INVESTIGATIONAL DEVICES	SOP 4.5.01

1. Purpose & Policy

The purpose of this SOP is to describe the requirements for research involving medical investigational devices and the process for IRB review of these devices, including those exempt from, or subject to Investigational Device Exemption (IDE) regulations. IRB Policy *Section 4.5*.

2. General Information

The Food and Drug Administration (FDA) IDE regulations [21 CFR 812] describe three types of device studies: 1) exempt, 2) significant risk (SR) and 3) nonsignificant risk (NSR).

The FDA requirements for studies involving investigational devices are proportional to the potential risk level (see SR and NSR definitions below). Certain investigational device studies are exempt from IDE requirements. An SR device study must be conducted under an FDA-approved IDE, and an NSR study may be conducted under an abbreviated IDE solely overseen by the Caltech IRB.

Each PI who uses an investigational medical device is responsible for control of the device in accordance with regulatory requirements. The PI is responsible for implementing the plan as approved by the IRB and/or FDA. (See flowchart in Figure 1).

A device that is used as a tool and not the focus of the study is not subject to FDA regulations.

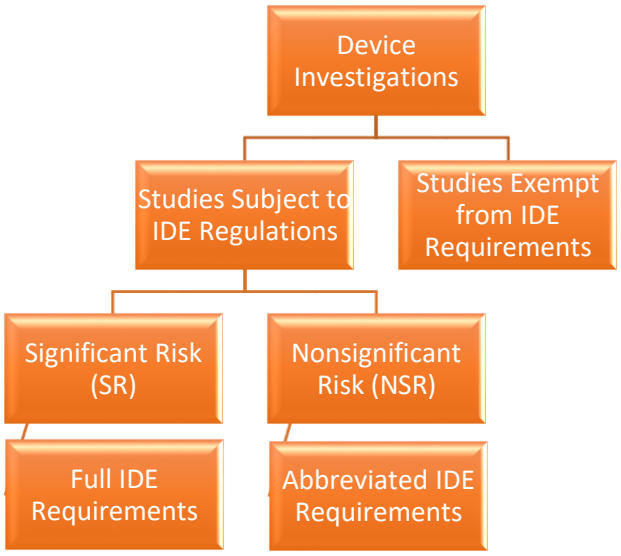


Figure 1. Types of FDA-governed Device Studies

Definitions

Medical Device: An instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is: A) recognized in the official National Formulary, or the United States Pharmacopoeia or any supplement to them, B) 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 C) 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 and which is not dependent upon being metabolized for the achievement of its primary intended purposes.

Any health care product that does not achieve its primary intended purposes by chemical action or by being metabolized.

Investigational Device: A medical device that is the subject of a clinical study designed to evaluate the effectiveness and/or safety of the device. The device is still in the developmental stage and is not considered to be in commercial distribution.

Investigational Device Exemption (IDE): An approved IDE exempts a device from specific FDA requirements as laid out under [21 CFR 812]. An approved IDE means that the IRB (and FDA for significant risk devices) has approved the investigators study application and all the requirements under [21 CFR 812] are met.

Significant Risk (SR) Device: An SR device is an investigational device that presents a potential for serious risk to the health, safety, or welfare of a participant and: (1) is intended as an implant; (2) is for use in supporting or sustaining human life; (3) is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease or otherwise preventing impairment of human health; or (4) otherwise presents a potential for serious risk to the health, safety, or welfare of a participant.

Nonsignificant Risk (NSR) Device: A NSR device is one that does not meet the definition for an SR device.

3. Training Requirements

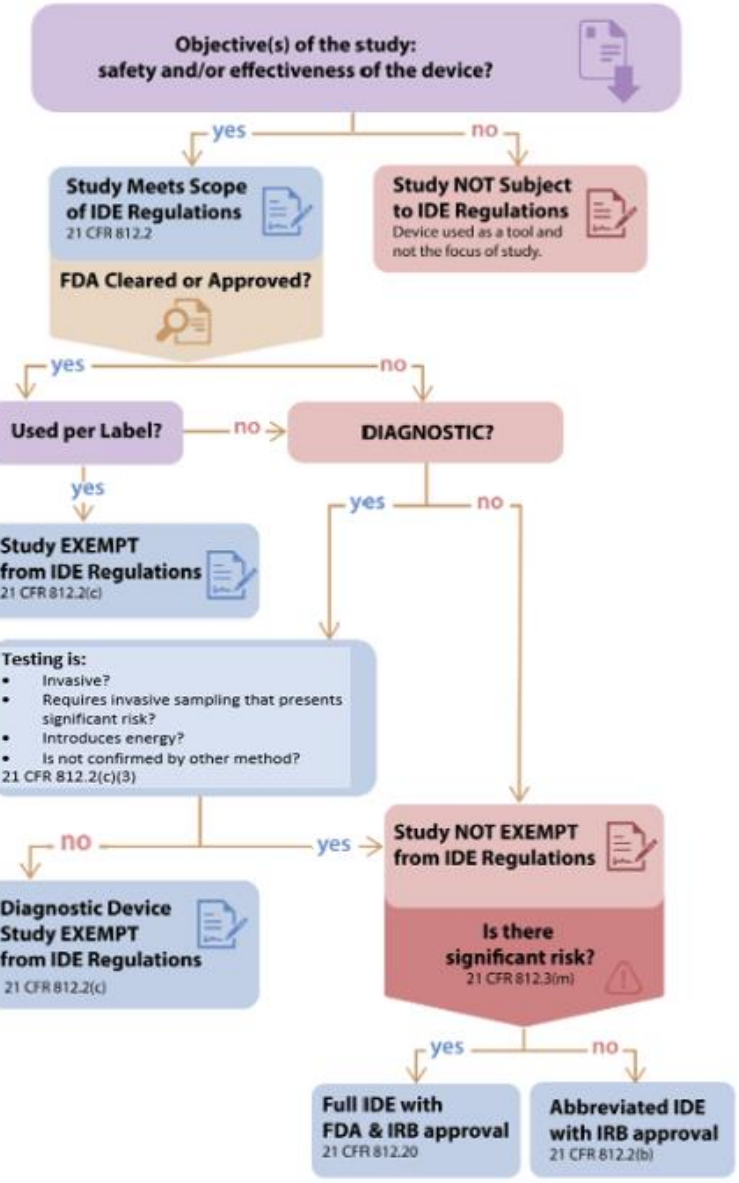
All investigators participating in studies involving medical investigational devices that are subject to FDA regulations must complete the CITI modules *FDA Regulated Research* and *GCP for Clinical Investigations of Devices*.

4. Procedure

A. An investigator conducting research that involves collection of safety or efficacy data on an investigational medical device must complete the applicable device section of the IRB protocol application. Investigators must provide sufficient information about the device, including:

1. Description of the device,
2. The FDA classification of the device, if applicable, (i.e., Class I (lowest risk), II, or II (highest risk)),
3. Reports of prior investigations using the device,
4. Risk assessment,
5. Rationale for why the study should be considered exempt or NSR, and
6. Any other substantial information.

The information entered in the protocol application will help the IRB determine whether the study is subject to or exempt from IDE requirements. The IRB will conduct its analysis in accordance with the flowchart shown in Figure 2.



FDA = U.S. Food and Drug Administration; IDE = Investigational Device Exemption; IRB = Institutional Review Board.

https://www.regardd.org/devices/is-my-study-exempt

Figure 2. Determination of whether a device is Exempt, Full IDE, or Abbreviated IDE

B. Studies that are NOT Subject to IDE Regulations
    1. A device that is used as a tool and is not the focus of the study.

C. Studies Exempt from IDE Requirements

    1. A device that is:
        i. The object of the study in people (For example, is the purpose to develop, calibrate or validate the device?);
        ii. Approved by the FDA for the purpose used in the study; and
        iii. Is not being modified in any way to improve efficacy.
    2. A diagnostic device, if the testing is:
        i. Non-invasive (A procedure that physically enters the body. For example, an endoscope);
        ii. Does not require an invasive sampling procedure that presents significant risk (greater than everyday life);
        iii. Does not by design or intention introduce energy into a subject (Energy that has the potential to introduce risk. Established diagnostic imaging does not apply. Thermal ablation would apply); and
        iv. Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure. (For example, comparing images to MRI images.)
        [21 CFR 812.2 (c)(3)]
    3. The IRB will make the final determination if the investigational device is exempt from FDA regulations.

D. Studies Subject to Abbreviated or Full IDE Requirements

    1. If the study is being conducted under a valid IDE, the PI must indicate this in the protocol and attach a copy of the FDA investigational device application and approval.
    2. If there is no existing IDE, the IRB makes its determination of the risk category (SR or NSR). The IRB may review reports of prior investigations conducted with the device, the proposed investigational plan, participant selection criteria, monitoring procedures, and any other information deemed necessary to make its decision.
    3. If the IRB determines that the study is NSR, there is no requirement for submission of an IDE application to the FDA. The PI conducts the study in accordance with FDA abbreviated IDE requirements [21 CFR 812.2(b)(1)]:

        PIs should use the Abbreviated IDE Requirements Checklist (Attachment 1) to ensure the study complies with abbreviated IDE requirements. The IRB will use this Checklist during the review of protocols that include the use of NSR device(s).

i. Banned Device: The device is not a banned device under [21 CFR 895];

ii. Labeling: The device will be labeled in accordance with [21 CFR 812.5] and must bear the statement "CAUTION – Investigational Device. Limited by Federal (or United States) law to investigational use;

iii. IRB Approval: The PI will obtain and maintain IRB approval of the study after presenting a brief explanation of why the device is not a significant risk device;

iv. Informed Consent: The PI ensures that each investigator participating in the study of the device obtains from each participant, informed consent unless documentation is waived by the IRB;

v. Monitoring: The PI complies with the requirements of [21 CFR 812.46] with respect to monitoring studies;

vi. Records and Reports: The PI maintains the records required under [21 CFR 812.140(b)(4-5)] and makes the reports required under [21 CFR 812.150(b)(1-3)(5-10)];

vii. Investigator Records and Reports: The PI ensures that participating investigators maintain the records required by [21 CFR 812.140(a)(3)(i)] and makes the reports required under [21 CFR 812.150(a)(1-2)(5)(7)]; and

viii. Prohibitions: The PI complies with the prohibitions in [21 CFR 812.7], including commercialization, promotion, test marketing, misrepresentation of an investigational device and prolongation of the study.

4. If the IRB determines that a study involves the use of an SR device, the PI must obtain an IDE and IRB approval before the study begins and must conduct the study in accordance with IDE requirements. See the FDA website for additional information on the IDE application submission process.

E. Unanticipated/Adverse Event

If an unanticipated or adverse event occurs with a participant or others during a study of an investigational device, the investigator must submit a report of the event per the requirements outlined in [21 CFR 812.140(b)(4-5)]

Unanticipated adverse device effects. A sponsor who conducts an evaluation of an unanticipated adverse device effect under § 812.46(b) shall report the results of such evaluation to FDA and to all reviewing IRB's and participating investigators within 10 working days after the sponsor first receives notice of the effect. Thereafter the sponsor shall submit such additional reports concerning the effect as FDA requests.

ATTACHMENT 1: ABBREVIATED IDE REQUIREMENTS CHECKLIST

PIs with nonsignificant risk (NSR) studies must comply with the abbreviated IDE requirements set forth in [21 CFR 812.2(b)].

If the IRB determines that the study is NSR, there is no requirement for submission of an IDE application to the FDA. The PI conducts the study in accordance with FDA abbreviated IDE requirements [21 CFR 812.2(b)(1)]:

☐ Banned Device: The device is not an FDA banned device under [21 CFR 895]; An FDA banned device is one that presents substantial deception or an unreasonable and substantial risk of illness or injury that the FDA determines cannot be, or has not been, corrected or eliminated by labeling or by a change in labeling, or by a change in advertising if the device is a restricted device. A list of banned devices can be found at 21 CFR 895.

☐ Labeling: The device will be labeled in accordance with [21 CFR 812.5];

- ☐ Contents. An investigational device or its immediate package shall bear a label with the following information: the name and place of business of the manufacturer, packer, or distributor (in accordance with § 801.1), the quantity of contents, if appropriate, and the following statement: "CAUTION—Investigational device. Limited by Federal (or United States) law to investigational use." The label or other labeling shall describe all relevant contraindications, hazards, adverse effects, interfering substances or devices, warnings, and precautions.

- ☐ Prohibitions. The labeling of an investigational device shall not bear any statement that is false or misleading in any particular way and shall not represent that the device is safe or effective for the purposes for which it is being investigated.

- ☐ Animal research. An investigational device shipped solely for research on or with laboratory animals shall bear on its label the following statement: "CAUTION—Device for investigational use in laboratory animals or other tests that do not involve human subjects."

- ☐ The appropriate FDA Center Director, according to the procedures set forth in § 801.128 or § 809.11 of this chapter, may grant an exception or alternative to the provisions in paragraphs (a) and (c) of this section, to the extent that these provisions are not explicitly required by statute, for specified lots, batches, or other units of a device that are or will be included in the Strategic National Stockpile.

☐ IRB Approval: The PI will obtain IRB approval of the study after presenting a brief explanation of why the device is not a significant risk device, and maintains such approval;

☐ Informed Consent: The PI ensures that each investigator participating in the study of the device obtains from each participant, informed consent unless documentation is waived by the IRB;

☐ Monitoring: The PI complies with the requirements of [21 CFR 812.46] with respect to monitoring studies;

☐ Securing compliance. A PI who discovers that an investigator is not complying with the signed agreement, the investigational plan, the requirements of this part or other applicable FDA regulations, or any conditions of approval imposed by the reviewing IRB or FDA shall promptly either secure compliance, or discontinue shipments of the device to the investigator and terminate the investigator's participation in the investigation. The PI shall also require such an investigator to dispose of or return the device, unless this action would jeopardize the rights, safety, or welfare of a participant.

☐ Unanticipated adverse device effects

☐ The PI shall immediately conduct an evaluation of any unanticipated adverse device effect. All unanticipated adverse events must be immediately reported to the IRB.

☐ An investigator who determines that an unanticipated adverse device effect presents an unreasonable risk to participants shall terminate all investigations or parts of investigations presenting that risk as soon as possible. Termination shall occur not later than 5 working days after the investigator makes this determination and not later than 15 working days after the investigator first received notice of the effect.

☐ Resumption of terminated studies. If the device is a significant risk device, the PI may not resume a terminated investigation without IRB and FDA approval. If the device is not a significant risk device, the PI may not resume a terminated investigation without IRB approval and, if the investigation was terminated under paragraph (b)(2) of this section, FDA approval.

☐ Records and Reports: The PI maintains the records required under [21 CFR 812.140(b)(4-5)] and makes the reports required under [21 CFR 812.150(b)(1-3)(5-10)];

☐ (4) For each investigation subject to § 812.2(b)(1) of a device other than a significant risk device, the records described in paragraph (b)(5) of this section and the following records, consolidated in one location and available for FDA inspection and copying:

☐ (i) The name and intended use of the device and the objectives of the investigation;

☐ (ii) A brief explanation of why the device is not a significant risk device:

☐ (iii) The name and address of each investigator:

☐ (iv) The name and address of each IRB that has reviewed the investigation:

☐ (v) A statement of the extent to which the good manufacturing practice regulation in part 820 will be followed in manufacturing the device; and

☐ (vi) Any other information required by FDA.

☐ (b) PI reports. The PI shall prepare and submit the following complete, accurate, and timely reports:

☐ (1) Unanticipated adverse device effects. Immediately report the unanticipated effect to the Caltech IRB. Work with the Caltech IRB to conduct an evaluation of an unanticipated adverse device effect under § 812.46(b) and report the results of such evaluation to FDA and to any additional reviewing IRB's and participating investigators within 10 working days after the PI first receives notice of the effect. Thereafter the PI shall submit such additional reports concerning the effect as FDA requests.

☐ (2) Withdrawal of IRB approval. The PI shall coordinate with the Caltech IRB to notify FDA and all other reviewing IRB's and participating investigators of any withdrawal of approval of an investigation or a part of an investigation by a reviewing IRB within 5 working days after receipt of the withdrawal of approval.

☐ (3) Withdrawal of FDA approval. The PI shall notify all reviewing IRB's and participating investigators of any withdrawal of FDA approval of the investigation, and shall do so within 5 working days after receipt of notice of the withdrawal of approval.

☐ (5) Progress reports. At regular intervals, and at least yearly, the PI shall submit progress reports to all reviewing IRB's. In the case of a significant risk device, the PI shall also submit progress reports to FDA. The PI of a treatment IDE shall submit semi-annual progress reports to all reviewing IRB's and FDA in accordance with § 812.36(f) and annual reports in accordance with this section.

☐ (6) Recall and device disposition. The PI shall notify FDA and all reviewing IRB's of any request that an investigator return, repair, or otherwise dispose of any units of a device. Such notice shall occur within 30 working days after the request is made and shall state why the request was made.

☐ (7) Final report. In the case of a significant risk device, the PI shall notify FDA within 30 working days of the completion or termination of the investigation and shall submit a final report to FDA and all reviewing IRB's and participating investigators within 6 months after completion or termination. In the case of a device that is not a significant risk device, the PI shall submit a final report to all reviewing IRB's within 6 months after termination or completion.

☐ (8) Informed consent. The PI shall submit to FDA a copy of any report by an investigator under paragraph (a)(5) of this section of use of a device without obtaining informed consent, within 5 working days of receipt of notice of such use.

☐ (9) Significant risk device determinations. If an IRB determines that a device is a significant risk device, and the PI had proposed that the IRB consider the device not to be a significant risk device, the PI shall submit to FDA a report of the IRB's determination within 5 working days after the sponsor first learns of the IRB's determination.

☐ (10) Other. The PI shall, upon request by a reviewing IRB or FDA, provide accurate, complete, and current information about any aspect of the investigation.

☐ Investigator Records and Reports: The PI ensures that participating investigators maintain the records required by [21 CFR 812.140(a)(3)(i)] and makes the reports required under [21 CFR 812.150(a)(1-2)(5)(7)]; and

☐ (a) Investigator records. A participating investigator shall maintain the following accurate, complete, and current records relating to the investigator's participation in an investigation:

☐ (3) Records of each participant's case history and exposure to the device. Case histories include the case report forms and supporting data including, for example, signed and dated consent forms and medical records including, for example, progress notes of the physician, the individual's hospital chart(s), and the nurses' notes. Such records shall include:

☐ (i) Documents evidencing informed consent and, for any use of a device by the investigator without informed consent, any written concurrence of a licensed physician and a brief description of the circumstances justifying the failure to obtain informed consent. The case history for each individual shall document that informed consent was obtained prior to participation in the study.

☐ (a) Investigator reports. An investigator shall prepare and submit the following complete, accurate, and timely reports:

☐ (1) Unanticipated adverse device effects. An investigator must immediately report an adverse device effect to the Caltech IRB. Working with the IRB, the investigator shall submit to the PI and to any other reviewing IRB a report of any unanticipated adverse device effect occurring during an investigation as soon as possible, but in no event later than 10 working days after the investigator first learns of the effect.

☐ (2) Withdrawal of IRB approval. An investigator shall coordinate with the Caltech IRB to report to the sponsor, within 5 working days, a withdrawal of approval by the reviewing IRB of the investigator's part of an investigation.

☐ (5) Informed consent. If an investigator uses a device without obtaining informed consent, the investigator shall report such use to the sponsor and the reviewing IRB within 5 working days after the use occurs.

☐ (7) Other. An investigator shall, upon request by a reviewing IRB or FDA, provide accurate, complete, and current information about any aspect of the investigation.

☐ Prohibitions: The PI complies with the prohibitions in [21 CFR 812.7] against promotion and other practices.

☐ A sponsor, investigator, or any person acting for or on behalf of a sponsor or investigator shall not:

☐ (a) Promote or test market an investigational device, until after FDA has approved the device for commercial distribution.

☐ (b) Commercialize an investigational device by charging the participants or investigators for a device a price larger than that necessary to recover costs of manufacture, research, development, and handling.

☐ (c) Unduly prolong an investigation. If data developed by the investigation indicate in the case of a class III device that premarket approval cannot be justified or in the case of a class II device that it will not comply with an applicable performance standard or an amendment to that standard, the sponsor shall promptly terminate the investigation.

☐ (d) Represent that an investigational device is safe or effective for the purposes for which it is being investigated.