

ARE YOU THE HOLDER OF AN IDE?

...CONSIDER YOUR LEGAL
OBLIGATIONS

INVESTIGATIONAL DEVICE



USC

**Office for the Protection of
Research Subjects (OPRS)**

About This Booklet

This booklet provides researchers with the regulations and responsibilities that apply when they are the holder of an Investigational Device Exemption (IDE). It is intended to be a useful reference for researchers, staff and study teams. USC has accountability obligations for all sponsor-investigator drug, device, or biological research at the University.

In addition, the sponsor-investigator is responsible for compliance with FDA regulations and communication.

Sometimes a faculty member serves as the principal investigator of an Investigational New Drug (IND) or IDE, whose sponsor is an outside company, institution, organization, or individual. Under federal law, the outside sponsor, not the University, is responsible for interactions with the FDA. The principal investigator, however, remains subject to all other University policies on clinical research.



What Is An IDE?

An Investigational Device Exemption (IDE) application is the document submitted to the FDA to allow for the conduct of a clinical study using a significant risk device that is new or not approved for a given use.

If you are the holder of an IDE and you assume the responsibilities of both an investigator and a sponsor, all of the following are true:

1. You obtained an IDE from the FDA (you are the “holder”)
2. You are responsible for clinical testing of the device (you are the “sponsor”)
3. You are conducting a clinical trial and dispensing or using the device in human subjects (you are the “investigator”). In order to conduct a clinical investigation of a device an IDE application must be filed with FDA, unless the study is exempt from IDE requirements*.

These terms may also be used to describe IDE holders:

- Sponsor-investigator**
- Investigator-initiated research
- IDE Investigator
- Investigator-sponsored IDE
- Physician-initiated research

****Exempt from IDE requirements:*** Certain device studies may be considered exempt from IDE requirements. These studies require documentation describing the specific reason for the exempt status.

*****The terms “sponsor-investigator” and “IDE holder” are used interchangeably throughout this pamphlet. The term sponsor-investigator is used particularly when the investigator has not yet submitted the IDE application to the FDA.***

When Do You Need An IDE?

Significant vs. Non-significant Risk Devices

An IDE is required to study an investigational device (including new intended use of an approved device) posing *significant risk** and must be submitted to the FDA before study initiation. If the investigation involves the use of a device that does not pose significant risk to humans (a non-significant risk device), an IDE application to FDA is not required.



Submissions for non-significant risk devices are made directly to the IRB. The sponsor-investigator must explain to the IRB why the device does not pose a significant risk. If the IRB determines that the device does pose a significant risk to subjects, the sponsor-investigator must notify the FDA within five working days. Sponsor-investigators conducting non-significant risk device studies must submit for IRB approval and comply with abbreviated IDE requirements listed in 21 CFR 812.2(b): www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?fr=812.2

Mobile Medical Applications

The intended use of a mobile application determines whether it meets the definition of a “device” that requires FDA oversight. When these items are marketed, promoted or intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, they are regulated by the FDA. The FDA will apply its regulatory oversight to those mobile apps that are medical devices and whose functionality could pose a risk to a patient’s safety if the mobile application were to not function as intended. IRB approval is necessary prior to commencing with an investigator-initiated study involving new mobile applications or devices – review can determine if an IDE, an abbreviated IDE, or no IDE is required. For more information visit:

FDA - Mobile Medical Applications:

<https://www.fda.gov/medicaldevices/digitalhealth/mobilemedicalapplications/default.htm>

*Significant risk: presents a potential serious risk to the health, safety, or welfare of subjects (e.g., stents, sutures)

What If Your Device Study is Exempt from IDE Requirements?

An approved IDE allows investigators to use an investigational device for the purpose of clinical testing. However, not all clinical trials using devices require permission from the FDA to proceed. The investigator must select the IDE exemption category in the IRB application in order to demonstrate that the study device is exempt.

Exempt IDE Categories

The following categories of devices are exempt from IDE requirements:

- devices in commercial distribution before 5/28/76
- devices determined by the FDA to be substantially equivalent to a device in commercial distribution before 5/28/76
- diagnostic devices that are noninvasive or do not require an invasive sampling procedure that presents significant risk, do not introduce energy into a subject or are not used as a diagnostic procedure without the confirmation of another medically established diagnostic product or procedure
- devices used for consumer preference testing or for any test that is not intended to determine safety or effectiveness and does not expose subjects to risk
- devices exclusively used for veterinary indications
- devices to be shipped exclusively for research on laboratory animals
- custom devices unless these are used to assess safety or effectiveness for commercial distribution

Device studies exempt from IDE requirements, generally still require IRB approval (21 CFR 56). Documentation of the IDE exemption category must be submitted to the IRB (choose exempt category in iStar). Contact the IRB for further guidance.

Preparing to Submit an IDE to FDA?

The FDA encourages prospective sponsors to communicate with the Office of Device Evaluation (ODE) prior to an IDE submission. Early communication with the FDA is a valuable resource, particularly for new IDE holders or for studies with new technology.

Preliminary information can be submitted to the FDA in the form of a pre-IDE submission when the applicant requires IDE application guidance.

The submission is reviewed by the FDA and the applicant receives a response within 60 days of submission. Pre-IDE submissions include correspondence between applicants and the FDA that transpire before the IDE submission and include pre-IDE meetings.

Pre-IDE meetings are classified as either informal or formal IDE meetings. Informal meetings can be utilized to obtain guidance for pre-clinical data and investigational plan development. The meeting format can be through telephone or video conferences as well as face-to-face conversations.

Formal meeting requests are submitted in writing and take place within 30 days of request submission. Formal meetings are either agreement or determination meetings and the type of meeting must be specified in the request.



Agreement vs. Determination Meetings

A formal agreement meeting is for the applicant of an IDE and the FDA to reach an agreement about the investigational plan. Meeting requests are submitted as pre-IDE submissions and must include a detailed description of the device and of the proposed conditions of use as well as the investigational plan and clinical protocol. If an agreement is made with the FDA about the investigational plan details, these are written into the IDE administrative record by the FDA.

Similarly, determination meetings are utilized to determine the type of valid scientific data necessary in a study for IDE applicants planning to submit a Pre-Market Approval (PMA). PMA is an FDA scientific and regulatory review process to evaluate the safety and effectiveness of Class III medical devices (e.g., devices that sustain human life).

Meeting requests are submitted along with summary information and the FDA provides a written determination within 30 days of the meeting.

USC Scientific Review

The USC Clinical Research Support Office of SC CTSI will complete a scientific review of IDE submissions. The OFFICE is also an available resource for assistance throughout the study process.

SC CTSI Contact Information: info@sc-ctsi.org

What to Include in an IDE Application?

The IDE application to the FDA must include the items listed below. Three copies of the signed IDE application must be submitted to the FDA with the following (812.20):

Required Items for IDE Application

1. The IDE holder's name and address
2. A report with all prior investigations of the device and a summary of the investigational plan. The complete investigational plan must be submitted to the FDA if no IRB has reviewed the investigational plan and report of prior investigations, if the FDA determines the IRB review is inadequate or if the FDA requests them.
3. A description of methods, facilities and controls used in the manufacture, processing, packing, storage, and, if applicable, installation of the device. The description will be used to assess quality control and good manufacturing practices, therefore, the level of detail should reflect the complexity of the process.
4. An example of the agreement to be signed by the investigators and a list of the names and addresses of all investigators.
5. A statement certifying that all investigators participating in the study will sign the agreement and that no investigator will take part in the study before signing the agreement.
6. An IRB list with the name, address and chairperson of each IRB that will review the investigation and a certification of IRB study-related action. Also, the name and address of any institution in which part of the study may be conducted but not yet identified in the application.
7. If the device will be sold, the amount to be charged for the device and a rationale of how its sale does not amount to commercialization of the device.

Note: FDA regulations allow for sponsors to sell a device and often the cost is passed onto participants.

