

IRB Review of Medical Device Research

The following question, definitions, and scenarios provide guidance for the evaluation of medical device research.

What is a Medical Device?

A medical device is 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 the official National Formulary, or the United States Pharmacopeia, or any supplement to them, intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body and which is not dependent upon being metabolized for the achievement of its primary intended purposes (Federal Food, Drug, and Cosmetic Act).

When do FDA regulations NOT apply?

FDA regulations would generally not apply to studies:

- using an FDA approved device to test a physiologic principle where no data is collected about the device;
- using an FDA approved device to address a research question and no data is collected about the device; or
- using an FDA approved device for clinical purposes (e.g., monitor a side effect, measure treatment progress);

as long as there is **no intent to collect safety or effectiveness data or develop the device for marketing.**

An example would be use of an MRI to measure a clinical outcome in a study that has nothing to do with the MRI itself.

However, if the device used for one of these purposes is **home-made by the principal investigator (PI)**, (e.g., a lever designed to raise the arm to measure flexibility), the informed consent should state that the device is not approved by the FDA.

When do FDA informed consent and IRB approval regulations apply?

FDA regulations apply when a study evaluates the safety or effectiveness of a medical device in subjects, healthy control subjects, or human specimens ★?

FDA [Informed Consent](#) and [IRB](#) (21 CFR 50, 56) regulations apply. The PI must include FDA language/references when developing the informed consent documents.

When is an Investigational Device Exemption (IDE) required?

FDA [Investigational Device Exemptions \(IDE\)](#) (21 CFR 812) regulations may apply for studies designed to:

- support marketing applications;
- collect safety and effectiveness information (e.g. for a new intended use of a legally marketed device); and

- sponsor-PI studies of an unapproved device or a new intended use of an approved device, even if no marketing application is planned.

What is an Investigational Device Exemption (IDE)?

An IDE allows the investigational device to be used in a clinical study in order to collect safety and efficacy data required to support a marketing application. The term “exemption” in this case means *exempt* from laws prohibiting unapproved products to move in interstate commerce.

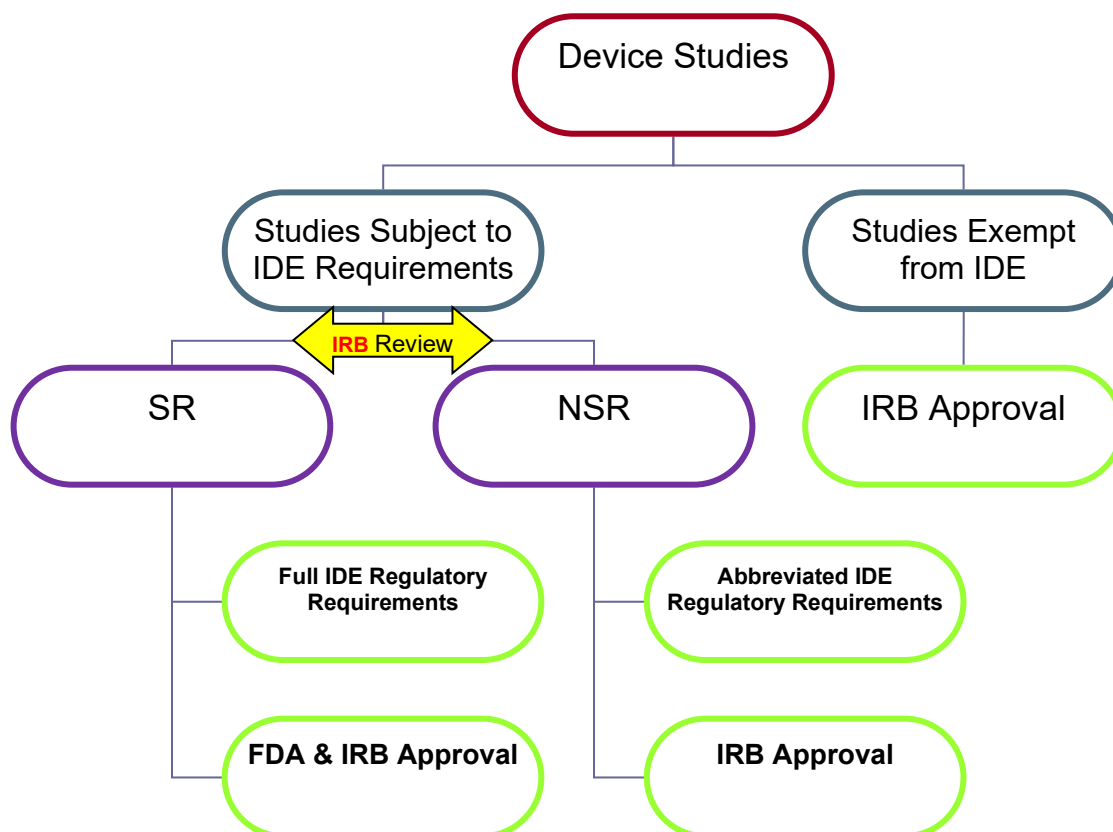
What are the three regulatory categories for device studies described in the IDE regulations (21 CFR 812)?

