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**Boston
Children's
Hospital**

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Applicability Boston Children's
Hospital- Policies
& Procedures

Investigational Devices (IDE) Policy/Procedure

Internal Approval

SVP, Research Administration

EVP, Chief Scientific Officer

Scope

This policy applies to the Boston Children's Hospital (BCH) Research department and the respective staff.

Definitions

Investigational Device Exemption (IDE): An exemption from certain regulations described in the medical device amendments that allows the shipment of an unapproved device for use in a clinical investigation. The sponsor of a Significant Risk device is required to apply to the U.S. Food & Drug Administration (FDA) for an IDE before the clinical research may begin. There are abbreviated requirements for Non-Significant Risk (NSR) devices that do not involve filing with the FDA.

Medical Device: A device is "an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is:

1. Recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them,
2. 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**
3. Intended to affect the structure or any function of the body of humans or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of humans or other animals and which is not dependent upon being metabolized for the

achievement of any of its primary intended purposes.

Medical devices include, among other things, surgical lasers, wheelchairs, sutures, pacemakers, vascular grafts, intraocular lenses, and orthopedic pins. Medical devices also include diagnostic aids such as reagents and test kits for *in vitro* diagnosis of disease and other medical conditions such as pregnancy.

Nonsignificant Risk device (NSR): A device that does not meet the definition of a significant risk device. However, NSR device studies should not be confused with the concept of "minimal risk," a term utilized in the Institutional Review Board (IRB) regulations.

Significant Risk device (SR): A device that presents a potential for serious risk to the health, safety, or welfare of a subject, and:

1. is intended as an implant;
2. is used in supporting or sustaining human life;
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 subject.

Policy Statements

This policy describes the various mechanisms for obtaining, testing, and using investigational devices in compliance with federal regulations, state law, and institutional policy.

Research that involves the use of investigational devices (must conform to the U.S. Food and Drug Administration (FDA) and Department of Health and Human Services (HHS) regulations.

The FDA regulations for investigational devices are listed in 21 CFR 812.

FDA informed consent and Institutional Review Board (IRB) regulations are listed in 21 CFR 50 and 56, respectively.

The IRB will document in their minutes any determination that a device is a significant risk or non-significant risk device.

Determining Exempt Status of Device

An Investigational Device Exemption (IDE) allows an investigational device to be used in a clinical study in order to collect safety and effectiveness data.

1. All clinical evaluations of investigational devices, unless exempt, must have an approved IDE before the study is initiated.
2. Investigational use also includes clinical evaluation of certain modifications or new intended uses of legally marketed devices.

When research is conducted to determine the safety and effectiveness of a device, the first step is to determine whether the device is subject to the IDE requirements.

Per regulations, a device can be exempt from the IDE requirements. A claim that the device is exempt

must reference the exemption category being claimed. There are seven exemption categories that may be claimed.

1. It is the sponsor's responsibility to provide sufficient justification to support the exemption category being claimed.
2. An exemption from the IDE requirements is not an exemption from the requirement for prospective IRB review or informed consent.

Exemption Categories (21CFR812.2)

1. 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.
2. 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.
3. A diagnostic device, if the sponsor complies with applicable requirements in Sec. 809.10(c) and if the testing:
 - i. Is noninvasive,
 - ii. Does not require an invasive sampling procedure that presents significant risk,
 - iii. Does not by design or intention introduce energy into a subject, and
 - iv. Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure
4. 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.
5. A device intended solely for veterinary use.
6. A device shipped solely for research on or with laboratory animals and labeled in accordance with Sec. § 812.5(c).
7. A custom device as defined in § 812.3(b), unless the device is being used to determine safety or effectiveness for commercial distribution

Exemption Category Summary

Categories 1 and 2 pertain to devices that were either manufactured before 1976 or similar products manufactured after 1976.

Categories 3 and 4 are the most commonly applied for exemptions.

Categories 5 and 6 are pertinent to the use of devices in animals.

Category 7 pertains to custom devices.

Control of Investigational Devices

Investigators are responsible for control of the investigational devices used in their studies.

The actual control plan will depend upon the type of device, the number of units to be received at any one time, and the proposed use. The protocol application submitted to the IRB must include a description of the following:

1. Location and manner of the receipt of the device
2. Location and manner of the secure storage of the device
3. Those who have access to the device and how access is controlled
4. How the device will be tracked when utilized in a patient

Procedures

Distinguishing Between Significant Risk (SR) and Non-Significant Risk (NSR) Device Studies

The consequences of the **Significant Risk (SR)** and **Non-Significant Risk (NSR)** determination are very important, and the regulatory responsibilities for sponsors and investigators of SR and NSR risk studies differ.

The major regulatory differences between the two concern:

1. The approval processes.
2. The record keeping and reporting requirements.

Significant Risk Device Studies

Before a study investigating a significant risk device can begin an IDE application must be first submitted and approved by the FDA.

If the IRB believes that a study is an SR device study, the investigation may not begin until both the IRB and the FDA approve the study

Non-Significant Risk Device Studies

Sponsors (or sponsor-investigators) of NSR device studies do not need to submit an IDE application to FDA; the IRB serves as the FDA's surrogate for review, approval, and continuing review of the NSR device studies. Additionally, for NSR device studies there are abbreviated regulatory sponsor responsibilities (e.g. labeling, IRB, consent, monitoring, reporting, prohibition on promotion).

The SR/NSR decision is also of consequence to the FDA because the IRB serves, in a sense, as the FDA's surrogate with respect to the review and approval of NSR studies.

1. Sponsors are responsible for making the initial risk determination and presenting it to the IRB.
2. The FDA is available to help the sponsor, clinical investigator, and IRB in making the risk

determination.

3. Sponsors/Investigators are encouraged to review the FDA Information Sheet: *Significant Risk and Nonsignificant Risk Medical Device Studies* for determining risk.

If an investigator or a sponsor proposes to the IRB to undertake an NSR investigation, the IRB must make a separate and independent determination that the study is, in fact, an NSR device study. The IRB's determination that a device is an NSR device must be documented in the convened IRB's minutes.

The SR/NSR Decision

The assessment of whether or not a device study presents an NSR is initially made by the sponsor.

1. If the sponsor identifies a study as an NSR, the sponsor is to provide the IRB with an explanation of its determination and any other information that may assist the IRB in evaluating the risk of the study.
2. The sponsor is expected to provide:
 - a. the IRB with a description of the device
 - b. reports of prior investigations with the device
 - c. the proposed investigational plan
 - d. a description of patient selection criteria and monitoring procedures,
 - e. any other information the IRB deems necessary to make its decision.
3. The IRB may also request an opinion from the FDA.
4. The IRB may agree or disagree with the sponsor's initial NSR assessment.
 - a. If the IRB agrees with the initial assessment and approves the study, the study may begin without submission of an IDE application to the FDA.
 - b. If the IRB disagrees, the sponsor is to notify the FDA that an SR determination has been made. The study may be conducted as an SR investigation following FDA approval of an IDE application.

The risk determination will be based on the proposed use of a device in an investigation, and not on the device alone.

1. In deciding if a study poses an SR, the IRB will consider the nature of the harm that may result from use of the device.
 - a. Studies considered to be SR, in which the potential harm to subjects may:
 - b. be life-threatening
 - c. result in permanent impairment of a body function or permanent damage to body structure
 - d. may necessitate medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to body structure
2. Moreover, if the subject must undergo a procedure as part of the investigational study (e.g., surgical procedure), the IRB must consider the potential harm that may be caused by the

procedure in addition to the potential harm that may be caused by the device.

3. If requested, the FDA will make the ultimate decision in determining if a device study is SR or NSR.
 - a. If the FDA does not agree with a IRB decision to identify a study as an NSR device study, an IDE application must be submitted to the FDA.
 - b. If a sponsor files an IDE with the FDA because it is presumed to be an SR study, but the FDA classifies the device study as NSR, the FDA will return the IDE application to the sponsor and the study must be presented to the IRB as an NSR investigation.

IRB Responsibilities Following SR/NSR Determination

SR Determination: If the IRB identifies the study as SR, then the IRB will notify the investigator who will, in turn, notify the sponsor of the SR determination. An IDE will be obtained by the sponsor, and the IRB will review the protocol, applying the requisite criteria (21 CFR 56.111).

NSR Determination: If the IRB identifies the study as NSR, the IRB will proceed to review the study, applying the requisite criteria (21 CFR 56.111). If the study is approved by the IRB, the sponsor and the investigator must comply with abbreviated IDE requirements (21 CFR 812.2(b)), informed consent, and IRB regulations (21 CFR 50 and 56). The determination that a device is an NSR device must be documented in the IRB minutes and final approval letter.

The Decision to Approve or Disapprove a Study

Once the SR/NSR decision is reached, the IRB is to consider whether or not the study should be approved.

1. The criteria for deciding if SR and NSR studies should be approved are the same as those for any other study.
 - a. If a device is classified as a SR device, the IRB will require written documentation from the sponsor which includes the IDE number.
 - b. If the investigator also serves as the sponsor of a SR device, a copy of the letter from the FDA will be requested which assigns the IDE number.
 - i. This information should be submitted as part of the protocol application. Protocol administrators will be responsible for making sure this information is obtained prior to release of the approval notification and informed consent document.
 - ii. The protocol approval will not be released until the information is provided.
2. The IRB is to ensure that:
 - a. the risks to subjects are minimized
 - b. The risks are reasonable in relation to the anticipated benefits and knowledge to be gained. To ensure that the risks to subjects are reasonable in relation to the anticipated benefits, the risks and benefits of the investigation are to be compared to the risks and benefits of alternative devices or procedures.
 - c. that subject selection is equitable

- d. that informed consent materials and procedures are adequate
 - e. and that provisions for monitoring the study and protecting the privacy of subjects are acceptable.
3. The minutes of IRB meetings must document:
- a. whether a device has been determined to be a SR or NSR
 - b. the rationale for SR/NSR decisions
 - c. the subsequent approval or disapproval decisions regarding the clinical investigation.

Any protocol that is considered SR is to be reviewed by the Convened IRB. Generally, IRB review, at a convened meeting, is also required when NSR studies are reviewed because the Committee must agree that the study is an NSR device investigation.

Sponsor-Investigators Responsibilities

Regulatory responsibilities for investigators and sponsors are detailed in 21 CFR 812 subpart C. A Sponsor-Investigator is responsible for all requirements as both a sponsor and an investigator. Prior to IRB approval of a protocol, any BCH staff member holding an IDE, either as the Sponsor or Sponsor-Investigator must meet with Boston Children's Hospital's Regulatory and Education Program to:

1. Review the responsibilities of a Sponsor or Sponsor-Investigator
2. Discuss study feasibility in context of available BCH resources and services.

Continuing Review

At the time of continuing review, the IRB may request additional documentation to be certain the investigator is following the IDE requirements.

1. If the investigator holds the IDE for a significant risk device, a copy of the annual report to the FDA may be requested.
2. In addition whenever a protocol that involves an IDE is randomly selected for a review by EQUIP (Education and Quality Improvement Program), all case report forms, adverse event reports, device storage and accountability information data and safety monitoring reports and informed consent documents will be reviewed to be certain the investigator complied with FDA requirements regarding sponsor requirements.

Related Content

- U.S. Food & Drug Administration
 - 21 CFR.50: Protection of Human Subjects
 - 21 CFR.56: Institutional Review Boards
 - 21 CFR 812: Investigational Device Exemptions
- U.S. Food & Drug Administration Guidance
 - [**Significant Risk and Nonsignificant Risk Medical Device Studies**](#)

Approval Signatures

| Step Description | Approver | Date |
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| Steering Committee | Dwight Mayfield | 2/25/2025 |
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Applicability

Boston Children's Hospital- Policies & Procedures

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