

Title:	Requirements for Investigational Device Exemption (IDE) for Human Subject Research
Department:	Human Research Affairs
Policy Type:	Mass General Brigham System-wide
Applies to:	Employees, Professional Staff or Other Agents of Mass General Brigham
Approved by:	Chief Academic Officer
Original Approval Date:	June 4, 2007
Original Effective Date:	June 4, 2007
Revision Approval Date(s):	December 6, 2007; September 8, 2010; March 7, 2014; August 18, 2015
Current Revision Effective Date:	October 1, 2021
Next Review Date:	October 1, 2022
Contact Person:	Director, Human Research Office

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 Mass General Brigham IRB follows to determine whether an IDE is needed for a device investigation.

POLICY STATEMENT:

Non-exempt human subject research and clinical investigations reviewed and approved by the Mass General Brigham IRB must comply with Food and Drug Administration (FDA) regulations for devices intended for human use, pursuant to 21 CFR 812, Investigational Device Exemptions.

PROCEDURES:

Investigators relying on the Mass General Brigham IRB for IRB review of human subject research and Clinical Investigations are required to complete Insight 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 Mass General Brigham

IRB 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 used in a Mass General Brigham hospital facility 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 in 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.
- An 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 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 Mass General Brigham IRB generally makes the determination of exempted device investigation; however, the Mass General Brigham IRB 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 Mass General Brigham IRB requires 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 under an IDE or requiring a nonsignificant risk determination are scheduled for review at a convened meeting of the Mass General Brigham IRB. The Mass General Brigham IRB must categorize the device investigation as either “significant risk” (SR) or “nonsignificant risk” (NSR) unless the study meets the definition of an exempted device investigation or is being conducted under an IDE.

The sponsor generally makes this determination regarding the need for an IDE; however, the Mass General Brigham IRB is responsible for making the determination when the sponsor has not submitted an IDE application to the FDA. The Mass General Brigham IRB bases its 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 Mass General Brigham IRB considers the potential harm that could be caused by the procedure as well as the device. The Mass General Brigham IRB may require the investigator to submit to the FDA for the determination of need for an IDE application, in which case the FDA decision will govern.

Nonsignificant risk device investigations

Nonsignificant risk device investigations include any investigation of a device other than those that meet the definition of 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. NSR studies are considered to have an approved IDE and must follow abbreviated requirements at 21 CFR 812.2(b).

When the Mass General Brigham IRB makes an NSR determination and the risk to the subjects is determined to be minimal in accordance with 21 CFR 56.102(i), the Mass General Brigham IRB 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 Mass General Brigham IRB concurs with the sponsor that the research is a nonsignificant risk device investigation, the investigation may proceed when fully approved by the Mass General Brigham IRB 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;
- (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 Mass General Brigham IRB or the sponsor or the FDA determines 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 Mass General Brigham IRB requires the IDE number be included in the application. As

confirmation that the IDE number is valid, the Mass General Brigham IRB requires documentation from the sponsor or the FDA of the IDE number. The IDE goes into effect 30 days after the FDA receives the IDE, unless the sponsor receives earlier notice from the FDA, and must be in effect before the Mass General Brigham IRB fully approves the research.

Sponsor-Investigator IDEs

When a Mass General Brigham investigator is the sponsor of the IDE, the Mass General Brigham IRB 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 Mass General Brigham sponsor-investigator, the Mass General Brigham IRB will require the investigator to undergo a review of FDA sponsor-investigator responsibilities with the Human Research Affairs Compliance and Education Office.

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 Mass General Brigham IRB even though the FDA does not consider such uses to be research. The Mass General Brigham IRB 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 undue 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 Mass General Brigham-affiliated entities have control.

REFERENCE:

21 CFR 812

DEVELOPMENT AND CONSULTATION:

Human Research Office

Human Research Affairs Compliance and Education Office