Research that involves assessing the safety or effectiveness of a medical device must fit in **ONE** of the following categories:

1. Studies exempt from IDE requirements (see scenario 1 & 3 below);
2. Significant Risk (SR)★ device research with formal IDE submission to FDA (see scenario 2 below);
3. Non-Significant Risk (NSR) device research which with IRB approval is “considered” to have an approved IDE; sometimes referred to as an Abbreviated IDE (see scenario 3 & 4 below).

★Significant risk device is an investigational device that: (1) is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject; (2) is for use in supporting or sustaining human life and represents a potential for serious risk to the health, safety, or welfare of a subject; (3) is for a use of substantial importance in 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 (4) otherwise presents a potential for serious risk to a subject. The IRB should evaluate the device as used in the study.

Figure 1: Diagram of regulatory categories for device studies.



Who decides whether a device study is SR or NSR?

Sponsors are responsible for making the initial risk determination and presenting it to the IRB. Unless FDA has already made a risk determination for the study, the IRB must review the sponsor's SR or NSR determination for every investigational medical device study reviewed and modify the determination if the IRB disagrees with the sponsor. If FDA has already made the SR or NSR determination for the study, the agency's determination is final.

The following scenarios illustrate category determinations and procedures.

1. The device section submitted in the IRB application indicates the device, as used in this study, is "Exempt" from IDE requirements.

The PI designates the applicable category for IDE exemption on the IRB application. The IRB considers information provided by the PI, sponsor, or FDA which indicates that the device meets one of the exempt categories ([21 CFR 812.2](#)). If the IRB agrees that the study is exempt from IDE requirements, the IRB does not need to make the SR/NSR determination (see Figure 1) and may proceed to evaluate study based on IRB approval criteria and informed consent regulations. However, if unsure, the IRB may request that the PI consult with FDA to verify the study is exempt from IDE requirements.

NOTE: IDE-exempt studies are still subject to informed consent and IRB review regulations (21 CFR 50, 56) therefore informed consent documents should still include reference to FDA (e.g., FDA may view portions of your records). While not subject to routine inspection, IDE-exempt trials could still be inspected in response to a problem or issue with the device.

A) Marketed Medical Device – Approved Indications

The most common IDE exempt studies are those involving a marketed medical device in which the device is used or investigated in accordance with the indications in the cleared labeling. For these studies the PI should provide, and the IRB should review, label information in order to compare the intended use in the protocol with the approved indications. Device approval indications may also be found by searching one of the FDA Device [Approvals and Clearances](#) databases.

