

University of Rochester	Office for Human Subject Protection		
	Research Subjects Review Board		Effective Date: 11/27/2019
	Research Involving FDA Regulated Devices		Policy 606
			Version: 1.2

POLICY

1. Purpose

Outline the responsibilities and regulatory requirements when conducting human subject research that involves the use of devices under the oversight of the Food and Drug Administration (FDA).

2. Scope

This policy applies to human subject research conducted or supported by employees or agents of the University of Rochester that involves the use of FDA regulated devices.

3. Definitions

3.1. *Clinical Investigation* – Research involving one or more subjects to determine the safety or effectiveness of a device.

3.2. *Expanded Access* – The use of an investigational device outside of a clinical trial for treatment of a patient.

3.3. *Humanitarian Device Exemption (HDE)* – An application approved by the FDA for use of a HUD which is exempt from the effectiveness requirements of section 514 and 515 of the Food, Drug, and Cosmetic Act.

3.4. *Humanitarian Use Device (HUD)* – A medical device intended to benefit patients in the treatment and diagnosis of diseases or conditions that affect fewer than 4,000 people in the United States per year.

3.5. *Implant* – A device this is placed into a surgically or naturally formed cavity of the human body if it is intended to remain there for a period of 30 days or more.

3.6. *Immediately Life Threatening Disease or Condition* – Stage of disease in which there is reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment (i.e., the patient has a disease or condition that causes major irreversible morbidity or the patient is in the stage of disease that requires intervention before review at a convened meeting of the IRB is feasible).

3.7. *Investigational Device* – A medical device, including a transitional device*, that is the object of a clinical study designed to evaluate the effectiveness and/or the safety of the device.

*Transitional device is one that was previously regulated as a new drug before 5/28/1976

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- 3.8. *Investigational Device Exemption (IDE)* – An application submitted to the FDA for an investigational device to be used in a research study in order to collect safety and effectiveness data required to support requests to legally market a device.
- 3.9. *Medical Device* – An instrument, apparatus, implement, machine, or other similar or related article which is intended for diagnostic purposes, or in the cure, mitigation, treatment, or prevention of disease, or which does not achieve its primary intended purposes by chemical action or by being metabolized.
- 3.10. *Non-Invasive* – As applied to a diagnostic device or procedure, is one that does not by design or intention, 1) Penetrate or pierce the skin or mucous membranes of the body, the ocular cavity, or the urethra, or 2) enter the ear beyond the external auditory canal, the nose beyond the nares, the mouth beyond the pharynx, the anal canal beyond the rectum, or the vagina beyond the opening of the cervix. Note that blood sampling that involves simple venipuncture and use of surplus samples of body fluids or tissues taken for non-investigational purposes is considered noninvasive.
- 3.11. *Non-Significant Risk Device* – An investigational device that does not present a potential for serious risk to the health, safety, or welfare of the subject. Examples include: most daily wear contact lenses, lens solutions, heel cups, antibacterial surgical garments, incontinence devices, oral training splints, and ultrasonic tooth cleaners.
- 3.12. *Significant Risk Device* – An investigational 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 to be used in supporting or sustaining human life, or 3) is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health. Examples include: catheters (other than urological), ventilators, cardiopulmonary resuscitation (CPR) devices, temporomandibular joint disorder (TMJ) prostheses, stents, lithotripters, sutures and absorbable bandages/materials, electroconvulsive therapy (ECT) devices, extended wear contact lenses, pacemakers, contraceptive devices, most laser systems, and most hemodialysis systems.
- 3.13. *Sponsor* – An entity who takes responsibility for and initiates a clinical investigation regardless of financial support, and may be an individual, company, governmental agency, academic institution, private organization, or other organization. This entity does not actually conduct the clinical investigation, unless the entity is a Sponsor-Investigator.
- 3.14. *Sponsor-Investigator* (or Investigator-held IDE) – An Investigator who is responsible for the initiation and conduct of a clinical investigation, as well as the responsibility for the direct oversight of the administration, dispensing and/or use of the test item across all

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sites (e.g., regulatory Sponsor). For example, when a physician submits an IDE application to the FDA to propose a study of an unapproved medical device or of an approved medical device for a new indication or in a new patient population.

3.15. *Treatment Use* – Use of an investigational device for treatment or diagnostic purposes.

