The Christ Hospital IRB
Section: 15
Effective Date: 02/07
Revised/Reviewed Date: 09/22
AAHRPP Element: I.7.A

IRB REFERENCE MANUAL
SECTION 15
INVESTIGATIONAL DEVICES

15.0 INVESTIGATIONAL DEVICES

15.1 Background

The U.S. Food and Drug Administration (FDA) defines a medical device, in part, as "an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part or accessory which is 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 within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes" (Food, Drug and Cosmetic Act [2012], Chapter 2, Section 201[h]).

Examples of medical devices include, but are not limited to, surgical lasers, wheelchairs, sutures, pacemakers, vascular grafts or stents, intraocular lenses, orthopedic pins, and radiographic imaging equipment. Medical devices also include diagnostic aids such as reagents and test kits for in vitro diagnosis of disease or other medical conditions such as pregnancy.

Except for certain low risk devices (Class I and Class II devices), device manufacturers who wish to bring new medical devices to the market must register their intent by submitting pre-market notification to the FDA. The FDA reviews pre-market notifications to determine if the new device is "substantially equivalent" to a device that was marketed prior to the passage of the Medical Device Amendments of 1976 (i.e., a "pre-amendments device") to the Federal Food, Drug and Cosmetics Act. If the new device is deemed to be substantially equivalent to a pre-amendments device, it may be marketed immediately and is regulated in the same regulatory class as the pre-amendments device to which it is equivalent. Devices determined by FDA to be "substantially equivalent" are often referred to as "510k devices" (i.e., the pre-market notification requirement for new devices is set forth in section 510(k) of the Federal Food Drug and Cosmetic Act). If a new device is deemed

not to be equivalent to a pre-amendments device, clinical studies of its safety and effectiveness must be performed and FDA approval granted before the device can be marketed.

When research involves a device with an IDE, the IRB Chairman or Primary Reviewer confirms that the IDE number is valid. Validation can occur by confirming the IDE number on the sponsor protocol, communication from the sponsor, or communication from the FDA. In cases of investigators who hold the IDE, validation can occur by confirming the number on the communication from the FDA. Note: Investigator brochures should not be used as confirmation that an IDE exists for the trial since one brochure may be used for multiple IDEs.

15.2 Regulatory Requirements for Clinical Studies

An investigational device is any unapproved medical device undergoing clinical trials to provide evidence to regulatory authorities that the product is safe and effective. Clinical studies of investigational devices must comply with FDA Investigational Device Exemption (IDE) regulations. Research involving investigational medical devices are reviewed by the IRB Chairman or Primary Reviewer to confirm that either (a), (b) or (c) is true:

a. The device has an IDE issued by the FDA

b. The device fulfills the requirements for an abbreviated IDE if the device is not a banned device and the sponsor *(ref. 21 CFR 812.2(b)(1))*:
   i. Labels the device in accordance with 21 CFR 812.5;
   ii. Obtains IRB approval of the investigation after presenting the reviewing IRB with a brief explanation of why the device is not a significant risk device, and maintains such approval;
   iii. Ensures that each investigator participating in an investigation of the device obtains consent from each subject under the investigator's care (ref. 21 CFR 50) and documents it, unless documentation is waived by an IRB under 21 CFR 56.109(c);
   iv. Complies with the requirements of 21 CFR 812.46 with respect to monitoring investigations;
   v. Maintains records required under 21 CFR 812.140(b)(4) and (5) and makes the reports required under 21 cfr 812.150(b)(1) through (3) and (5) through (10);
   vi. Ensures that participating investigators maintain the records required by 21 CFR 812.140(a)(3)(i) and make the reports required under 21 CFR 812.150(a) (1), (2), (5), and (7); and
   vii. The sponsor complies with the prohibitions in 21 CFR 812.7 against promotion and other practices, OR

c. The device fulfills one of the IDE exemption categories (ref 21 CFR 812.2(c)):
    i. A device, other than a transitional device, in commercial distribution immediately before May 28, 1976, when used or investigated in accordance with the indications in labeling in effect at that time
    ii. A device, other than a transitional device, introduced into commercial distribution on or after May 28, 1976, that FDA has determined to be substantially equivalent to a device in commercial distribution immediately before May 28, 1976, and that is used or investigated in accordance with the indications in the labeling FDA reviewed under subpart E of part 807 in determining substantial equivalence
    iii. A diagnostic device, if the sponsor complies with applicable requirements in 21 CFR 809.10(c) and if the testing:
        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
        4) Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure
    iv. A device undergoing consumer preference testing, testing of a modification, or testing of a combination of two or more devices in commercial distribution, if the testing is not for the purpose of determining safety or effectiveness and does not put subjects at risk
    v. A device intended solely for veterinary use
    vi. (6) A device shipped solely for research on or with laboratory animals and labeled in accordance with § 812.5(c)
    vii. A custom device as defined in 21 CFR 812.3(b), unless the device is being used to determine safety or effectiveness for commercial distribution

