

Guidance and Procedures: Use of Devices in Clinical Research and Treatment (last updated August 30, 2011)

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Brief Overview

This guidance is intended to assist UCLA investigators in meeting the various Food and Drug Administration (FDA) requirements as well as UCLA requirements when using devices in clinical research (clinical investigations) and in treatment.

FDA IDE regulations [21 CFR 812](#) contain procedures and requirements for the conduct of the clinical research of devices. Clinical research involving devices **to determine safety and effectiveness** are subject to these regulations, unless certain exemptions apply. The responsible branch of the FDA is the [Center for Devices and Radiological Health \(CDRH\)](#). For most studies involving devices, an investigator or sponsor must obtain an Investigational Device Exemption (IDE) from the FDA.

All investigational device studies involving human subjects must be submitted to the IRB for review and approval before the investigation can begin.

Investigational Device Exemption Applications (IDEs)

A device is considered investigational if either condition applies:

- The device is not approved for marketing in the United States or
- The device is approved for marketing but is being clinically evaluated for a new indication.

All device studies involving human subjects must be reviewed and approved by the UCLA IRB before the research can begin.

When is an IDE required?

- **Studies involving unapproved devices that are considered to be significant risk:** An IDE from the FDA is required to perform clinical research using an unapproved device that poses a **significant risk** to subjects. Typically these studies are conducted to collect safety and effectiveness data used to support **Premarket Approval (PMA)** applications submitted to the FDA. (See definitions below.)
- **Studies involving an approved device being tested for a new indication:** IDE regulations apply to **significant risk** studies testing an FDA-approved device for **a new indication**, and/or are being used or tested in **a new way that significantly increases the risks** associated with the device.

Example: Significant risk (SR) studies involve implantable devices such as cardiac pacemakers, orthopedic implants, and stents. SR studies can also involve products not introduced into the body, such as computer software used for prenatal risk evaluation. Each of these studies would require an IDE.

For more information, see FDA guidance on [Significant and Non-Significant Risk Medical Devices](#).

Example: A legally marketed coronary stent would be considered an investigational device and would require an IDE if used as part of a study to collect **safety and effectiveness data** for treating conditions involving other vascular sites.

When is an IDE *not* required?

- **Studies involving approved devices used within their approved labeling.** Devices used within their approved labeling are exempt from IDE regulations.
- **Studies involving devices that are considered to be non-significant risk (NSR):** An IDE is not needed for research use of **non-significant risk devices** or **devices that are substantially equivalent** (510K) to currently marketed devices.
 - UCLA IRB review and approval is required for all NSR studies.
 - The FDA authorizes IRBs to conduct the risk assessment of all proposed non-significant risk studies.
 - Study approval is dependent on the investigator supplying the IRB with sufficient information, usually provided by the sponsor, regarding the device and its intended use so that the Board may conduct the risk assessment.

IMPORTANT NOTE: Although FDA approval is not required, the agency can assume study jurisdiction at any time deemed necessary.

Example: Non-significant risk devices include daily wear contact lenses and associated care products; conventional gastroenterology and urology endoscopes; externally worn monitors for insulin reactions; general catheters (biliary, urological); and, non-implantable electrical incontinence devices.

For more information, see FDA guidance on [Significant and Non-significant Risk Medical Devices](#).

- **Practice of Medicine:** A physician can use a legally marketed device without UCLA IRB approval for any condition or disease within a “legitimate healthcare practitioner-patient relationship”. However, the results of an off-label use of a medical device cannot be presented as research.
- **Specific IDE-Exempt Studies:** FDA regulations describe specific IDE-exempt studies. Please review the [OHRPP Tip Sheet: Exemptions from IDE Requirements](#) for a complete list of all types of investigations which are exempt from FDA IDE requirements according to [21 CFR 812.2](#).

The two more common IDE-exempt investigations submitted to the IRB meet the following criteria:

- Investigations conducted with legally marketed devices used according to labeling.
- Studies using in vitro diagnostic devices labeled “for research purposes only” may be IDE-Exempt as per regulations ([21 CFR 809.10\(c\)](#)) if the testing:
 - Is noninvasive;
 - Does not require invasive sampling procedures that presents significant risk;
 - Does not introduce energy into a subject; and
 - Is not used as a diagnostic procedure without confirmation by another medically established diagnostic product of procedure;

What is the Difference between a “Sponsor” and a “Sponsor- Investigator” IDE?

The FDA makes the following distinction between a “sponsor” and a “sponsor-investigator” and a “commercial IDE” and an “Investigator-Initiated IDE.”

- **“Sponsor”** means a person who takes responsibility for and initiates a clinical investigation. The sponsor may be an individual or company, governmental agency, academic institution, private organization, or other organization. The sponsor does not actually conduct the investigation unless the sponsor is a sponsor-investigator. A person other than an individual that uses one or more of its own employees to conduct an investigation that it has initiated is a sponsor, not a sponsor-investigator, and the employees are investigators.
- **“Sponsor-Investigator”** means an individual who both initiates and conducts an investigation, and under whose immediate direction the investigational device is used. The term does not include any person other than an individual. The requirements applicable to a sponsor-investigator under this part include both those applicable to an investigator and a sponsor.
- A **“Commercial IDE”** is submitted by a sponsor seeking FDA clearance to market a medical device.
- An **“Investigator-Initiated IDE”** is submitted by a physician who both initiates and conducts the clinical investigation.

How Should an Investigator Time the Request for an IDE?

- **Pre-IDE Process:** Investigators considering submitting an IDE application to the FDA should communicate with the reviewing division of the Office of Device Evaluation (ODE) prior to the submission of an IDE application. See the FDA [IDE Approval Process](#) website for details.
- **The IDE Submission:** The IDE submission to the FDA and the IRB application should be initiated at the same time. The FDA has 30 days to review the IDE application. Likewise, the IRB typically reviews an application within a 30-day window, but it may take longer to secure approval. Subjects may not be recruited or enrolled before FDA **and** IRB approval.

Situations and Methods that Allow for Expanded Access to Unapproved Devices for Treatment

What are the situations in which expanded access to unapproved devices may be allowed?

There are several regulatory mechanisms that allow **expanded access** to investigational medical devices while clinical studies and/or FDA review are on-going. Because the FDA is primarily concerned with protecting public safety, the number of patients who can be treated under these special access mechanisms is limited and generally determined by the existence of sufficient safety and efficacy data.

FDA allows **a limited number** of certain individuals **not enrolled in clinical trials to obtain expanded access to investigational devices** through the methods described below, under the following circumstances:

- Patient(s) have a **serious or immediately life-threatening disease or condition**, and there is no comparable or satisfactory alternative therapy to diagnose, monitor or treat the disease or condition;
- Potential **patient benefit justifies the potential risks of the treatment use** and those potential risks are not unreasonable in the context of the disease or condition to be treated; and
- Providing the investigational device for the requested **use will not interfere with clinical investigations that could support marketing approval** of the expanded access use or otherwise compromise the potential development of the expanded access use.

IMPORTANT NOTES:

1. Use of investigational devices through these methods requires prior review and approval by the IRB and the FDA.
2. The sponsor will likely hold the IDE for these programs.

What are the Various Expanded Access Programs?

- **Compassionate Use IDE:** Under an existing IDE, the FDA may allow treatment of a small number of seriously ill patients who have no acceptable alternatives. The FDA requires the sponsor/investigator to supply a supplement to an existing IDE justifying the compassionate use.

IMPORTANT NOTES:

1. Compassionate use requires FDA review and approval and concurrence of an IRB Chair before treatment can be initiated. The study involving the existing IDE must already be approved by the IRB.
2. "Compassionate Use" is not the same as "Emergency Use" which is much more restrictive. Please see the [OHRPP Guidance on Emergency Use of a Test Article](#).