4. References

- 4.1. FDA 21 CFR 812; FDA 21 CFR 814
- 4.2. Guidance for HDE Holders, Institutional Review Boards (IRBs), Clinical Investigators, and Food and Drug Administration Staff: Humanitarian Device Exemption (HDE) Regulation: Questions and Answers
- 4.3. [Policy 404 Criteria for Approval of Research](#);
[Policy 502 Types of RSRB Submissions](#);
[Policy 504 RSRB Reliance for Review](#);
[Policy 607 Emergency Use of Investigational Drugs, Biologics and Medical Devices](#);
[Policy 901 Investigator Responsibilities](#)
- 4.4. [Treatment Use Protocol Template](#);
[Treatment Use Consent Template](#)

5. Responsibilities

- 5.1. In addition to the responsibilities indicated in *Policy 901 Investigator Responsibilities* “Requirements for Principal Investigators Conducting FDA Regulated Research”, Investigators conducting research involving investigational devices are responsible for providing the RSRB with all applicable information and documentation requested in the RSRB protocol template and IRB review system, when the RSRB is the Reviewing IRB, including but not limited to the following, as applicable:
 - A plan for storage, control and accounting of the investigational device;
 - Manufacturer’s brochure or other document with risk information;
 - Documentation of FDA approval for use of a marketed device in accordance with an FDA approved indication, when applicable (e.g. 510K or PMA documentation);
 - If an IDE application was submitted to the FDA, documentation (e.g., letter or email) from the FDA verifying the IDE number and indicating the study is safe to proceed. If the safe to proceed letter has not been received, the RSRB will accept documentation from the Sponsor or Investigator indicating the FDA’s confirmation that the study may proceed;
 - If an IDE application was not submitted to the FDA and the Investigator is requesting the RSRB grant an abbreviated IDE, justification written in the protocol to document why the use of the investigational device(s) in this application should be considered non-significant risk (NSR) [21 CFR

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812.2(b)(1)]. If the FDA has already made an NSR determination, provide documentation.

- If an IDE application was not submitted to the FDA and the Investigator is requesting the RSRB to confirm that the study is exempt from the IDE requirements, justification written in the protocol as to why the use of the investigational device(s) in this application meets requirements for IDE exemption under 21 CFR 812.2(c). If the FDA has already made a determination that the study is exempt from IDE requirements, provide documentation.
- If the UR Investigator is the Sponsor-Investigator, provide documentation of UR IDE training.

5.1.1. When the UR Investigator holds the IDE (Sponsor-Investigator), he/she assumes all responsibilities of both the Investigator (as listed in 5.1 above) as well as the Sponsor responsibilities as stated in Subpart C of 21 CFR 812, including but not limited to:

- Submitting the IDE application for FDA review;
- Ensuring RSRB approval is obtained;
- Complying with FDA regulatory requirements including device labeling, informed consent, IDE safety reporting, recordkeeping, prohibition against promotion, Annual Reports, Final Study Report, and withdrawal or inactivation of the IDE;
- Ensuring proper monitoring of the research.

5.1.2. When an abbreviated IDE is granted by the RSRB as an NSR device, the UR Investigator assumes all responsibilities of the Investigator (as listed in 5.1 above) as well as the Sponsor responsibilities as stated in 21 CFR 812.2(b) when the research is not industry sponsored, including but not limited to:

- Submitting an NSR determination to the RSRB for review;
- Ensuring RSRB approval is obtained;
- Complying with FDA regulatory requirements including device labeling, consent, IDE Safety reporting, recordkeeping, and prohibition against promotion;
- Ensuring proper monitoring of the research.

5.1.3. When the RSRB is the Relying IRB, Investigators are responsible for following the submission requirements of the Reviewing IRB as described in *Policy 504 RSRB Reliance for Review*, as well as any institutional requirements described within this policy.

5.2. When the RSRB is the Reviewing IRB, the RSRB is responsible for the review and approval of research involving devices under the FDA regulations 21 CFR 812 and

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according to *Policy 404 Criteria for Approval of Research*. Prior to considering whether the research may be approved, the RSRB will first review the research application to confirm that one of the following is true:

- 5.2.1. The device has an IDE issued by the FDA, or presents significant risk (SR) and the Investigator/Sponsor must go to the FDA to obtain an IDE prior to receiving RSRB approval;
- 5.2.2. The device presents non-significant risk (NSR) and meets requirements for an abbreviated IDE [21 CFR 812.2(b)(1)], if the FDA already made the NSR determination, the RSRB does not need to do this, or
- 5.2.3. The device meets one of the IDE exemption categories [21 CFR 812.2(c)(1-7)].