15.3 Significant Risk and Non-significant Risk Medical Device Studies

15.3.1 Non-significant Risk Device Studies

A non-significant risk device study is an investigation of a device that does not pose a significant risk to human subjects. Examples include most daily wear contact lenses, ultrasonic dental scalers, and Foley catheters.

Non-significant risk device studies are conducted in accordance with abbreviated requirements of the IDE regulations and may be

approved by the IRB and commence without the requirement of submission of an IDE application or other notification to the FDA (i.e., the IRB serves as the FDA's surrogate with respect to study review and approval of non-significant risk device studies).

15.3.2 Significant Risk Device Studies

IDE regulations (21 CFR part 812.3(m)) describe a significant risk device as an investigated device that:

a. Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject.
b. Is purported or represented to be for a use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject;
c. Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or
d. Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

Note that risk determination should be based not only on the nature of the device, but also on the proposed use of the device in the research study. Two examples:

- The research evaluation of a pacemaker that is a modification of a commercially available pacemaker is a "significant risk" device study because the use of any pacemaker involves the potential for serious harm to patients involved. This is true even though the modified pacemaker may pose less risk, or only slightly greater risk, in comparison with the commercially available product.

- The research evaluation of contact lens wherein the proposed study involves its extended wear constitutes "significant risk." Although the contact lens, itself, poses minimal risk, wearing it continuously for several days/nights presents a potential for injuries not normally seen with limited daily use.

Significant risk device studies must be conducted in accordance with the complete requirements of the IDE regulations and necessitate the prospective approval of an IDE application by the FDA and approval by the IRB.

15.3.3 Sponsor/Investigator and IRB Responsibilities

The sponsor/investigator initially makes the determination of whether a device study falls under non-significant risk or significant

risk. If the sponsor/investigator considers the device study to be of non-significant risk, the sponsor/investigator must provide the IRB with an explanation of this determination and copies of the respective research protocol and informed consent document. The sponsor should inform the IRB of the FDA's assessment of the risk status of the proposed device study, if such an assessment has been made. The IRB may question whether other IRBs have reviewed the proposed device study and what determination the IRBs made, or the IRB may consult with the FDA for its opinion.

The IRB may agree or disagree with the sponsor's/investigator's initial non-significant risk assessment.

a. **IRB Agreement with Non-significant Risk**
If the IRB agrees with the determination that the device study presents "non-significant risk" and approves the research study and informed consent document(s), the study may proceed without further notification of the FDA. Under this scenario, the sponsor and principal investigator are required to comply with the abbreviated requirements of the IDE regulations (21 CFR 812.2(b)).

b. **IRB Disagreement with Non-significant Risk**
   i. If the IRB disagrees with the determination that the device study presents non-significant risk, the sponsor/investigator must notify the FDA that the device study has been determined to be of significant risk and, if electing to proceed with the study, must submit an IDE application. The device study may not commence until the FDA approves the IDE and the IRB approves the device study and informed consent document(s). Under this scenario, the sponsor and principal investigator are required to comply with the complete IDE regulations under 21 CFR 812.
   ii. If a sponsor/investigator submits an IDE to the FDA because it is presumed to be a significant risk study, but the FDA classifies it as a non-significant risk, the FDA will return the IDE application with the recommendation that it be presented to the IRB as a non-significant risk device study.

15.3.4 FDA Final Authority

The FDA has the ultimate authority in determining whether a device study presents as non-significant risk or significant risk. If the FDA,

upon review of IRB activities, disagrees with the IRB's decision that a device study presents a non-significant risk, an IDE application must be submitted to the FDA.

On the other hand, if a sponsor/investigator submits an IDE to the FDA because it is presumed to be a significant risk study, but the FDA classifies it as a non-significant risk, the FDA will return the IDE application with the recommendation that it be presented to the IRB as a non-significant risk device study.

15.4 Unanticipated Device Effect (UADE) Reporting

See Section 8.0 “Reporting Unanticipated Problems Involving Risks to Human Subjects/Adverse Events.”