Clinical trials involving devices that have not been cleared for marketing, devices with certain modifications, or legally marketed devices with a new intended use requires an investigational device exemption (IDE). This exemption allows the investigational device(s) 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 FDA. An approved IDE also permits a device to be shipped lawfully for the purpose of conducting investigations of the device.

Investigations covered under the IDE regulation are subject to differing levels of regulatory control depending on the level of risk. The IDE regulation distinguishes between:

- Significant Risk Devices
- Nonsignificant Risk Devices
- Exempt Device Studies

The procedures for obtaining initial approval and sponsor/investigator responsibilities of the study differ according to the assigned risk.

**Significant Risk Device:**
A significant device presents a potential for serious risk to the health, safety, or welfare of a subject. Significant risk devices may include implants, devices that support or sustain human life, and devices that are substantially important in diagnosing, curing, mitigating or treating disease or in preventing impairment to human health. Examples include cardiac pacemakers, sutures, shunts, and orthopedic implants. Studies of devices that pose a significant risk require both FDA and an IRB approval prior to initiation of a clinical study.

A. **FDA Submission (For Sponsor-Investigator Trials)**
   A sponsor of a significant risk device study must submit a complete IDE application to the FDA. There are no preprinted forms for an IDE application; however, the FDA encourages sponsors to contact the FDA for guidance prior to submission of an IDE application. The communication with the FDA can include an "Informal Guidance Meeting", a "Formal Guidance Meeting", "Pre-IDE Submissions".
   The IDE application includes certain required information; such as sponsor, investigator(s), IRB, and institution names/addresses, prior investigations, investigational plan, labeling, device manufacturing, storage and installation processes. Three copies of the signed IDE application are submitted to the FDA. More detailed information regarding FDA submission can be found at the end of this guidance. Investigators interested in filing his/her own IDE should contact the office of Clinical Research support for assistance.

B. **IRB Submission**
The IRB will require a copy of the FDA letter approving the IDE and providing the IDE number or IDE Supplement Number in addition to the standard regulatory documents submitted for IRB approval.

**Nonsignificant Risk Device:**
Nonsignificant risk devices are devices that do not pose a significant risk to the human subjects. Examples include most daily-wear contact lenses, foley catheters, and lens solution. A nonsignificant risk device study requires only IRB approval prior to initiation of a clinical study. The sponsors of studies involving nonsignificant risk devices are not required to submit an IDE application to the FDA for approval.

A. **IRB Submission**
Guidance: Investigational Device Exemption

In addition to the standard regulatory documents submitted to an IRB for initial approval, the sponsor must provide a letter stating and explaining why the device is non-significant. The FDA considers an investigation of a nonsignificant risk device to have an approved IDE when IRB concurs with the nonsignificant risk determination and approves the study. If the IRB disagrees and determines that the device poses a significant risk, the sponsor must report this finding to the FDA within 5 working days.

**IDE Exempt Investigations:**
Studies exempt from the IDE regulation, in general are legally marketed devices used according to label, and a noninvasive diagnostic device that complies with labeling requirements. Devices used for veterinary use or use in laboratory animals can also be exempt. At Ochsner, the trials involving human subjects are submitted to the IRB with other written documentation that sufficiently establishes the regulatory status of the device. This may include a statement by the sponsor that the device is not of a regulatory status for which individual written FDA documentation exists, or a letter from the FDA declining to issue an IDE number, stating it was not necessary. Ochsner’s IRB will review the documents and make the determination of exempt.

Regardless of the type of device trial, no subject should be consented on a clinical trial until all proper approvals have been obtained.

**Principal Investigator Responsibilities**
Sponsors require investigators participating in significant risk device trials are required to sign an investigator agreement (21 CFR 812.43). The agreement includes:
- The investigator's curriculum vitae;
- A statement of the investigator's relevant experience;
- An explanation of any research that has been terminated;
- A statement of the investigator's commitment to:
  - conduct the trial according to the investigational plan, the IDE and other applicable FDA regulations, and conditions of approval imposed by the IRB or FDA;
  - supervise all testing of the device involving human subjects; and
  - ensure that the requirements for obtaining informed consent are met;
- financial disclosure.

For all other device trial investigator responsibilities, see the Ochsner policy and guidance on Principal Investigator Responsibilities.

**Sponsor-Investigator Responsibilities**
Investigators that are also sponsors of IDE trials are required to adhere to sponsor responsibilities. These additional responsibilities vary based on the level of risk. Sponsor Responsibilities include:
- Obtain IDE, if applicable
- Proper monitoring of the investigation. (21 CFR 812.40)
- Inform the IRB and FDA promptly of any significant new information. (21 CFR 812.40)
- Create an investigational plan, including prior investigations of the device. (21 CFR 812.45)
- Monitor the trial for device compliance (21 CFR 812.46)
• Evaluate unanticipated adverse device effects (UADE) immediately (21 CFR 812.46), report findings to the FDA, and terminate investigations that are determined to present unreasonable risk to subjects.
• Obtain IRB and FDA approval prior to resuming terminated studies.
• Maintain accurate device disposition, shipping records, correspondence, adverse device effects records, and any other records required by the FDA (21 CFR 812.140)
• UADEs, Withdrawal of IRB or FDA approval, List of Investigators, Progress Reports, Recalls and Device Disposition, Informed Consent, Risk Determination, the Final Report and other reports must be provided to the FDA and IRB in a timely manner (21 CFR 812.150).
• Device Control – to ensure the device is only shipped to qualified investigators participating in the trial. (21 CFR 812.43)
• Labeling of the device (21 CFR 812.5).

Resources:
FDA website for IDE applications:

21 CFR 812, *Investigational Device Exemptions*, covers the procedures for the conduct of clinical studies with medical devices including application, responsibilities of sponsors and investigators, labeling, records, and reports.