B) Studies not testing safety or effectiveness (e.g., consumer preference)

Other examples of studies exempt from IDE requirements are consumer preference testing, testing of a device modification or testing of a combination of two or more devices in commercial distribution if the testing does NOT collect safety or effectiveness data, or put subjects at additional risk.

C) In Vitro Diagnostic (IVD) Devices

In addition, diagnostic device studies (e.g., *in vitro* diagnostic studies) are exempt from the requirements under certain circumstances. The study is exempt as long as the sponsor complies with the requirements at 21 CFR 809.10(c) for labeling, and if 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)(3)].

2. The study is being conducted under a valid FDA approved IDE.

Office of Research Integrity (ORI) staff validate the IDE number and no further IDE determination is required.

The PI includes the IDE number in the IRB submission and ORI staff use one of the following to validate the IDE number:

- 1) Written communication from the sponsor;
- 2) Written communication from FDA (*required for PI held IDE;*)
- 3) Sponsor protocol imprinted with IDE #.

3. The study is submitted with correspondence from the FDA indicating that the device is NSR or that the study is exempt from IDE requirements.

The IRB does not have to make the SR or NSR determination as FDA is considered the final arbitrator.

4. The device, as used in study, is NOT exempt and study does NOT have a valid IDE or FDA correspondence stating device is NSR. **THE CONVENED IRB MUST MAKE A SR/NSR DETERMINATION.**

The IRB makes the SR or NSR determination based on the proposed use of the device in the study. The SR/NSR determination is made by the full IRB at a convened meeting using information such as the sponsor's risk designation and justification criteria, a description of the device, reports of prior investigations, proposed investigational plan, and subject selection criteria.

- If the IRB determines the study is NSR, the IRB may approve the study using the standard approval criteria at [21 CFR 56.111](#). The study may begin without submission of an IDE application to FDA. The PI must still follow abbreviated regulatory requirements including labeling, informed consent, monitoring, records, reports, and prohibition on promotion. Progress and final reports are submitted only to the IRB.
- If the IRB disagrees with the sponsor's NSR assessment and decides the study is SR, the IRB must tell the clinical PI, and where appropriate, the sponsor. ([21 CFR 812.66](#))
SR device studies must have an IDE application approved by FDA before they may proceed. The PI follows full regulatory requirements under the purview of both the FDA and the IRB.
- **NOTE:** The device SR/NSR determination should not be confused with the "minimal risk" determination or "risk-benefit" assessment for the study in general.

ORI staff document the decision of the IRB (both risk assessment and approval) in meeting minutes and in correspondence sent to the PI.

What if the FDA must be consulted when the IRB is unsure whether an IDE is needed?

The IRB, at its discretion, may contact or require that the PI contact the FDA for a determination. Call 240-276-4040 with general questions about whether a product is subject to IDE regulations. *FDA also recommends that the sponsor-PI contact Center for Devices and Radiological Health (CDRH) if unsure about exemption from IDE requirements. To obtain a written risk determination from FDA submit correspondence labeled "Study Determination" in triplicate to USFDA, CDRH, Document Mail Center – WO66-G609, 10903 New Hampshire Ave., Silver Spring, MD 20993-0002. CDRH Manufacturer's Assistance may be reached at 800-638-2041, 301-796-7100, or industry.devices@fda.hhs.gov.*

Does device classification (Class I, II, III) factor into IRB determinations?

A sponsor's detailed protocol may list a device as [Class I, II or III](#). FDA classifies devices based on the level of control necessary to assure safety and effectiveness of the device for marketing (not research). Controls range from general requirements such as labeling, not misbranding, and good manufacturing practices to special controls such as specific instructions for use or post marketing surveillance requirements.

The classification is risk based so is indicative of the type of submission required for FDA to clear a device for marketing. Class II and Class III devices require the type of marketing route that most often involves clinical trials. Therefore, these are the types of devices seen in research for which the IRB is involved in the regulatory determinations addressed in the questions above.

Which regulatory device categories may be eligible for Expedited IRB review?

For a device study to be eligible for Expedited Review under Expedited Category 1, the device must present no more than minimal risk to the subject, and meet one of the criteria in Category 1b:

Expedited Category 1b- Research on medical devices for which

- (i) an IDE application (21 CFR Part 812) is not required^{*}; or
- (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling^{**}.

^{}Example: Study presents documentation from FDA indicating that an IDE application is not required or study meets all criteria to be IDE exempt in vitro diagnostic device [21 CFR 812.2\(c\)\(3\)](#).*

*^{**} An approved Device used in research according to its approved labeling is considered Exempt from IDE requirements- [21 CFR 812.2\(c\)\(1 or 2\)](#). See scenario 4 above.*

Note: Expedited Category 1 should not be used for studies that involve use of a device only, (no testing or data collected on or about the device), as FDA regulations do not apply. Expedited Category 4 may be considered for studies that use, but not test, a device.

What else must the IRB consider in regard to PI responsibilities?

The IRB reviews the PI's plan for management, control, and accountability of the investigational device. The [ORI quality improvement program \(QIP\) resource website](#) provides tools and sample standard operating procedures for device accountability. The ORI performs periodic QIP reviews of device studies to assess device control, access, and accountability.

What if the PI is also the sponsor of a device study?

The PI must indicate in the IRB submission that he/she is aware of his/her [regulatory responsibilities](#) in acting as both the PI and sponsor for an FDA regulated investigation. The PI indicates if any responsibilities have been formerly transferred to a contract research organization or other entity. Sponsor-PIs must complete a required [Device Development for Sponsor-PI's Good Clinical Practice course](#) available on CITI. ORI receives course completion notices directly from CITI.

What if the submission involves a Humanitarian Use Device (HUD)?

There are different requirements for HUDs depending on the device use in the study. See the [IRB HUD SOP](#), [IRB Summary - Humanitarian Use Devices](#) or [FDA's Humanitarian Device Exemption \(HDE\) Regulation: Questions and Answers](#).

What if the submission involves a combination product?

A combination product comprises two or more regulated components (i.e., drug/device, biologic/device, drug/biologic) such as a prefilled insulin injector pen, transdermal patch or metered dose inhaler. FDA considers the whole combination when determining need for Investigational New Drug (IND) or IDE application. An application may be indicated if one part is new, one part increases risk of an approved device/drug, or both drug and device are approved for different indications, and when two are used together present a new risk. The [FDA Office of Combination Products website](#) provides answers to frequently asked questions. They may also be reached by email (combination@fda.gov) or phone (301-796-8930).

What if the submission involves a Compassionate Use or Treatment IDE?

Compassionate use allows access for patients who do not meet the requirements for inclusion in a clinical investigation but for whom the treating physician believes the device may provide a benefit in treating and/or diagnosing a serious disease or condition. A treating physician or PI would contact the sponsor to request access to the device for an individual or small group of patients. The sponsor submits an IDE supplement requesting approval of the compassionate use from the FDA. The IRB chair documents concurrence with the use, ensures FDA has approved the use, and after administration, receives and reviews reports of the use.

Treatment IDEs facilitate availability of promising new devices to patients with life-threatening or serious diseases for whom no comparable or satisfactory alternative exists. Standard IDE regulations for conduct and IRB review apply to the Treatment IDE as data is collected on the device's safety and effectiveness. A treating physician who uses a device under a Treatment IDE is responsible for meeting all applicable IDE responsibilities.

Sources:

- Information Sheet Guidance For IRBs, Clinical PIs, and Sponsors , [Significant Risk and Nonsignificant Risk Medical Device Studies](#), January 2006
- Information Sheet Guidance For IRBs, Clinical PIs, and Sponsors [Frequently Asked Questions About Medical Devices](#), January 2006
- Code of Federal Regulations, [Title 21 CFR 812](#), Investigational Device Exemptions
- [IDE Definitions and Acronyms](#)