Investigational Devices

What is an Investigational Medical Device?

A medical device is considered investigational if either condition applies:

- The device is not approved for marketing in the U.S. or
- The device is approved for marketing but is being *clinically* evaluated for a new indication.

The Food and Drug Administration (FDA) [2] regulates research involving medical devices (see FDA definition [3]), as well as all aspects of device manufacturing, marketing and distribution (*Code of Federal Regulations* Title 21, parts 800-1299). The FDA website contains several sets of useful and readable guidance documents about investigational devices, including mobile devices.

For many studies involving devices, an investigator or sponsor must obtain an Investigational Device Exemption (IDE) from the FDA. See the **UCSF Investigator Checklist for IDE Exempt, Non-Significant, and Significant Risk Device Studies [4]** for a quick overview of when an IDE from the FDA is required or not required.

FDA Regulatory Support at UCSF [5] provides free consultations to the UCSF community on compliance with FDA regulations, including IDE requirements.

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

When Is an Investigational Device Exemption (IDE) Required?

There are two types of clinical studies involving medical devices that require than an Investigational Device Exemption (IDE) be obtained from the FDA in addition to IRB approval before a research study may commence.

1. A clinical study involving an unapproved device that poses significant risk to subjects

The majority of IDE studies are conducted to collect safety and effectiveness data used to support Premarket Approval (PMA) applications submitted to the FDA.

Examples: Significant risk [6] studies involve implantable devices such as cardiac pacemakers, orthopedic implants and stents. Significant risk 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.

Note: See UCSF guidance on Significant and Non-Significant Risk Devices [6] for more information.

2. A clinical study involving an approved (legally marketed) device being tested for a new indication

This includes both a device being used or tested in a new way that significantly increases the risks associated with the device and/or significant risk studies testing an FDA-approved device.

Examples: 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?

There are four types of clinical studies involving medical devices that do *not* require that an IDE from the FDA be obtained be obtained. However IRB approval is required before the study may commence.

1. **Studies involving approved devices used with their approved labeling** *or* **devices that are substantially equivalent** [7] (already granted an 510(k) by the FDA) to currently marketed devices

2. Studies involving approved devices that are determined by the IRB or the FDA to pose non-significant risks to the subjects

- IRB review and approval is required for all non-significant risk device [6] studies.
- The FDA authorizes institutional review boards to conduct a risk assessment of all proposed non-significant risk studies. However, IRB cannot override NSR FDA determination if one has previously been made.
- Study approval is dependent on the investigator supplying the IRB with sufficient information, generally provided by the study sponsor, regarding the device and its intended use.
- If the IRB determines that a proposed non-significant risk study is actually a significant risk study, the sponsor must submit a report to the FDA as explained here [6].

For more information, see UCSF guidance on Significant and Non-Significant Risk Devices [6].

Examples: Non-significant risk devices include daily wear contact lenses and associated care products; conventional gastroenterology and urology endoscopes; externally worn monitors for insulin reactions; and non-implantable electrical incontinence devices.

3. Practice of medicine

A physician can use a legally marketed device without 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.

4. Specific IDE-exempt studies, as described by FDA regulations

Review 21 CFR 812.2 [8] for a complete list of all types of investigations which are exempt from FDA IDE requirements. The 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 diagnostics labeled for ?research purpose only? as per regulations [21 CFR 809.10(c)] and if the testing:
    - is noninvasive;
    - does not require invasive sampling procedure 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 or procedure;

Additional FDA guidance on studies using in vitro diagnostics [9] is available. Also review the ? UCSF Investigator Checklist for IDE Exempt, Non-Significant, and Significant Risk Device Studies [4]? for a quick overview of when an IDE from the FDA is required or not required.

IRB Submission and Reporting Requirements

If your study involves a device, you must provide information about the device in the IRB Application and consent form [10], and submit other supporting documents.

