



Introduction to Investigational Device Exemption (IDE)

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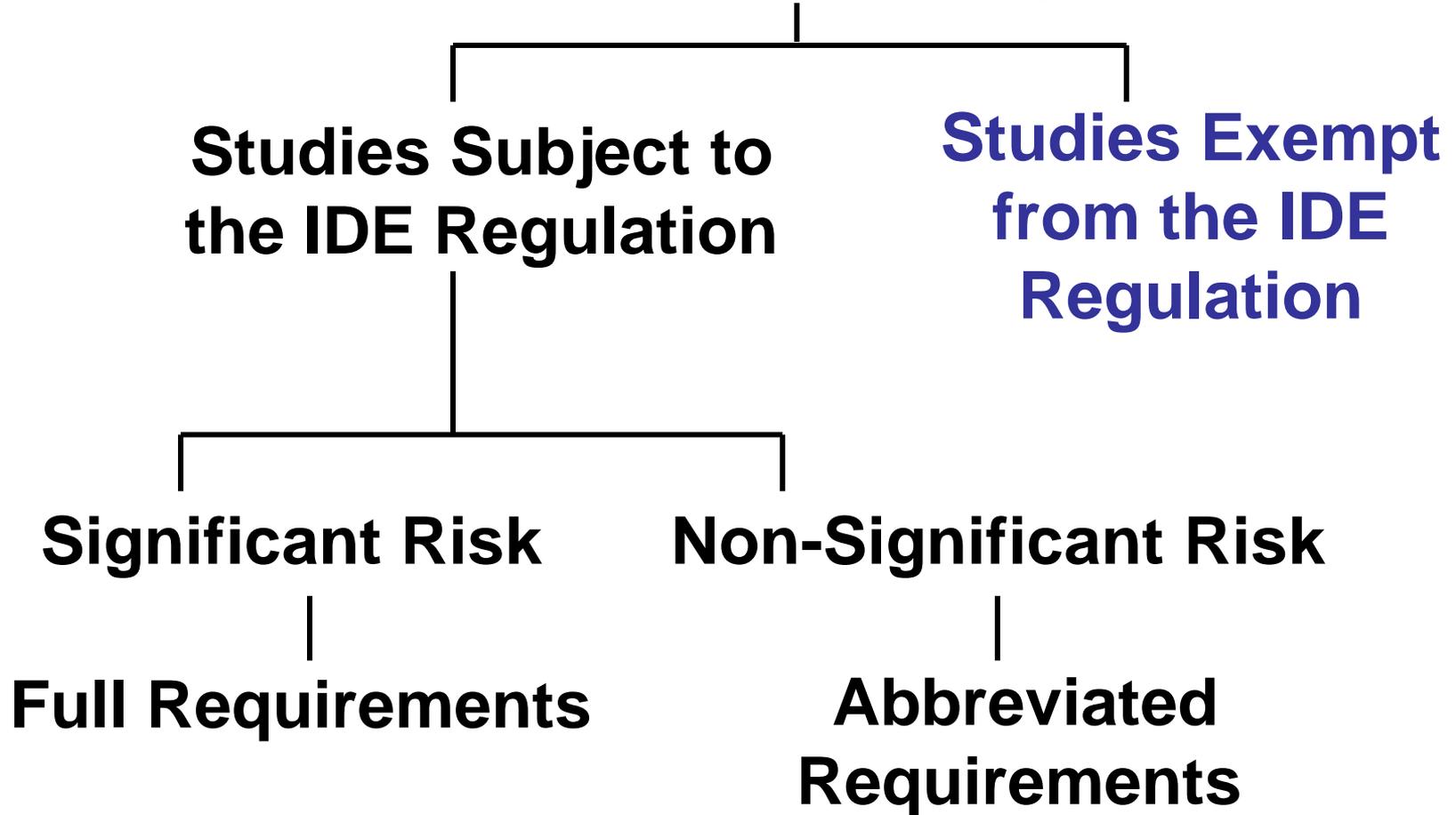
Outline of Presentation

- What is an IDE?
- The purpose of an IDE submission
- What an IDE does and does not permit?
- When should one 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
- The term “IDE” stems from this description in 21 Code of Federal Regulations (CFR) 812.1
- An approved IDE permits a device to be shipped lawfully for the purpose of conducting investigations of the device without complying with other requirements of the Food, Drug, and Cosmetic Act (Act) that would apply to devices in commercial distribution. Sponsors need not submit a PMA or Premarket Notification 510(k), register their establishment, or list the device while the device is under investigation.
- Sponsors of IDE's are also exempt from the Quality System (QS) Regulation **except for the requirements for design control.**

All Device Investigations

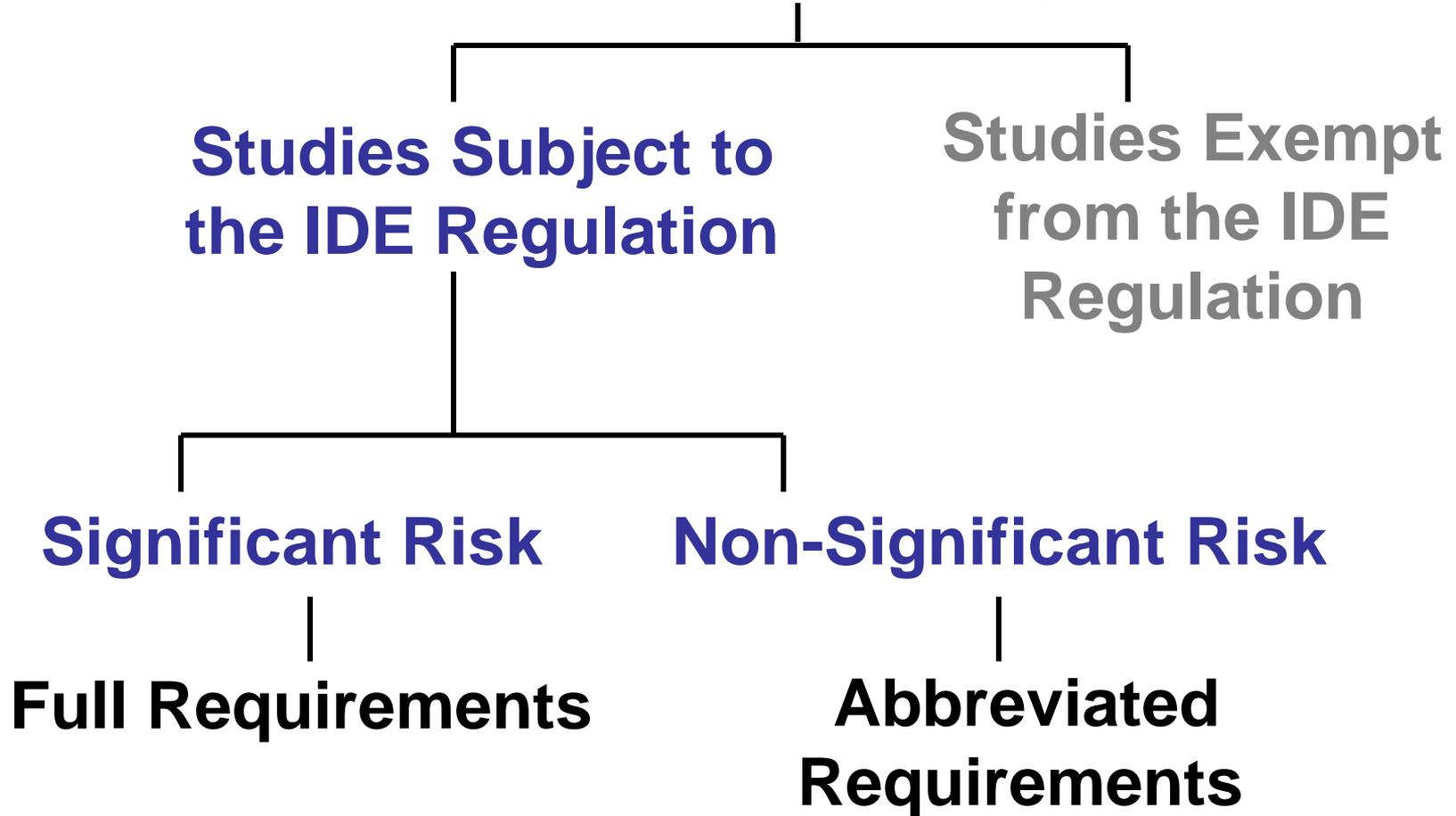


IDE Exempt Investigations

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

- Non-invasive
- Does not require an invasive sampling procedure that presents 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
- Is not used to predict the therapeutic outcome and therefore used to stratify patients in a clinical trial₅

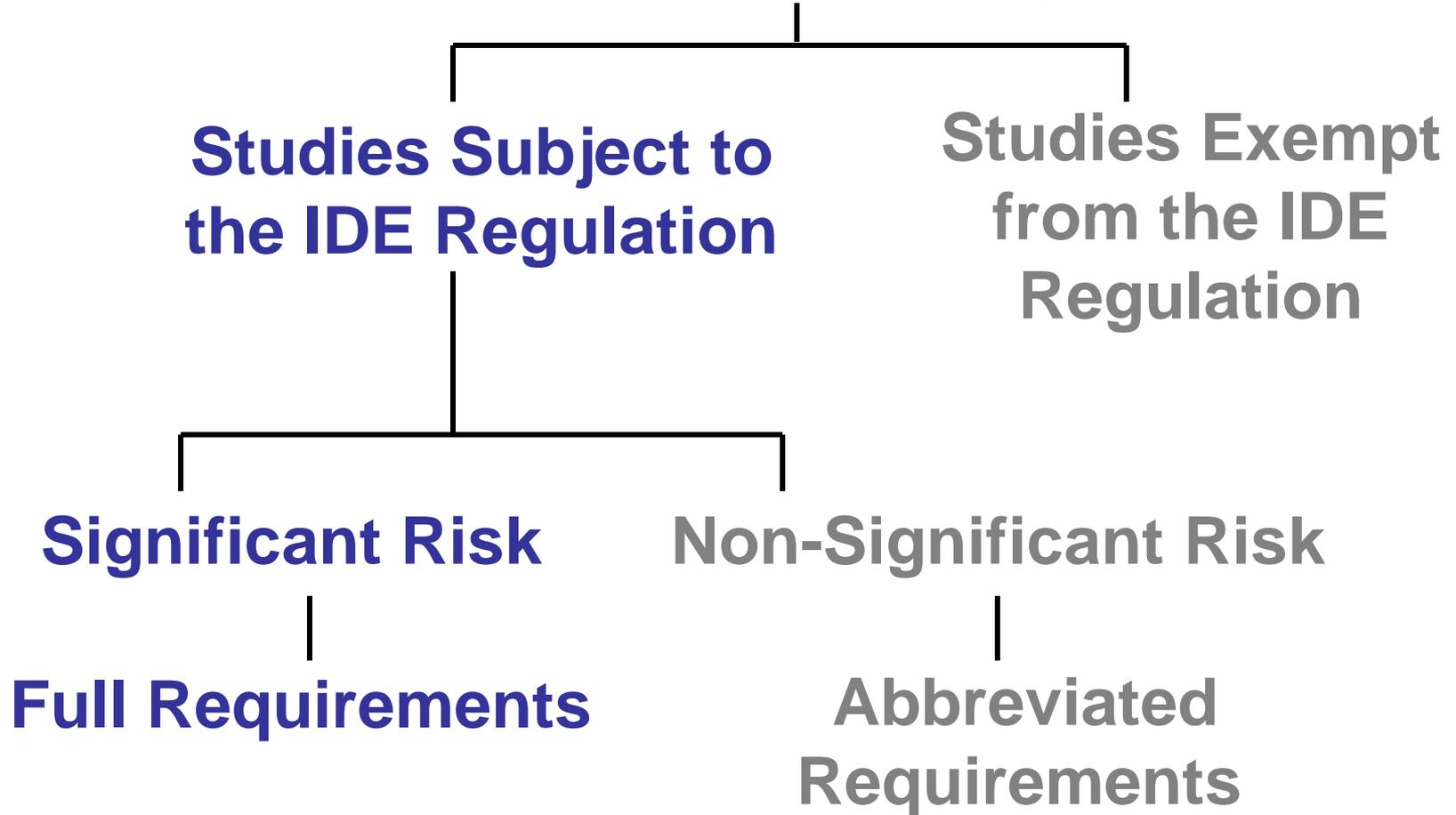
All Device Investigations



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



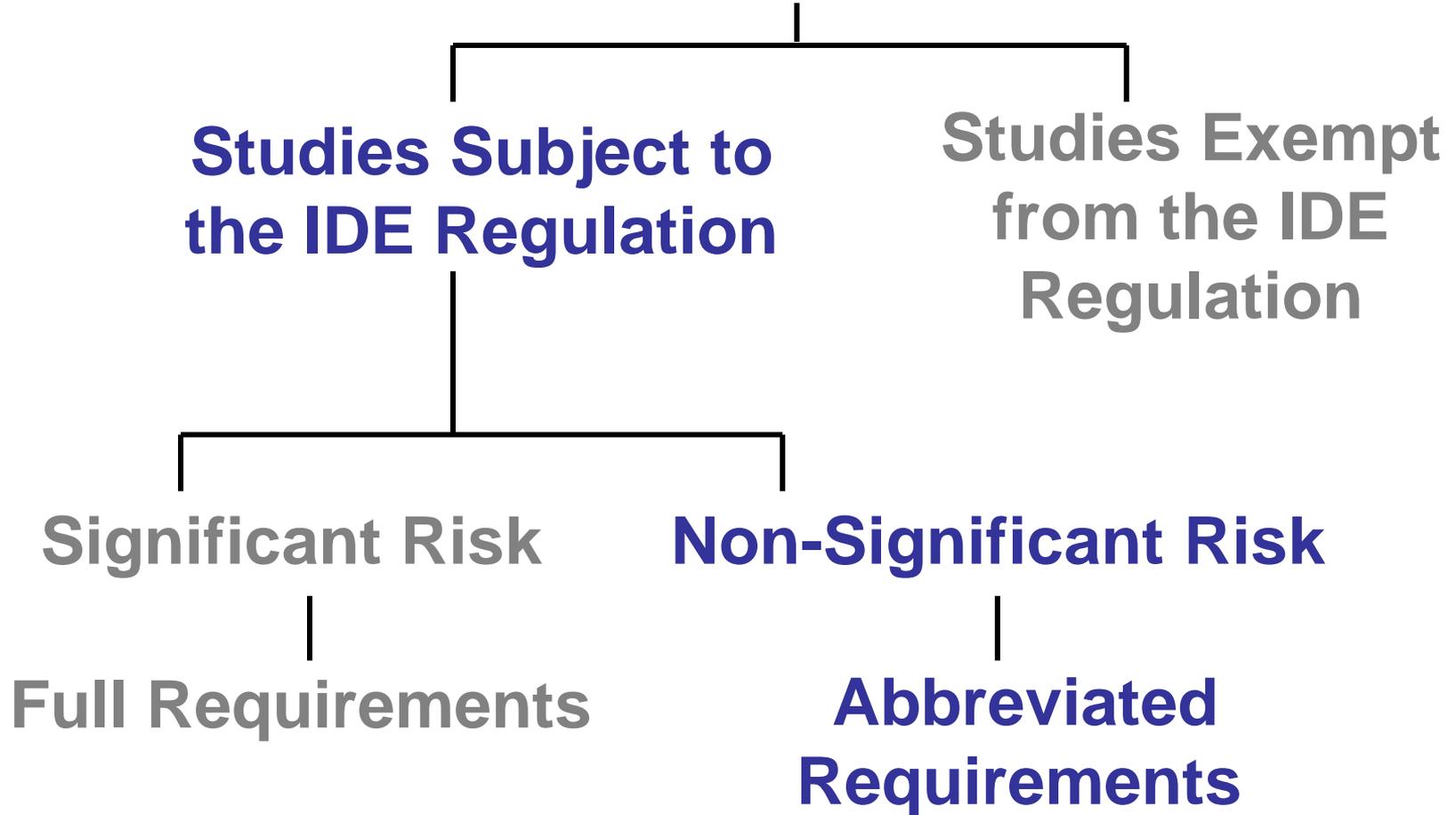
Significant Risk Study

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

For example: Using a biomarker in deciding if they will be accrued to a clinical trial for an investigative compound/biologic

All Device Investigations

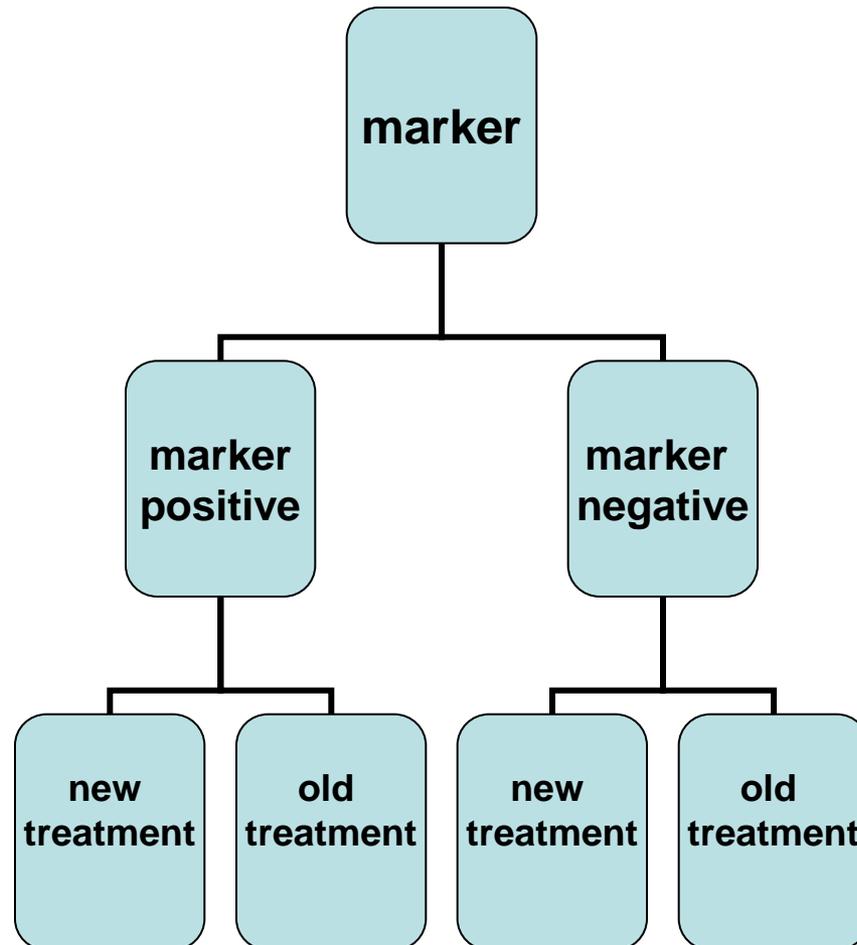


Non-Significant Risk Studies

- Sponsor presents protocol to IRB and a statement why the study does not pose a significant risk to the study participants
- If IRB approves the investigation as NSR, the sponsor may begin the study
- **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

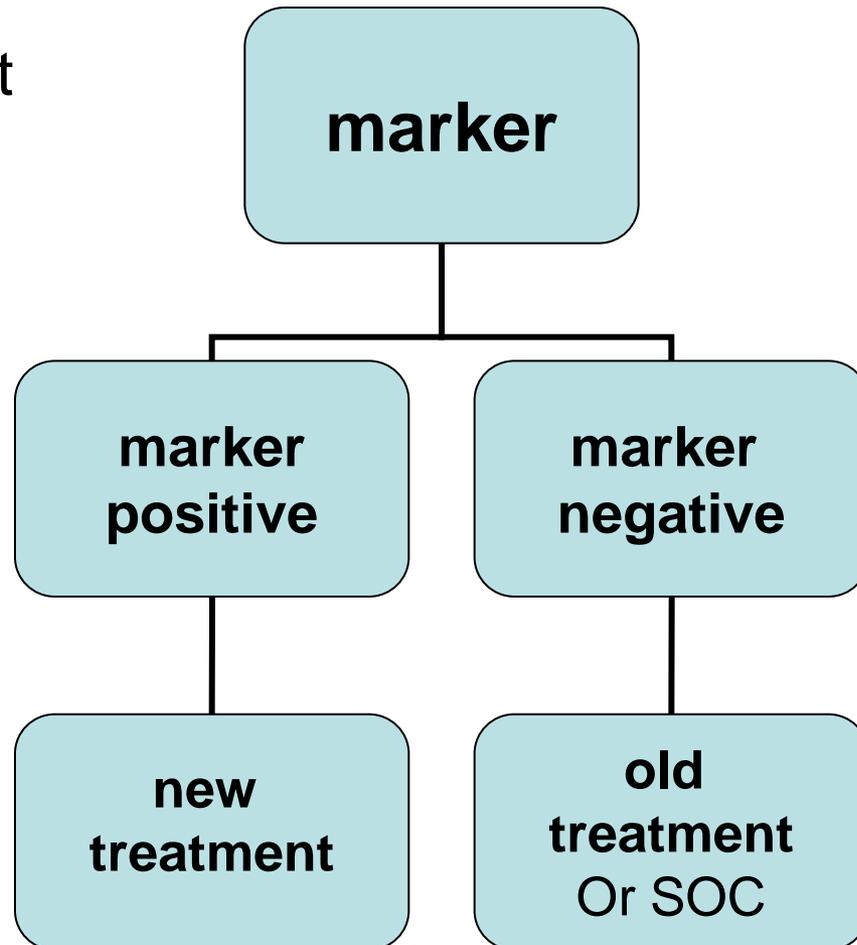


Example of Significant Risk Study

- 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 OR, if needed
 - Analytical performance requirements
 - Potential clinical impact
- Pre-IDE (Pre-Sub) are Not for data review - actual data will be reviewed in IDE or IND
- Pre-IDE (Pre-Sub) interactions are to seek FDA feedback prior to the start of a study - include study design; statistical considerations; planned outcomes etc.

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 – Include, as part of the IDE, the actual text of the Informed consent that will be used in the proposed study.
- If there are physician investigators in the study ensure that they have a current license to practice medicine, and this will be included in the IDE and subsequent annual reports.

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 (based on if the drug is a compound or biologic)
- CDER/CBER will consult CDRH when appropriate and vice versa
- Study may be IND-exempt but still require an IDE – CDRH will make that determination

IDE Requirements for LDTs

While Enforcement Discretion is applied with reference to Laboratory Developed Tests (LDTs), **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>



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