PARTNERS HEALTHCARE | FOUNDED BY BRIGHAM AND WOMEN'S HOSPITAL AND MASSACHUSETTS GENERAL HOSPITAL

Title:	Requirements for Investigational Device Exemption (IDE) for Human-Subjects Research
Department:	Human Research Affairs
Policy Type:	☑ Partners System-wide ☐ Partners System-wide Template ☐ Partners Corporate ☐ Partners Corporate Departmental ☐ Entity
Applies to:	Employees, Professional Staff or Other Agents of Brigham and Women's Hospital (BWH), Faulkner Hospital (FH), Massachusetts General Hospital (MGH), McLean Hospital (McLean), and North Shore Medical Center (NSMC)
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Contact Person:	Director, Human Research Review and Compliance

KEYWORDS:

IRB, Institutional Review Board

PURPOSE:

The purpose of this policy is to define the applicability of the United States Code of Federal Regulations Title 21 – Food & Drugs Part 812 – Investigational Device Exemptions (IDE) and the procedures the Partners Human Research Committees (PHRC) follow to determine whether an IDE is needed for a device investigation.

DEFINITIONS:

See Definition of Human-Subjects Research

Device means an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any 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 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.

Investigational device means a device, including a transitional device, that is the object of an investigation. [21 CFR 812.3(g)]

Transitional device means a device subject to section 520(l) of the act, that is, a device that FDA considered to be a new drug or an antibiotic drug before May 28, 1976. [21 CFR 812.3(r)]

Custom device means 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 or 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. [21 CFR 812.3(b)]

Investigator means an individual who actually conducts a clinical investigation, i.e., under whose immediate direction the test article is administered or dispensed to, or used involving, a subject, or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team. [21 CFR 812.3(i)]

Sponsor means a person who initiates, but who does not actually conduct, the investigation, that is, the investigational device is administered, dispensed, or used under the immediate direction of another individual. A person other than an individual that uses one or more of its employees to conduct an investigation that it has initiated is a sponsor, not a sponsor-investigator, and the employees are investigators. [21 CFR 812.3(n)]

Sponsor-investigator means an individual who both initiates and actually conducts, alone or with others, an investigation, that is, under whose immediate direction the investigational device is administered, dispensed, or used. The term does not include any person other than an individual. The obligations of a sponsor-investigator under this part [21 CFR 812 Subpart C] include those of an investigator and those of a sponsor. [21 CFR 812.3(o)]

POLICY STATEMENT:

Non-exempt human-subjects research and clinical investigations reviewed and approved by the PHRC must comply with FDA regulations for devices intended for human use 21 CFR 812 Investigational Device Exemptions.

PROCEDURES:

Investigators relying on the PHRC for IRB review of human-subjects research and clinical investigations are required to complete Insight/eIRB application forms and provide all required

information and documents for review as described in the Protocol Submission Instructions and instructions and forms for continuing review, amendments, and unanticipated problems involving risks to subjects or others, including adverse events.

When the research involves a device, the investigator is required to provide the PHRC with sufficient information about the device, including FDA status, to assess the risks and potential benefits to subjects.

With the exception of implantable devices, electrically-powered devices must be reviewed for electrical safety by Biomedical Engineering. Electrically-powered devices include devices that are battery-powered or line-powered (i.e., devices that plug into an electrical outlet).

1. Clinical investigations of devices

   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 an exempted investigation; i.e., investigations of the following categories of devices:

   - A device, other than a transitional device, introduced into commercial distribution before May 28, 1976, when used or investigated in accordance with the indications in labeling in effect at that time.
   - A FDA-approved device, which means 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 21 CFR 807 in determining substantial equivalence.
   - A diagnostic device, if the sponsor complies with applicable requirements in 21 CFR 809.10(c) and if the test is: (i) 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.
   - 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.
   - A device intended solely for veterinary use.
   - A device shipped solely for research on or with laboratory animals and labeled in accordance with 21 CFR 812.5(c).
   - A custom device as defined in 812.3(b), unless the device is being used to determine safety or effectiveness for commercial distribution.

   Studies of an already cleared medical device in which the device is used or investigated in accordance with the indications in the cleared labeling are exempt from Part 812. Studies of a cleared device for a new use must comply with the human subject protection (informed consent and additional safeguards for children in research), IRB and IDE regulations. Similarly, studies of a PMA approved device are exempt from the IDE requirements if the device is being studied for the indications in the approved labeling.

The PHRC generally make determination of exempted device investigation; however, the PHRC may consult with the FDA or request the investigator seek a written determination from the FDA. Exempted device investigations must comply with the FDA requirements for IRB review (21 CFR 56) and Informed Consent (21 CFR 50).

When an investigator is conducting a clinical investigation of a device, the PHRC require the investigator to have a standard operating procedure for control of the investigational device and device accountability to ensure that the device is used only by investigators listed on the protocol and in subjects enrolled in the research study. The investigator is responsible for the control of the investigational device and device accountability in accordance with institutional policy and FDA regulations.