IRB Application and Supporting Documentation Requirements

For significant risk device studies

- **IRB Application:**
    - Indicate that the study involves a device in the "Initial Screening Questions" section.
    - Check the appropriate box in the "Drugs and Devices" section of the IRB Application.
- **An IDE number:** If the sponsor?s protocol does not list the IDE number, you must submit documentation from the sponsor or FDA identifying the IDE number for this study. The IRB will not issue final approval until the IDE number is reported to and verified by the IRB. However, the IRB will review the research before the IDE application is submitted to the FDA.
- **Investigator?s Brochure**
- **Directions for use**, typically provided by the manufacturer and **device labeling** consistent with federal regulations [21 CFR 812.5 [11]]
- **Scientific/sponsor's protocol**: This document should describe the methodology to be used and offer an analysis that the study is scientifically sound.
- **An explanation of the device cost,** which is determined by the reimbursement category [12] provided by FDA with each approved IDE. This information is needed for the consent form.
- **Clearance from the Radiation Safety Committee [13]** for radiation-emitting devices.

For non-significant risk device studies

- **IRB Application:**
  - Indicate that the study involves a device in the "Initial Screening Questions" section.
  - Check the appropriate box in the "Drugs and Devices" section of the IRB Application
  - Check Yes when asked if a Non-Significant Risk (NSR) determination is being requested for the investigational device. Then complete the "Non-Significant Risk Determination for an Investigational Device" section to provide the IRB with adequate justification why the use of the device in this study poses non-significant risk.
- **Detailed device information from the sponsor,** such as a description of the device and how it is used.
- **Diagrams and/or *in situ* photographs of the device** are very useful (attach as "Other Study Documents").
- **Directions for use**, typically provided by the sponsor or manufacturer and **device labeling** consistent with federal regulations [21 CFR 812.5].
- **Scientific/sponsor's protocol:** This document should describe the methodology to be used and offer an analysis that the study is scientifically sound.
- **An explanation of the device cost:** Non-significant risk devices are placed in Category B and are most likely eligible for reimbursement. See the reimbursement category [12] overview provided by the FDA.

See our guidance on Significant and Non-Significant Risk Devices [6] for more info.

Consent Form Requirements

All medical device studies involving human subjects require informed consent. Include the following key points within the consent form template [14] sections noted below:

Purpose and background

- Must include a clear statement that the device is investigational and has not been approved by the FDA for clinical use or, if applicable, that the device has been approved for specific clinical indications but not for the use being studied.
- Should include a brief lay description of the device and what it is designed to do.
- Must not describe the issuance of an IDE as an approval or endorsement by the FDA.

Confidentiality

Must state that the FDA may review research and subjects? medical records to verify study data.

Alternatives

Must include a list of the various alternatives to participation in the study. This should name

the standard therapies available with approved devices, as well as other experimental treatments with investigational devices.

Cost

- Provide specific information regarding the participation in the device study. If applicable,
  - state if the sponsor is supplying the device at no charge.
  - state whether the subject or their insurance carrier will be billed for the device,
  - state that the cost may not be covered by insurance because the therapy is experimental,
  - provide a discussion of the cost of implanting and, if anticipated as part of the study, the cost of explanting the device.
- Describe how the subject can obtain more detailed information about the possible financial risks, if needed.

Adverse Event Reporting

Adverse events associated with research participation must be reported expeditiously to both the IRB [15] and to the FDA (21 CFR 812.150).

Investigator?s responsibilities

- All investigators have an obligation to report certain adverse events [15] directly to the IRB.
- Under IDE regulations, there are additional and separate federal requirements for reporting adverse events to the FDA. 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.

Investigator-sponsor responsibilities

- Investigators who hold an IDE have responsibilities for reporting adverse events associated with the investigational device.
- In addition to reporting to the IRB [15], an investigator-sponsor must report unanticipated adverse events investigated under a sponsor?s monitoring requirements directly to FDA within 10 working days after the sponsor receives notice of the effect. See FDA regulations [16] and the UCSF HUB [17] for more info.

Types of IDE Applications

Commercial IDE

An IDE application submitted by a sponsor seeking FDA clearance to market a medical device.

Investigator-initiated IDE

By submitting an IDE application to the FDA and conducting the clinical investigation, a physician takes on the responsibilities of both ?sponsor? and ?investigator.?

Emergency Use IDE

This is an exception to investigational device regulations permitting the *one-time treatment of one patient per institution* without prior FDA approval.

- Every effort must be made to obtain prior authorization from the IRB; at minimum at UCSF an IRB Chair must concur before treatment begins.
- Strict reporting requirements apply.
- The emergency use of an investigational device must meet all of the following criteria:
    - the patient has a life-threatening or severely debilitating condition, and
    - there are no other available treatments, and
    - there is not sufficient time for prior IRB review and approval.

Note: Research may not be conducted under an emergency use IDE. Subsequent use(s) of the emergency use investigational device require prior IRB review and approval. For more information, please review the UCSF guidelines for Emergency Use of Experimental Drugs and Devices [18].

Expanded Access, Humanitarian Use and Combination Products

Expanded Access

There are three regulatory mechanisms that allow expanded access to investigational medical devices while clinical studies and/or FDA review are on-going. Because 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. See FDA Guidance on Expanded Access for Medical Devices [19] or more details.

Important Notes:

1. Except for Emergency Use, both FDA and IRB review and approval is required before treatment can begin using these mechanisms. See guidance on Emergency Use [18]for requirements for details of that process.
2. Expanded access programs are not considered research but rather treatment, and those enrolled in these programs should be referred to as ?patients? and not ?subjects.?

1. Emergency Use ? See discussion in section above.

2. Compassionate Use (or Individual Patient/Small Group Access)

Under an existing IDE, the FDA may allow treatment for an individual or a small number of seriously ill patients who have (a) a life-threatening disease or condition(b) with no other generally acceptable alternative treatment for the condition and (c) there is an existing concurrent clinical trial but the patient(s) do not meet the inclusion criteria and (d) the treating physician believes the device may provide a benefit in treating and/or diagnosing their disease. The FDA requires the sponsor/investigator either to supply a supplement to an existing IDE justifying the compassionate use or to request a new IDE.

Note: Compassionate use requires FDA review and IRB approval before treatment can be initiated. The study involving the existing IDE must already be approved by the IRB. See the Emergency Use and Compassionate Use of Experimental Drugs and Devices [18] page for more info.

3. Treatment Use

If during the course of a clinical trial the data suggests that the device is effective, then the trial may be expanded to include additional patients with life-threatening or serious diseases for whom no comparable or satisfactory alternative is available. In addition, the sponsor of the controlled trial must be pursing marketing approval/clearance of the device. Note: Treatment use may begin 30 days after the FDA has received the treatment IDE submission, or earlier if FDA notifies the sponsor in writing. Prior IRB review and approval are also required.

Continued Access (Example of Treatment Use)A common type of treatment use occurs when after the completion of a controlled clinical trial, a supplement to an existing IDE is submitted and the FDA allows continued access to the device provided there are no safety concerns. The Continued Access Policy creates a bridge and allows access to promising devices while the marketing application is being prepared by the sponsor or reviewed by the FDA.

Humanitarian Use

A Humanitarian Device Exemption (HDE) allows the FDA to grant an exemption from the effectiveness provisions of the Premarket Approval (PMA) regulations. Devices approved under an HDE are referred to as 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 no more than 8,000 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 IRB requires a standard application and use of a consent form similar to research consent. The initial review for this application must be done by the full committee; however, the annual continuing reviews can be done through expedited procedures.

The IRB has posted a sample consent form for Humanitarian Use Devices [20]. However, you may also adapt the sample consent supplied by the study sponsor.

Drug-Device Combination Products

The Office of Combination Products (OCP) [21] was created to facilitate the review process for combination products by coordinating interactions between reviewing branches. The OCP provides guidance documents for combination products.

Some recent combination product approvals [22] include drug-eluting coronary stents and antibiotic bone cement.

Timing the IDE Submission

Pre-IDE Process

Applicants are encouraged to request feedback from the FDA regarding potential or planned IDE applications or other premarket submissions. For more info, review the UCSF HUB's Pre-IDE Process [17] page and FDA's Pre-Submission Program guidance document [23].

The IDE Submission

The completed IDE submission to the FDA and the IRB Application should be initiated at the same time. However, because the IDE application process is more complicated than the IND process, inexperienced investigators may wish to allow extra time to complete the paperwork for the FDA and complete this before preparing the IRB Application. The FDA has 30 days to review the completed IDE application. An investigator cannot initiate a clinical study until the FDA and IRB have granted approval.

Responsibilities of Investigators and Sponsors

While conducting significant risk and non-significant risk device studies, investigators and sponsors have many specific responsibilities [24]. The obligations span a broad range, including FDA and IRB approvals, informed consent, study monitoring, and multiple reporting requirements. See the FDA website [24] for more info.

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:

- The investigator must ensure that the investigational device is used only in accordance with the IRB-approved protocol, the signed agreement, the investigational plan and applicable FDA regulations.
- The investigator must administer 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.
- The investigator must not supply the investigational device to any person not authorized to receive it.
- The investigation must maintain the following accurate, complete, and current records relating to the investigator?s participation in an investigation.
    - Records of receipt, use or disposition of a device that relate to a) The type and quantity of the device, the dates of its receipt, and the batch number or code mark; b) the names of all persons who received, used, or disposed of each device; c) why and how many units of the device have been returned to the sponsor, repaired, or otherwise disposed of.
- If the investigation is terminated, suspended, discontinued, or completed, the investigator must return 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.

Here is a sample Investigational Device Accountability Log [25] you can use.

Import/export of investigational devices

A complete overview of medical device import/export regulations [26] is provided by the CDRH. Clinical investigators should be aware that 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 Resources

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 a new device is as safe and effective as the predicate device(s).
- Guidelines describing streamlined 510(k) options [27] are available.
- Clinical studies using 510(k) devices may be subject to IDE regulations. Prior FDA and IRB approval are required.

Premarket Approval (PMA) [28] has more stringent requirements for high risk Class II devices. In most cases an IDE is required to clinically evaluate devices subject to PMA regulations.

Humanitarian Device Exemption [29] **(HDE)**, as discussed above, is aimed at encouraging device development for conditions with no more than 8000 patients.

Device classification

The level of regulatory controls placed on a medical device is determined by the risk classification. Most of the clinical studies at UCSF requiring IDEs from the FDA are significant risk, Class III devices. The FDA provides an overview of the risk-based classification scheme. To help determine device classification, regulatory controls, and exemptions, the Center for Devices and Radiological Health (CDRH) maintains:

- A searchable classification database [30] containing information about all approved Class I, Class II, and Class III devices.
- A device listing categorized by medical speciality [31].
- A Listing of Class I and Class II devices deemed exempt [32] from Preparmet Notificatiion (510(k) regulations.
- Guidance for devices that emit radiation [33].

Resources

- FDA Regulatory Support at UCSF [5]
- Significant and Non-significant Risks Devices:
    - UCSF Guidance [6]
    - FDA Guidance [34]
- UCSF HUB: IDE Submissions for Sponsor-Investigators [17]
- FDA: IDE Definitions and Acronyms [35]
- FDA: Device Advice: Comprehensive Regulatory Assistance [36]
- FDA: Mobile Medical Applications Guidance [37]
- FDA: 21 CFR 812: Investigational Device Exemptions [38]
- FDA: 21 CFR 814: Premarket Approval of Medical Devices [39]
- FDA: 21 CFR 860: Medical Device Classification Procedures [40]

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Links
[1] https://irb.ucsf.edu/sites/hrpp.ucsf.edu/files/device-checklist.pdf
[2] http://www.fda.gov/MedicalDevices/
[3] http://www.fda.gov/AboutFDA/Transparency/Basics/ucm211822.htm
[4] http://irb.ucsf.edu/sites/hrpp.ucsf.edu/files/device-checklist.pdf

[5] https://compliance.ucsf.edu/fda-support
[6] https://irb.ucsf.edu/significant-vs-non-significant-risk-devices
[7]
http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions
[8] http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=812.2
[9]
http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/IVDRegulatoryAssistance/ucm123682.htm
[10] https://irb.ucsf.edu/#consent
[11] http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?FR=812.5
[12]
http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceE
[13] http://www.research.ucsf.edu/rspc/techcomm.asp
[14] https://irb.ucsf.edu/consent-and-assent-form-templates
[15] https://irb.ucsf.edu/adverse-event
[16]
http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=812&showFR=1
[17] http://hub.ucsf.edu/ide-development-process
[18] https://irb.ucsf.edu/emergency-use-and-compassionate-use-experimental-drugs-and-devices
[19]
http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceE
[20] http://irb.ucsf.edu/sites/hrpp.ucsf.edu/files/hud-consent.doc
[21] http://www.fda.gov/CombinationProducts/default.htm
[22] http://www.fda.gov/CombinationProducts/AboutCombinationProducts/ucm101598.htm
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[25] http://hrpp.ucsf.edu/sites/hrpp.ucsf.edu/files/investigational-device-accountability-log.doc
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