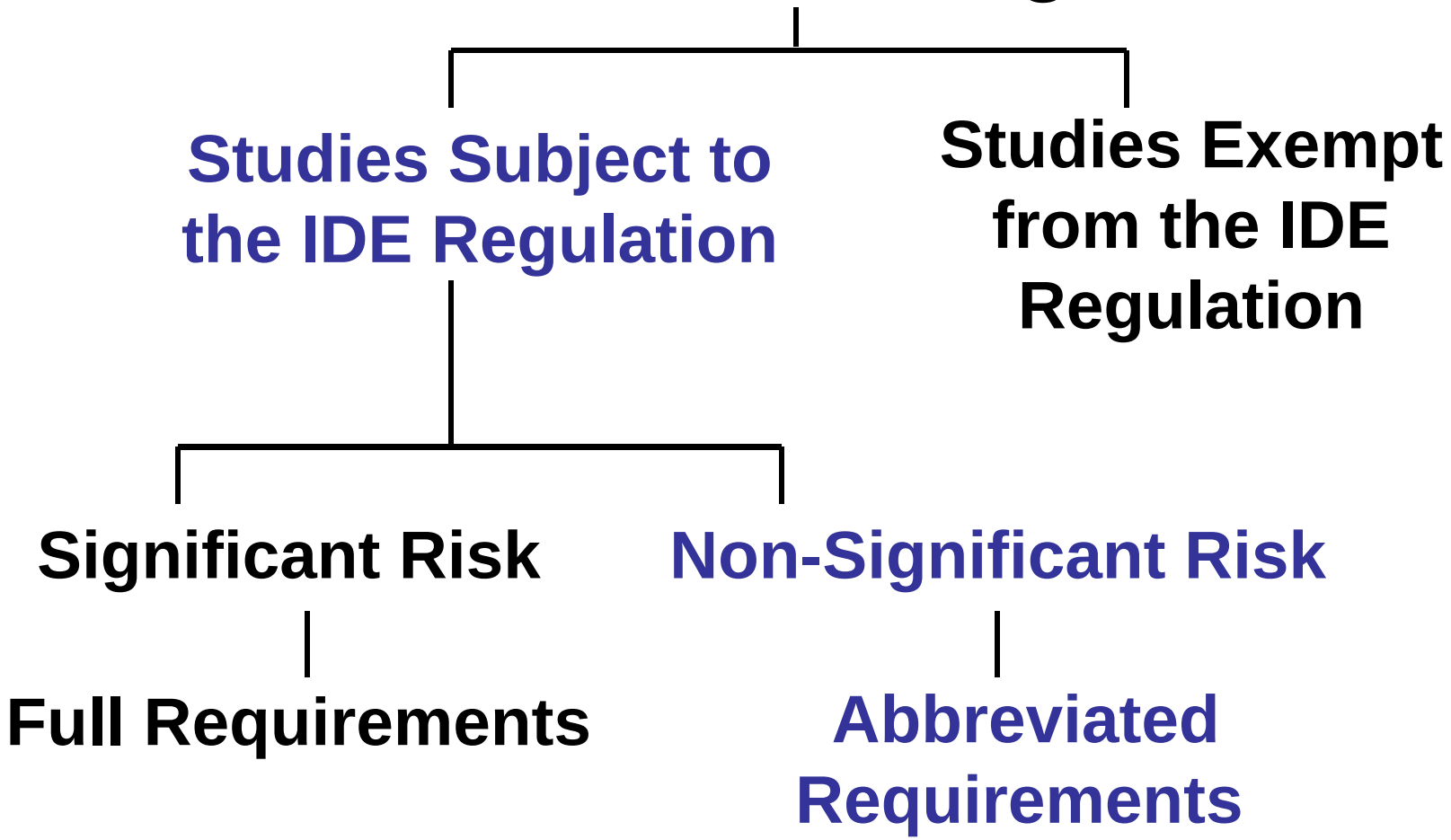
- **Studies Subject to the IDE Regulation**
  - **Significant Risk**
    - **Full Requirements**
  - **Non-Significant Risk**
    - **Abbreviated Requirements**
- **Studies Exempt from the IDE Regulation**

# Significant Risk Study

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

- an implant; or
- used in supporting or sustaining human life; or
- of substantial importance in diagnosing, curing, mitigating, or treating disease or preventing impairment of human health

# All Device Investigations

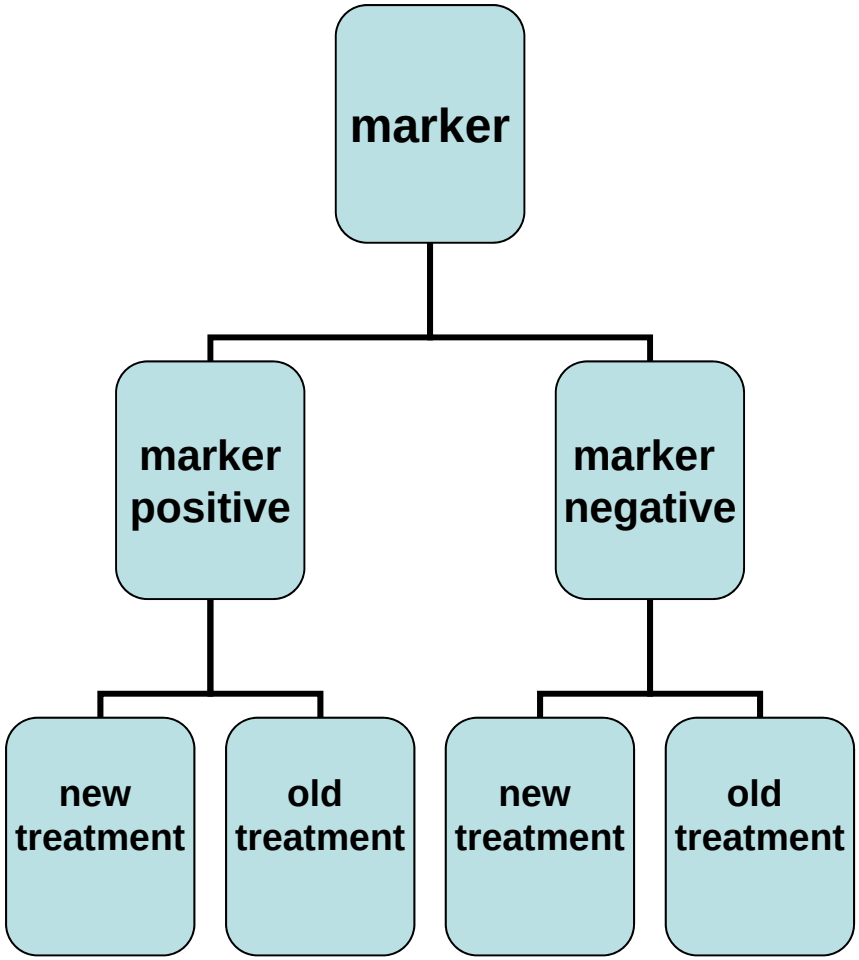


# Non-Significant Risk Studies

- Sponsor presents protocol to IRB and a statement why investigation does not pose significant risk
- If IRB approves the investigation as NSR, it may begin
- **Abbreviated** IDE requirements (labeling, IRB, informed consent, monitoring, reporting, prohibition of promotional activities)
- **No IDE** submission to FDA needed

# Example of Non-Significant Risk Study

- Marker used for stratification

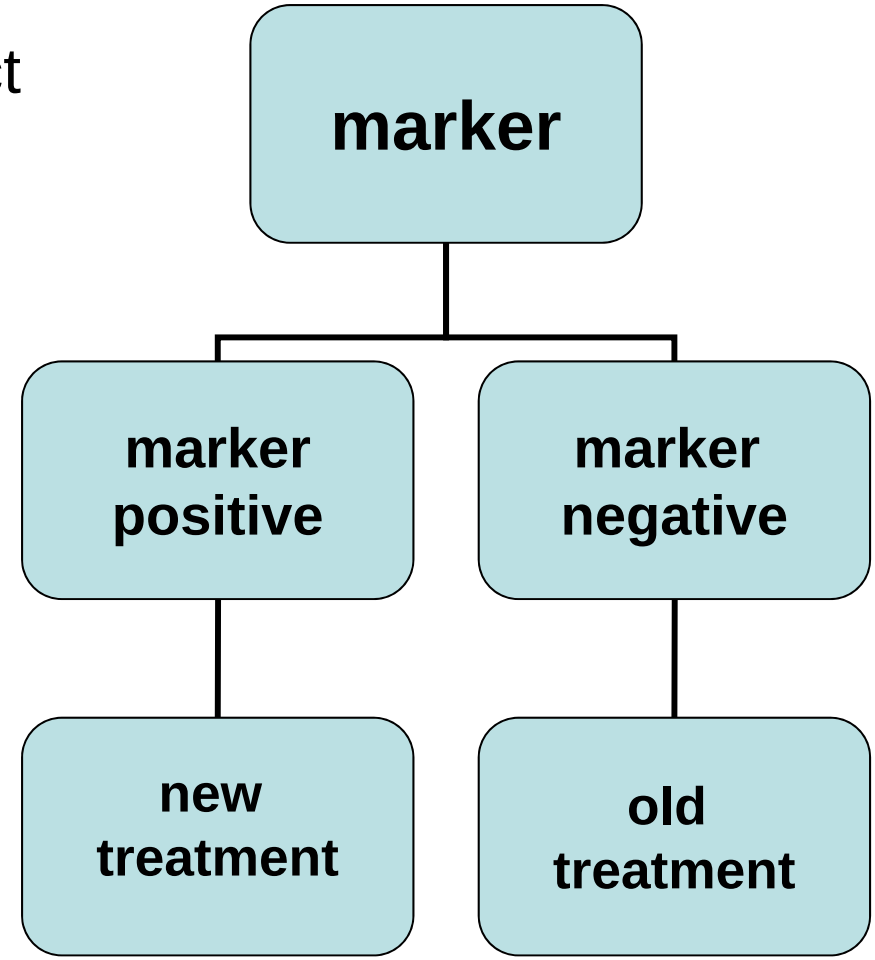


# Example of Significant Risk Study

- Investigational device-driven accrual to the trial and/or assignment to treatment arms alters therapy that would be undertaken absent the trial
- Additional **risk(s)**

# Example of Significant Risk Study

- Marker used to select treatment



# Before Submitting Your IDE

- Encourage interactions with OIVD, if needed
  - Analytical performance requirements
  - Potential clinical impact
- Not for data review, actual data will be reviewed in IDE or IND

# Significant Risk Studies

- Sponsor submits IDE application to FDA
- FDA **approves, approves with conditions,** or **disapproves** IDE within 30 calendar days
- Sponsor obtains IRB approval
- After **both** FDA and IRB approve the investigation, study may begin

# Significant Risk Studies

- Changes → supplement, another 30 days, etc…
- **"Approved with Conditions"** signifies that the study may begin, but that certain conditions have been stipulated and must be met by the sponsor within 45 calendar days
- Annual reports

# Significant Risk Studies

- Example of “approved with conditions” letter:

  Your application is conditionally approved, and you may begin your investigation at the following institutions after you have obtained IRB approvals and submitted certifications of IRB approvals to FDA: Centers X, Y, and Z. Your investigation is limited to 3 institutions and 20 subjects.

  This approval is being granted on the condition that, within 45 days from the date of this letter, you submit information correcting the following deficiencies:

# IDE Requirements (non-inclusive)

- Fully specified device
- Sufficient analytical validation and clinical information
- Pre-specified investigational plan
- Informed consent

# Companion Diagnostics: IDEs and Investigational New Drug Applications (INDs)

- Companion diagnostics
- May submit an IDE to CDRH or device validation information in an IND to CDER or CBER
- No need for both as CDER/CBER will consult CDRH when appropriate and vice versa
- Study may be IND-exempt but still require an IDE

# IDE Requirements for LDTs

Investigational LDTs may be exempt from IDE requirements, as are many IVDs, but investigational use of LDTs is not treated under enforcement discretion (i.e., NSR or SR IDE requirements apply).

# Federal Food, Drug, and Cosmetic Act ⇒ Regulation

Several parts of the Code of Federal Regulations (21 CFR) pertain to IDEs:

- Part 812 - Investigational Device Exemptions
- Part 50 - Protection of Human Subjects and Informed Consent
- Part 54 - Financial Disclosure of Investigators
- Part 56 - Institutional Review Boards

# Resources

- Information Sheet Guidance For IRBs, Clinical Investigators, and Sponsors http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126418.pdf
- Device Advice: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/default.htm
- CDRH Learn (including information about sponsor responsibilities, investigator responsibilities, IRBs, and the Bioresearch Monitoring Program): http://www.fda.gov/Training/CDRHLearn/default.htm

# Contact Information

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