Device investigations are scheduled for review at a convened meeting of the PHRC. The PHRC must categorize the investigation as either "significant risk" (SR) or "nonsignificant risk" (NSR) unless an exempted device investigation.

The sponsor generally makes this determination; however, the PHRC are responsible for making the determination when the sponsor has not submitted an IDE application to the FDA. The PHRC base their determination on the proposed use of the device in the investigation, and not on the device alone. If the proposed use of the device involves a procedure, e.g., a surgical procedure, the PHRC consider the potential harm that could be caused by the procedure as well as the device. The PHRC may require the investigator to seek the guidance of the FDA on the need for an IDE application, in which case the guidance of FDA will govern.

Nonsignificant risk device investigations

Nonsignificant risk device investigations include any investigation of a device other than a significant risk device, if the device is not a *banned device* and the sponsor labels the device in accordance with 21 CFR 812.5 and meets all other sponsor requirements in 812.2(1). A *banned device* means a device that has been banned by the Commissioner of the FDA.

When the PHRC make an NSR determination and the risk to the subjects is determined to be minimal in accordance with 21 CFR 56.102(i), the PHRC may vote to allow continuing review to be conducted using the expedited review procedure, as long as the research poses no more than minimal risk to subjects and no additional risks have been identified.

When the PHRC concur with the sponsor that the research is a nonsignificant risk device investigation, the investigation may proceed when fully approved by the PHRC and relevant ancillary committee(s).

Significant risk device investigations

A significant risk device investigation means a device that:

(1) Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject;

(2) 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; or

(3) 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

(4) Otherwise presents potential for serious risk to the health, safety, or welfare of a subject.

When the PHRC determine that the research is a significant risk device investigation, the sponsor must submit an IDE application to the FDA, unless the investigation of the device is exempt from the requirements of the IDE regulations 21 CFR Part 812. The PHRC require documentation of IDE number before the research is fully approved.

Sponsor-Investigator IDEs

When a Partners investigator is the sponsor of the IDE, the PHRC is responsible for ensuring that the investigator is knowledgeable about the following additional regulatory requirements of sponsors and will follow them:

- 21 CFR 11 (Electronic Records and Electronic Signatures)
- 21 CFR 54 (Financial Disclosure by Clinical Investigators)
- 21 CFR 803 (Medical Device Reporting)
- 21 CFR 807 (Establishment Registration and Device Listing for Manufacturers and Initial Importers of Devices)
- 21 CFR 812 (Investigational Device Exemptions)
- 21 CFR 814 (Premarket Approval of Medical Devices)
- 21 CFR 820 (Quality System Regulation)
- 21 CFR 860 (Medical Device Classification Procedures)

Before allowing the sponsor-investigator to conduct the research as a first time Partners sponsor-investigator, the PHRC will require the investigator to undergo a review of FDA sponsor-investigator responsibilities with the Human Research Quality Improvement Program (QI Program). Should the PHRC or QI Program identify the need for additional expertise to fulfill FDA regulatory requirements, the PHRC will require the investigator to: (1) undergo an audit by a Contract Research Organization to ensure that procedures are in place so that all FDA regulatory requirements of sponsors will be met; (2) assign responsibility of compliance with all FDA regulatory requirements to a Contract Research Organization; or (3) assign responsibility of compliance with some FDA regulatory requirements to a Contract Research Organization and have the investigator obtain an audit from a Contract Research Organization to ensure that procedures are in place so that all other FDA regulatory requirements of sponsors will be met.

2. Humanitarian Use Devices (HUD)

HUDs with approved Humanitarian Device Exemptions (HDEs) may be used for the FDA-approved indication only with approval of the PHRC even though the FDA does not consider such uses to be research. The PHRC may vote to allow continuing review to be conducted using the expedited review procedure, as long as the use of the HUD is within the scope of its approved labeling.

When HUDs are being evaluated for safety and effectiveness beyond the scope of the FDA-approved HDE indication, they are subject to the requirements of investigations of non-FDA approved devices as described elsewhere in this Policy.

3. Non-FDA Approved Devices Used as Tools to Measure Data or to Study Human Physiology

Non-FDA approved devices used in research as tools to measure data or to study human physiology are not subject to the 21 CFR 812 IDE regulations. However, any non-FDA approved devices used to measure data or study human physiology must be safe for use in humans and must not place subjects at more than minimal risk of harm. This does not include studies designed to evaluate the sensitivity or specificity of a non-FDA approved device or to collect safety and effectiveness data for submission to the FDA now or in the future for device approval/change in labeling.

4. Non-Hospital Inventory FDA-Approved Medical Devices Used for Monitoring or Data Collection

   Commercially available FDA-approved medical devices used in research according to the FDA-approved labeling are not subject to the 21 CFR 812 IDE regulations, but must meet the same hospital safety standards as medical devices being used for patient care; such devices are subject to the requirements of the Medical Equipment Management Program when used within the hospitals or sites over which the applicable Partners-affiliated entities have control.

REFERENCE:

21 CFR 812

DEVELOPMENT AND CONSULTATION

Human Research Office
Human Research Quality Improvement Program

Reviewed by:	Original Review Date:	Revision Approval Dates: