

 OHSU Research Integrity Office	Human Research Protection Program Policies & Procedures	
Title: Research with Medical Devices	Date Effective 4/21/2008	Supersedes P&P dated:
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BACKGROUND

Federal requirements governing investigations involving medical devices were enacted as part of the Medical Device amendments of 1976 and the Safe Medical Devices Act of 1990. These amendments to the Federal Food, Drug, and Cosmetic Act define the regulatory framework for medical device development, testing, approval, and marketing.

AUTHORITY

The purpose of 21 CFR 812.2 is to encourage, to the extent consistent with the protection of public health and safety and with ethical standards, the discovery and development of useful devices intended for human use, and to that end to maintain optimum freedom for scientific investigators in their pursuit of this purpose. This part provides procedures for the conduct of clinical investigations of devices.

Studies of devices that pose a significant risk require both FDA and an Institutional Review Board (IRB) approval prior to initiation of the clinical study. FDA approval to conduct the study is obtained by submitting an IDE application to FDA (§812.20).

Under 21 CFR 812.66, if an IRB determines that an investigation, presented for approval under 812.2(b)(1)(ii), involves a significant risk device, it shall so notify the investigator and, where appropriate, the sponsor. A sponsor may not begin the investigation except as provided in 812.30(a).

FDA Information Sheets www.fda.gov/oc/ohrt/irbs/devices.html

Under 21 CFR 56, which contains the general standards for the composition, operation, and responsibility of an Institutional Review Board (IRB) that reviews clinical investigations regulated by the Food and Drug Administration. Compliance with this part is intended to protect the rights and welfare of human subjects involved in such investigations.

21 CFR 50 applies to all clinical investigations regulated by the Food and Drug Administration including medical devices for human use. Compliance with these parts is intended to protect the rights and safety of subjects involved in investigations filed with the Food and Drug administration.

SCOPE

The procedures for Institutional Review Board (IRB) review of significant risk (SR) and non-significant risk (NSR) investigational device use, and the IRB's procedures for evaluating principal investigators' plans to use investigational devices.

I. Policy

- A. All studies involving investigational medical devices must be reviewed and approved for use in accordance with Federal regulations (FDA and OHRP) and Institutional policies. Clinical investigations of medical devices must comply with the Food and Drug Administration (FDA) informed consent and Institutional Review Board (IRB) regulations [21 CFR parts 50 and 56, respectively].
- B. The IRB may approve or disapprove the proposed research based on local context and its responsibilities to protect human subjects in research even when approval of the device has been granted by the FDA.
- C. All clinical investigations of devices must have an approved Investigational Device Exemption (IDE) or have been determined to be exempt from the IDE regulation. Investigations that are exempted from 21 CFR 812 are described in §812.2(c) of the IDE regulation.
- D. Unless exempt from the IDE regulations, an investigational device must be categorized as either "significant risk" (SR) or "nonsignificant risk" (NSR).
 - 1. The sponsor makes the initial determination that a device presents a nonsignificant or significant risk.
 - 2. The principal investigator (PI) submits the proposed study to the IRB for SR and NSR studies for formal determination of the appropriate SR/NSR category.
 - 3. If the IRB agrees that the study is NSR, a submission of an IDE application to FDA is not required but the sponsor is required to conduct the study in accordance with the "abbreviated requirements" of the IDE regulations [21 CFR 812.2(b)]. Unless otherwise notified by the FDA, an NSR study is considered to have an approved IDE if the sponsor fulfills the abbreviated requirements.
 - 4. A SR device study may not commence until FDA has approved the IDE application and the IRB has approved the study.
- E. During review of the research proposal, the IRB evaluates PI's on these responsibilities and plans to control investigational devices.
 - 1. Each PI using an investigational medical device is responsible for control of the devices received in accordance with regulatory requirements.
 - 2. PI's develop and submit to the IRB their plan for control, storage and accountability of the device.
 - 3. The investigator is responsible for implementing the plan as approved by the IRB.

II. PROCEDURE

- A. **Studies Exempt From the IDE Regulation**
 - 1. The OHSU IRB will review studies involving devices to determine whether they meet the exemption criteria. If the IRB feels that the exemption criteria are not met and an IDE has not been obtained, they will ask the investigator to have the FDA make a determination of the requirement for an IDE.
 - 2. Exempt studies include:
 - a. A legally marketed device when used in accordance with its labeling
 - b. A diagnostic device if it complies with the labeling requirements in §809.10(c) and if the testing:
 - is noninvasive;
 - does not require an invasive sampling procedure that presents significant risk;
 - does not by design or intention introduce energy into a subject; and
 - is not used as a diagnostic procedure without confirmation by another medically established diagnostic product or procedure;
 - c. Consumer preference testing, testing of a modification, or testing of a combination of devices if the device(s) are legally marketed device(s) [that is, the devices have an

approved PMA, cleared Premarket Notification 510(k), or are exempt from 510(k)] AND if the testing is not for the purpose of determining safety or effectiveness and does not put subjects at risk;

3. The OHSU IRB will review studies involving devices to determine whether they meet the above exemption criteria. If the IRB feels that the exemption criteria are not met and an IDE has not been obtained, they will ask the investigator to have the FDA make a determination of the requirement for an IDE.