8. Copies of all device labeling
9. Copies of all informational material to be presented to subjects in the informed consent process
10. Any other information requested by the FDA for inclusion in the IDE application

Note: a categorical exclusion claim as listed under 21 CFR 25.30 or 25.34 or an environmental assessment as required by 21 CFR 25.40 is no longer required.

A Form FDA 3674 (Certification of Compliance with Requirements of ClinicalTrials.gov Data Bank) must also be submitted to the FDA

The FDA website provides additional guidance on the IDE application including required elements, suggested content and format, and common problems submitting IDEs. Refer to:

IDE Approval Process:

<https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionIDE/ucm046164.htm>

IDE Application:

<https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionIDE/ucm046706.htm>

eCopy Program for Medical Device Submissions Guide:

<https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/howtomarketyourdevice/ucm370879.htm>

USC Sponsor-Investigator Agreements

Principal Investigator's Assurance

All investigators must read and agree to the Principal Investigator's Assurance. The agreement is located in iStar and acceptance is required of all Principal Investigator (PI) responsibilities before submitting a completed application for IRB review.

USC Sponsor-Investigator Agreement

For investigator-initiated device studies in which the PI is the IDE holder, the investigator must upload a signed USC Sponsor-Investigator Agreement form on the iStar application. By signing this form, the investigator agrees to comply with both sponsor and investigator responsibilities and assure compliance with applicable regulations. A copy of the USC Sponsor-Investigator Agreement form can be found at:

https://oprs.usc.edu/files/2017/05/Invest_Sponsor_Form.doc

USC Educational Requirements

In addition to federal and state requirements, USC IDE holders must comply with applicable USC educational training requirements. All trainings are online.

1. Human Subjects Education Training

All investigators and key personnel conducting human subjects research at USC, whether IDE holders or not, must complete the CITI human subjects training. The mandatory training is a condition of IRB study approval. For CITI access, FAQs:

<https://oprs.usc.edu/education/citi/>

2. Good Clinical Practice (GCP)

Good Clinical Practice training is required for all principal investigators and key personnel conducting full board clinical trials (not applicable to personnel who conduct expedited or exempt studies exclusively). More information can be found at:

<https://oprs.usc.edu/education/citi/>

3. HIPAA

All USC faculty, staff, employees, students, volunteers and agents with access to patient protected health information (PHI) from USC providers must complete the online HIPAA compliance program:

<http://ooc.usc.edu/hipaa-privacy-regulations>

Maintaining Regulatory Compliance

In studies sponsored by a pharmaceutical or device company, study monitors, provided by the sponsor, visit sites on a regular basis to ensure regulatory compliance. However, when investigators act as their own sponsors, they normally do not have study monitors to verify that the study is conducted in compliance with the protocol, IRB application, and applicable regulations. IDE holders must ensure that all federal, state and institutional regulations are being met. The monitoring functions may be delegated to a contract research organization. The monitoring plan should include the following:

- The protocol/investigational plan is being followed
- Changes to the protocol have been approved by the IRB and/or reported to the sponsor and the IRB
- Records are accurate, current, and complete
- Informed consent has been documented in accordance with 21 CFR Parts 50 and 56

More information can be found on the FDA website:

<https://www.fda.gov/medicaldevices/deviceregulationandguidance/howtomarketyourdevice/investigationaldeviceexemptionide/ucm046702.htm#resofspofor>

Products Manufactured in California

If an IDE product is manufactured in California, the following requirements must be met:

License and Inspection

A license application (one per place of manufacture) must be submitted to the Food and Drug Branch (FDB) of the California Department of Health Care Services. A license is valid for two calendar years from the date of issue and a license renewal application should be filed before its expiration date to maintain compliance and avoid penalties.

Device Manufacturing Requirements

When a device is manufactured in the state of California, IDE holders must abide by additional requirements according to the CA Sherman Food, Drug, and Cosmetic Law.

IDE Reporting Requirements

Changes to Investigational Plan

21 CFR 812.35

IDE holders must notify the FDA within 5 working days of implementing the change to the plan.

Adverse Events / Unanticipated Adverse Device Effects

21 CFR 812.3

A reportable event is any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious event associated with a device that relates to the rights, safety, or welfare of subjects.

A reportable event must be submitted to the FDA, all reviewing IRBs and participating investigators within 10 working days after the IDE holder receives notice of the effect.

Progress Reports or Annual Reports

21 CFR 812.150(b)(s), 812.35(a)(4)

A progress report must be submitted at least once a year to the reviewing IRB and the FDA.

Study Completion or Termination

21 CFR 812.150(b)(7)

Holders of an IDE must notify the FDA of the completion or termination of a study of a significant risk device within 30 working days of termination and submit a final report to the FDA and all reviewing IRBs within 6 months after completion or termination.

Potential Conflicts of Interest

The University of Southern California defines Conflict of Interest (COI) as “a situation in which financial or other personal considerations compromise, or have the appearance of compromising an individual’s professional judgment in proposing, conducting, supervising or reporting research” (USC Conflict of Interest in Research: Policy and Procedure). USC Conflict of Interest reporting requirements are found at:



<https://policy.usc.edu/research-conflict-interest/>

Researchers who are proposing or have received support from the United States Department of Health and Human Services (including NIH, CDC, HRSA, and AHRQ) must also make an annual disclosure of all financial interests related to their institutional responsibilities to USC, regardless of whether any of these interests give rise to a conflict of interest related to their research.

Link: <https://disclose.usc.edu/>

Investigators must also disclose Conflicts of Interest in the iStar application.

An IDE holder must disclose COIs as a sponsor and as an investigator. If the IDE holder does not have an identifiable disclosable financial arrangement to report, an FDA 3454 Form (Certification: Financial Interests and Arrangements of Clinical Investigators) must be completed and submitted to the FDA. However, if an identifiable disclosable financial arrangement will be reported, an FDA 3455 Form (Disclosure: Financial Interest and Arrangement of Clinical Investigators) must be submitted to disclose the financial arrangement.

If the IDE holder is the only investigator for the study, only one form is submitted to the FDA. If other investigators are involved in the study, the IDE holder can attach a list of all investigators without a disclosable financial arrangement to report to FDA 3454 Form. However, an individual FDA 3455 Form must be completed by each investigator in the study reporting a disclosable financial arrangement.

Other Resources

State Resources

California Dept. of Health for Manufacturers, Processors, and Distributors

California Food and Drug Branch

University of San Fransisco Resource

Investigational Device Exemption (IDE) Submission for Sponsor-Investigators

<http://hub.ucsf.edu/ide-development-process>

Virginia Commonwealth Resource

Investigational Device Exemption (IDE) Flowchart

http://research.vcu.edu/IND_IDE/IDE_flowchart.pdf

USC Resources

USC Resources

Office for the Protection of Research Subjects (OPRS)

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Los Angeles, CA 90089-0706

Tel: (213) 821.1154 Fax: (213) 740.9299 E-mail: oprs@usc.edu

<https://oprs.usc.edu/>

<https://oprs.usc.edu/hsirb/biomedical/investigator-initiated-trials/>

<https://oprs.usc.edu/hsirb/biomedical/drugs-and-devices/>

USC Institutional Review Board

1640 Marengo Street, Suite 700

Los Angeles, CA 9033-9269

Tel: (323) 442.0114 Fax: (323) 224.8389 E-mail: irb@usc.edu

<https://oprs.usc.edu/irb-review/>

USC Office of Compliance

University Gardens Building, Room 105 3500 Figueroa Street

Los Angeles, CA 90089-8007

Tel: (213) 740.8258 E-mail: complian@usc.edu

www.usc.edu/compliance/

USC Clinical Trials Office

2011 North Soto Street, 2nd Floor

Los Angeles, CA 90032

Tel: (323) 442-7218 E-mail: clinicaltrialsoffice@med.usc.edu

<http://clinicaltrials.usc.edu>

Southern California Clinical and Translational Science

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2250 Alcazar Street, CSC 200

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