6. Requirements for Use of Investigational Devices

- 6.1. Investigators (or Sponsor-Investigators as applicable) are required to conduct research involving investigational use of medical devices according to the FDA Investigational Device Exemption (IDE) regulations at 21 CFR 812, as appropriate, which includes obtaining IRB approval before the study is initiated. When the RSRB is the Reviewing IRB, the requirements below under 6.2 through 6.6 apply to the review.
- 6.2. The RSRB will consider the following during its review of research involving a device approved by the FDA and used as indicated:
 - 6.2.1. The RSRB will review the manufacturer’s brochure and the FDA [510k](#) or [PMA](#) databases, as needed, to confirm the protocol shows that the device will be used according to its FDA approved indication(s).
 - 6.2.2. The study will be reviewed by the RSRB based on the risk category of the study and according to *Policy 501 Levels of Review*.
- 6.3. During its review of research involving a device with an established IDE, the RSRB review will be based upon the risk category of the study and according to *Policy 501 Levels of Review*.
- 6.4. The RSRB review of research involving a device that qualifies for exemption from the IDE regulations will be based upon the risk category of the study and conducted according to *Policy 501 Levels of Review*.
- 6.5. Research involving a device not approved by the FDA, which does not have an established IDE and is not exempt from the IDE regulations, must be presented to the convened board for a device risk determination of significant risk (SR) or non-significant risk (NSR).
 - 6.5.1. During its review, the RSRB will consider the following in determining whether a device poses SR or NSR:
 - 6.5.1.1. Information provided by the Investigator (or Sponsor) describing the rationale used in making a SR or NSR determination,
 - 6.5.1.2. Whether the proposed research meets the definition of “significant risk”,

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- 6.5.1.3. The proposed use of the device in the study, not just the device alone, as well as any protocol related procedures and tests (e.g., surgery for an implant), and any potential for serious risk to the health, safety or welfare of the subject.
- 6.5.2. If the board categorizes the device as SR, further review of the study is deferred and the Investigator will be instructed to apply for an IDE with the FDA. Once the Investigator provides written documentation of the FDA’s approval of the IDE application or its NSR classification, RSRB review may resume.
- 6.5.3. If the board categorizes the device as NSR, the risk determination of the RSRB approved research will be documented.
 - 6.5.3.1. Research involving NSR devices *may* be considered for subsequent RSRB review under the expedited review procedures outlined in *Policy 502 Types of RSRB Submissions*.
 - 6.5.3.2. For NSR determinations, if new information is presented to the RSRB during the conduct of the study, the RSRB has the authority to reconsider its prior NSR decision and, if necessary, request FDA review.
- 6.6. During its review of research involving a device approved by the FDA, **but not used as indicated**, and not exempt from the IDE requirements, the RSRB will:
 - 6.6.1. Review the manufacturer’s brochure and the FDA [510k](#) or [PMA](#) databases, as needed, to confirm that protocol shows that the device will not be used according to its FDA approved indication(s).
 - 6.6.2. Conduct a risk assessment of the device as indicated in Section 6.5 above.
- 7. Requirements for Humanitarian Use Devices (HUD)**
 - 7.1. HDE regulation 21 CFR 814.124 requires convened board review prior to use when the RSRB is the Reviewing IRB (except as applies to emergency use according to Section 8.1 below) for Investigators using a HUD according to its HDE-approved indication(s) for patient treatment or diagnosis. Investigators must provide the RSRB with the following, as applicable:
 - 7.1.1. Documentation from the FDA verifying the HDE number, and the approved HDE indication.
 - 7.1.2. Summary of the proposed use of the HUD, to include a description of any screening procedures, the HUD procedure, and any patient follow up activities, as applicable;
 - 7.1.3. Manufacturer’s brochure;
 - 7.1.4. HUD patient information packet,
 - 7.1.5. Documentation designating the individual(s) who will use/insert the device and proof of training with the HUD.
 - 7.2. Investigators using a HUD outside the FDA approved indication(s) (i.e., off-label) for patient treatment or diagnosis requires convened board review and approval and a treatment use consent form, when the RSRB is the Reviewing IRB. The protocol should address the following:

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- 7.2.1. Provide reference to the literature supporting the off-label use;
 - 7.2.2. Any alternative therapeutic options for the patients;
 - 7.2.3. Description of any greater risk from the use of the HUD than that of the disease and whether the risks and procedures for patients differ from those for the approved recipients;
 - 7.2.4. Description of any additional monitoring of the patient;
 - 7.2.5. Indication that follow-up reports will be filed with the HDE holder;
 - 7.2.6. Indication that patients will receive the HUD patient information packet in addition to the treatment use consent form that describes additional information pertinent to the patient's condition.
- 7.3. Investigators conducting research with a HUD is considered an investigational device, and 21 CFR Parts 50 (protection of human subjects) and 56 (IRB review) apply. If the research is following the FDA approved use and labeling, no IDE is required; however, any other research use (e.g., different indication or different population) must follow the requirements under Section 6.5 above.
- 7.4. When the RSRB is the Reviewing IRB, the RSRB will review the use of a HUD for treatment or diagnosis according to the criteria at 21 CFR 56.111 and *Policy 404 Criteria for Approval of Research* (with the exception of emergency use of a HUD as described under Section 8.1 below).
- 7.5. When using a HUD according to its HDE-approved indication(s) for treatment or diagnosis, the RSRB will confirm the HDE number and indications for which the HUD may be used according to the FDA [Humanitarian Device Exemptions database](#).
- 7.6. When using a HUD outside its HDE-approved indication(s) for treatment or diagnosis, the RSRB will consider:
- 7.6.1. The patient population's need for the HUD;
 - 7.6.2. The likelihood that the device is appropriate for the patient population's condition or disease state.
 - 7.6.3. Whether any limitations on the use of the HUD should be applied.
- 7.7. The HDE holder must have a HUD designation and approved HDE application from the FDA before the device is shipped to the institution, and must ensure that RSRB approval is obtained prior to administering or implanting the HUD in a patient.
- 7.8. The investigator is required to report to the FDA deaths and serious injuries that the HUD has or may have caused, or was a contributing factor. These reports are coordinated through the [Office of Counsel](#).

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7.9. RSRB approved uses of a HUD for treatment or diagnosis may be considered for subsequent RSRB review under the expedited review procedures outlined in *Policy 502 Types of RSRB Submissions*.

8. Requirements for Expanded Access of Investigational Devices

The following mechanisms expand access to investigational devices without compromising the protection of human subjects or the thoroughness and scientific integrity of product development and marketing approval ([FDA Expanded Access for Medical Devices](#)). All expanded access uses require review by the RSRB as the Reviewing IRB.

8.1. Emergency Use

8.1.1. The use of an investigational device or of a HUD in an emergency situation before it is approved by an IRB may be permitted without prior FDA or RSRB approval when necessary to protect the life or physical well-being of a subject according to 21 CFR 812.35(a)(2), 21 CFR 814.124, and according to *Policy 607 Emergency Use of Investigational Drugs, Biologics and Medical Devices*.

8.1.2. Prospective RSRB review is required for emergency use, unless conditions for exemption from prior RSRB review and approval are met (see *Policy 607 Emergency Use of Investigational Drugs, Biologics and Medical Devices*).

8.2. Treatment Use

8.2.1. The FDA may permit an unapproved device to be used under a treatment IDE (i.e., use of a device for treatment or diagnostic purposes) for a group of patients not in the clinical trial if the following requirements are met [21 CFR 812.36]:

- 8.2.1.1. The device is intended to treat or diagnose a serious or life-threatening disease or condition;
- 8.2.1.2. There is no comparable or satisfactory alternative device or therapy to diagnose, monitor, or treat the disease or condition in the intended population;
- 8.2.1.3. The device is under investigation in a controlled clinical trial for the same use under an approved IDE, or all clinical trials have been completed; and,
- 8.2.1.4. The sponsor of the controlled clinical trial is actively pursuing marketing approval of the investigational device with due diligence.

8.2.2. Prospective RSRB review and informed consent is required for treatment use studies (refer to the RSRB *Treatment Use Protocol Template* and *Treatment Use Consent Template*).

8.3. Compassionate Use

8.3.1. The FDA may permit access to an investigational device for a patient (or small group of patients) for which the treating physician believes the device may provide a benefit in treating and/or diagnosing their disease or condition and no generally

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acceptable alternative treatment for the condition exists; however, prior FDA approval is required prior to compassionate use of the device. Refer to the [FDA Expanded Access for Medical Devices](#) information regarding the criteria and requirements for this type of expanded access.

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Appendices:

None

Revision History:

03/2017: Added definitions 3.1 and 3.2; added references and hyperlinks; language to account for single IRB review; added Sect 7.8, added Sect 8.3 compassionate use
11/2019: Update links, editorial changes, and update signatories

Supersedes Date:

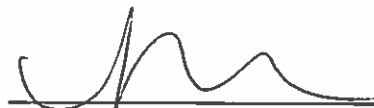
03/17/19

Approved By:



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12/5/2019
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