B. Significant vs. Nonsignificant Risk Determination

1. The PI includes in the IRB application the sponsor's initial assessment of the risk (SR or NSR) and the rationale used in making the risk determination.
2. The IRB assesses the proposed device use to assign a risk category.
 - a. The IRB reviews reports of prior investigations conducted with the device;
 - b. The proposed investigational plan;
 - c. A description of subject selection criteria;
 - d. Monitoring procedures; and
 - e. Any other information the IRB deems necessary to make its decision.
3. The IRB makes its own risk determination:
 - a. The risk determination should be based on the proposed use of a device in an investigation, and not on the device alone.
 - b. In deciding if a study poses an SR, an IRB must consider the nature of the harm that may result from use of the device.
 - Studies where the potential harm to subjects could be life-threatening, could result in permanent impairment of a body function or permanent damage to body structure, or could necessitate medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to body structure should be considered SR.
 - If the subject must undergo a procedure as part of the investigational study, e.g., a surgical procedure, the IRB must consider the potential harm that could be caused by the procedure in addition to the potential harm caused by the device.
4. After the IRB makes the risk determination, the IRB conducts the review of the study using the same criteria it would use in considering approval of any full review application. The IRB considers the risk and benefits of the medical device compared to the risks and benefits of alternative devices or procedures as listed in the Research Description in the application.
5. The IRB may request that the PI consult with the FDA for an opinion as appropriate.
6. If the IRB determines that a protocol submitted for approval involves a SR device, which has been deemed NSR by the sponsor
 - a. The IRB notifies the investigator who notifies the sponsor.
 - b. The sponsor notifies the FDA that the IRB has made an SR determination.
 - c. The study can be conducted as an SR investigation following FDA approval of an IDE application.
7. If the FDA determines that a study involves the use of a SR device.
 - a. The PI must obtain an IDE and IRB approval before the study begins and must conduct the study in accordance with IDE requirements.
8. If the study is determined to be NSR by both the FDA and IRB, there is no requirement for submission of an IDE application to the FDA. The FDA will return the IDE application to the sponsor and the study would be presented to IRBs as an NSR investigation.
9. Minutes of IRB meetings must document the rationale for SR/NSR and subsequent approval or disapproval decisions for the clinical investigation.
10. Devices may have an unanticipated problem or adverse event to subjects or others. An investigator submits to the sponsor and to the IRB a report of any unanticipated problems or adverse event to subjects or others occurring during an investigation. (See Unanticipated/Adverse Event Reporting)

C. IRB Determines the Study is Significant Risk

1. Sponsor Responsibilities:

D. IRB Determines the Study is a Nonsignificant Risk

1. IRB proceeds to review study applying requisite criteria [21 CFR 56.111]
2. If the study is approved by the IRB, the sponsor and PI must comply with “abbreviated IDE requirements” [21 CFR 812.2(b)], and informed consent and IRB regulations [21 CFR parts 50 and 56]

E. Principal-Investigator Responsibilities

1. Sponsor and investigator must comply with IDE regulations [21 CFR part 812], as well as informed consent and IRB regulations [21 CFR parts 50 and 56]
2. If the PI is also the sponsor, the IDE must be submitted to FDA or, if electing not to proceed with study, notify FDA (CDRH Program Operations Staff 301-594-1190) of the SR determination (if one has been made).
3. The investigator must provide the IRB with:
 - a. All available information regarding the use of the device, including IDE #, if applicable.
 - b. When IDE is required, PI must complete FDA’s investigator agreement form and send copy.
 - c. All correspondence from the sponsor and/or FDA regarding SR or NSR.
4. Notify sponsor of the SR decision of the IRB;
5. Provide a description of the device including, ingredients, properties, etc.;
6. Maintain all case report forms;
7. Be accountable for storage, dispensing, tracking, and oversight of device;
8. Appropriately report continuing reviews, adverse events, or unanticipated problems and clinical outcomes of each participant, if known.
9. Study may not begin until FDA approves IDE and IRB approves the study.

F. Custom Devices

1. Custom devices made in a specific form for a given patient on the order of a physician or dentist as part of their professional practice are not subject to the requirements for device investigations unless the devices are being evaluated for safety and effectiveness.
2. In such cases, custom devices are subject to the requirements of device investigations.

III. DEFINITIONS

Medical device: any health care product that does not achieve its primary intended purposes by chemical action or by being metabolized

Investigational new device (IND): a medical device which is the subject of a clinical study designed to evaluate the effectiveness and/or safety of the device.

Investigational device exemptions (IDE): Documentation 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 that use.

Significant risk device (SR): an investigational device that:

- (1) is intended as an implant; or
- (2) is used in supporting or sustaining human life; or
- (3) is of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise prevents impairment of human health; or
- (4) otherwise presents a potential for serious risk to the health, safety, or welfare of a participant.

Guidance on distinguishing between significant risk and nonsignificant risks studies are outlined in the document found at <http://www.fda.gov/oc/ohrt/irbs/devices.html>.

Non-significant risk device (NSR): an investigational device that does not meet the definition for an SR study. An investigational device is considered a NSR if it:

- (1) is noninvasive;

- (2) does not require an invasive sampling procedure that presents significant risk;
- (3) does not by design or intention introduce energy into a subject; and
- (4) is not used as a diagnostic procedure without confirmation of the diagnosis by another medically established diagnostic product or procedure.

Unanticipated adverse device effect: any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, 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 problem associated with a device that relates to the rights, safety, or welfare of subjects.

Custom Device: A device that:

- (1) Necessarily deviates from devices generally available or from an applicable performance standard or premarket approval requirement in order to comply with the order of an individual physician or dentist;
- (2) Is not generally available to, or generally used by, other physicians or dentists;
- (3) Is not generally available in finished form for purchase or for dispensing upon prescription;
- (4) Is not offered for commercial distribution through labeling or advertising; and
- (5) Is intended for use by an individual patient named in the order of a physician or dentist and is to be made in a specific form for that patient, or is intended to meet the special needs of the physician or dentist in the course of professional practice.

Device Investigations: Investigations of FDA-approved devices off-label or non-FDA approved devices intended for human use. When a device is being evaluated for safety and effectiveness, the device is considered "investigational" and is subject to the requirements of the IDE regulations 21 CFR part 812, unless exempt.