- **Treatment IDE:** If FDA has reviewed sufficient safety and efficacy data obtained under an existing IDE, wider access to an unapproved device may be granted to desperately ill patients under [Treatment IDE Regulations](#).
- **Continued Access:** After the completion of a controlled clinical trial, a supplement to an existing IDE can be submitted and the FDA may allow continued access to the device provided there are no safety concerns. The FDA continued access policy allows access to promising devices while the marketing application is being prepared by the sponsor or reviewed by the FDA.

IRB Requirements

What is required for IRB review of the study application?

If the study involves a device, the investigator should check the appropriate box in the webIRB application. By doing so, the investigator will be prompted to answer the appropriate questions and provide the information needed for IRB review. The following is required for IRB review:

- **An Appropriate Level of IRB Review:**
 - The investigators should specify whether they believe the device to **pose significant or non-significant risk**, however, the **Full Committee** is required at the time of initial review to determine what they believe to be the risk level.
 - If the IRB determines that the device poses a non-significant risk and that the study itself poses no more than minimal risk, then the IRB may determine that expedited category #1¹ will apply for future reviews.
 - If the IRB determines that the device poses a significant risk, then the study will continue to be reviewed at the Full Committee level for future submissions.
 - For studies that are **exempt from submitting an IDE application to the FDA** — see [Tip Sheet on Exemptions from IDE Requirements for Clinical Research](#) — the level of IRB review will depend on the risk assessment of the study including the use of the device. Expedited Category #1 may apply (see footnote below) if the IRB determines that the study otherwise poses no more than minimal risk to the subjects.
- **IDE Number:** When a clinical investigation requires an IDE number, the IRB will not issue final approval until the IDE number is reported to and verified by the IRB. Verification can be accomplished by providing a copy of the sponsor's protocol with the IDE number listed, or by submitting correspondence from the sponsor or FDA indicating the IDE number for the study.

However, the IRB will review the research before the IDE application is submitted to or approved by to the FDA. The FDA does not require local IRB approval before issuing an IDE number.

- **Investigator's Brochure** for any study involving an investigational device for **a significant risk study** a copy of the brochure should accompany the IRB application. For **non-significant risk studies** diagrams and/or *in situ* photographs or the device are helpful.
- **Clinical Protocol** (also known as “sponsor protocol” or “multicenter protocol”) should be included with the application and it should describe the methodology to be used and offer an analysis that the study is scientifically sound.

¹ Expedited Category #1: Clinical studies of drugs and medical devices only when condition (a) or (b) is met:
 a. Research on medical devices for which (i) an investigational device exemption 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.

- **Information about the device** including the trade (brand) name of device, common (generic) name of device, manufacturer of the device (if UCLA research lab, identify the lab), source of the device, directions for use, package insert (if appropriate and/or available).
- **An explanation of the device cost.** Non-significant risk devices are placed in Category B and are most likely eligible for reimbursement. See "[Implementation of the FDA/HCFA Interagency Agreement Regarding Reimbursement Categorization of Investigational Devices](#)" overview provided by the FDA.
- **FDA Form 1572:** This form is required for FDA purposes and does not need to be submitted to the IRB.
- **Clearance from the Medical Radiation Safety Committee** for radiation-emitting devices.

What information must be included in the consent documents?

The basic requirements for UCLA IRB approval of all consent documents are outlined in federal and state regulations as well as UCLA guidance and the UCLA consent templates. Specific information is required for the use of devices in clinical research and for the use of unapproved devices for treatment as described below:

- **Purpose and Background Section:**
 - Must include a clear statement that the device is investigational and has not been approved by the FDA for clinical use, or it has been approved for specific clinical indications but not for the use being studied.
 - Should include a brief lay description of what the device is and what it is designed to do.
 - Must *not* state or imply that the issuance of an IDE is an approval or endorsement by the FDA.
- **Confidentiality Section:**
Must state that the FDA and the study sponsor may review subject medical records and research records which identify the subjects.
- **Alternatives Section:**
Must inform participants of any alternatives to participating in the study, including any standard treatments available with approved devices, or other experimental treatments with investigational devices.
- **Costs Section:**
Must provide specific information about how the costs of the study device will be covered, including the costs of the device itself, and when applicable:
 - State if the sponsor is supplying the device at no charge.
 - State whether the participant or their insurance provider will be billed for the device.
 - State that the cost of the device might not be covered by insurance because the device is investigational.
 - Discuss any costs associated with implanting and/or removing the device.
- **Agreement to Participate Section:**
Must include information that subject will be given a copy of the "Research Participants Bill of Rights."

For additional guidance on preparing a consent form for review and approval by the UCLA IRB please refer to OHRPP Guidance on [Informed Consent Process and Documentation](#) and copies of the [templates for the UCLA consent forms](#).

Control of Investigational Devices

Investigators conducting studies in which an investigational device will be used must ensure adequate control of the device. Adequate control and handling of investigational devices include all of the following:

- **Ensuring** that the investigational device is used only in accordance with the UCLA IRB approved protocol, the signed agreement, the investigational plan and applicable FDA regulations.
- **Administering** the investigational device only to participants under the investigator's direct personal supervision or under the supervision of a sub-investigator directly responsible to the investigator.
- **Supplying** the investigational device to only persons authorized to receive it.
- **Maintaining** accurate, complete, and current records relating to the investigator's participation in an investigation, including records of receipt, use or disposition of a device that relate to:
 - The type and quantity of the device, the dates of its receipt, and the batch number or code mark.
 - The names of all persons who received, used, or disposed of each device.
 - Why and how many units of the device have been returned to the sponsor, repaired, or otherwise disposed of.
- **Returning any unused supplies** of the investigational device to the study sponsor, or otherwise provide for disposition of the unused supplies as directed by the sponsor if the investigation is terminated, suspended, discontinued, or completed.
- See [Sample Investigational Device Accountability Log](#).

Reporting Requirements

What are the post-approval reporting requirements?

The UCLA IRB and the FDA require adverse events (AE) associated with the use of devices under an IDE be reported in a timely manner. When an IDE is issued, there are additional and separate federal requirements for reporting adverse events to the FDA. The UCLA IRB also requires that the reporting of unanticipated problems, protocol violations and incidents and updated safety information.

- **When the study sponsor holds the IDE,**
 - Investigators need to report *all* adverse events to the sponsor and the sponsor will submit appropriate reports to the FDA.
 - Investigators need to understand and comply with the similar but separate reporting requirements for the UCLA investigator as described in the [UCLA Summary Sheet of Post-Approval Reporting Requirements for Investigators](#) .
 - Investigators need to determine if their department or unit has any additional reporting requirements.
- **When the investigator holds the IDE** for a specific study protocol (as in the case of investigator-initiated/investigator-sponsor IDEs),
 - The investigator has responsibilities for reporting adverse events to the FDA.
 - Investigators need to understand and comply with the similar but separate reporting requirements for the UCLA investigator as described in the [UCLA Summary Sheet of Post-Approval Reporting Requirements for Investigators](#) .
 - Investigators need to determine if their department or unit has any additional reporting requirements.

Additional Guidance

- See FDA regulations [21CFR812](#) for complete reporting information.
- Investigators should also review the OHRPP Guidance [Post-Approval Reporting Requirements for Investigators: Reporting of Unanticipated Problems, Including Adverse Events, Protocol Violations, Deviations and Incidents and the Reporting of Updated Study Safety Information](#) for a detailed description of the UCLA reporting requirements.

Special Medical Device Regulations

Humanitarian Device Exemption (HDE)

An HDE is a type of Premarket Application described under the Safe Medical Devices Act (SMDA) of 1990 and allows the FDA to grant an exemption from the effectiveness requirements of the Premarket Approval (PMA) regulations. Devices approved an HED are referred to as a Humanitarian Use Devices (HUD). The provisions for obtaining an HDE are:

- The device is designed to treat or diagnose a disease or condition that affects fewer than 4,000 individuals per year in the U.S.
- The device is not available otherwise, and there is no comparable device available to treat or diagnose the disease or condition; and
- The device will not expose patients to unreasonable or significant risk, and the benefits to health from the use outweigh the risks.

Treatment under an HDE is not considered research, but the FDA requires IRB review prior to use. The UCLA IRB requires a standard application and use of a consent form similar to research consent. A [sample consent form](#) for use of an HUD is available on the OHRPP website.

Drug-Device Combination Products

If an investigator is interested in evaluating a combination product, the following links may be useful:

- The [Office of Combination Products](#) (OCP) was created in 2002 to facilitate the review process for combination products by coordinating interactions between reviewing branches.
- The OCP provides applicable [guidance documents](#) for combination products.
- Some recent combination product approvals include:
 - Drug-eluting coronary stents;
 - Spinal fusion putty; and
 - An influenza vaccine administered via an intranasal delivery device.
- A complete listing of [recently approved combination products](#) is available.

Import/Export of Investigational Devices

A complete overview of [medical device import/export regulations](#) is provided by the CDRH. Clinical investigators should be aware that the FDA does not recognize regulatory approvals from other countries. Therefore, an imported medical device must meet all FDA requirements.

- The IDE sponsor must be located in the United States.
- Anyone who intends to import an investigational device takes on the [responsibilities of a sponsor](#).

Definitions and Quick Links

- **Significant and Non-Significant Risk Devices:** See [OHRPP Guidance on Significant and Non-Significant Risk Devices](#).
- **Types of Marketing Applications**
 - [Premarket Notification \(510\(k\)\)](#) applies to Class I, Class II, and some Class III devices.
 - A sponsor must demonstrate “substantial equivalence,” meaning that the new device is as safe and effective as the predicate device(s).
 - New guidelines streamlined 510(k) options are available.
 - Clinical studies using 510(k) devices may be subject to IDE regulations. Prior FDA and IRB approval are required.
 - [Premarket Approval \(PMA\)](#) has more stringent requirements for high risk Class III devices. In most cases an investigational device exemption (IDE) is required to clinically evaluate devices subject to PMA regulations.
 - [Humanitarian Device Exemption \(HDE\)](#) is part of the FDA Modernization Act aimed at encouraging device development for conditions with fewer than 4000 patients.
- **Device Classification**

The level of regulatory controls placed on a medical device is determined by the risk classification. Most research reviewed by the IRB involves significant risk, Class III devices. To help determine device classification, regulatory controls, and exemptions, the Center for Devices and Radiological Health (CDRH) maintains:

- A searchable [classification database](#) containing information about all approved Class I, Class II, and Class III devices.
- A listing of Class I and Class II devices deemed [exempt](#) from Premarket Notification 510(k) regulations.
- Guidance for devices that [emit radiation](#).

References and Regulations

FDA References:

- [Device Advice: Comprehensive Regulatory Assistance](#)
- [Significant Risk and Non-significant Risk Medical Device Studies](#)
- [Expanded Access to Unapproved Medical Devices](#)
- [Guidance for Humanitarian Device Exemptions](#)

FDA Regulations:

- Investigational Device Exemptions: [21 CFR 812](#)
- Premarket Approval of Medical Devices (includes HUDs): [21 CFR 814](#)
- Medical Device Classification Procedures: [21 CFR 860](#)
- Requirements for Device Registration and Listing: [21 CFR 807](#)
- Electronic Records; Electronic Signatures: [21 CFR 11](#)
- Financial Disclosure by Clinical Investigators: [21 CFR 54](#)
- Quality System Regulation: [21 CFR 820](#)