6.2 Research Involving Investigational and Marketed Devices

1.0 Purpose

The purpose of this policy and procedure is to describe the Organization’s requirements for research involving investigational and marketed devices.

2.0 Policy

- 2.1. It is the policy of the Organization that the IRB will review all research involving investigational devices and FDA-approved devices (test articles) in full accordance with the following: 21 CFR 50, 56; 21 CFR 812, 814; 45 CFR 46.
- 2.2. It is the policy of the Organization that investigators will conduct such research in full accordance with the above cited regulations and applicable HRPP policies.
- 2.3. It is the policy of the Organization that sponsors and any CRO acting on behalf of the sponsor will fully comply with FDA regulations at 21 CFR 812.

3.0 Definitions

- 3.1. Investigational Device means a device, including a transitional device, which is the object of a clinical investigation. As further defined, a device is any healthcare product that does not achieve its primary intended purpose by chemical action or by being metabolized.
- 3.2. Clinical Investigation means any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the FDA under Section 505(i) or 520(g) of the Act or need not meet the requirements for prior submission to the FDA under these sections of the Act but the results of which are intended to be later submitted as part of an application for a research or marketing permit. The terms research, clinical research, clinical study, and clinical investigation are deemed to be synonymous.
- 3.3. Investigator means the individual under which immediate direction the test article is administered or dispersed to a subject. Under HRPP policy 1.26 (PI Qualifications and Responsibilities), this individual is referred to as the PI.
- 3.4. Human Subject means an individual who is or becomes a participant in a clinical investigation either as a recipient of the test article or as a control. A subject may be either a patient or a healthy individual.
- 3.5. Significant risk device (SRD) is a device that
  - 3.5.1. Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject; or
  - 3.5.2. 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
  - 3.5.3. 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
  - 3.5.4. Otherwise presents a potential to the health, safety or welfare of a subject.
    Note: SR device studies must follow all the IDE regulations at 21 CFR 812, and must have an IDE application approved by FDA before they may proceed.
- 3.6. Non-significant risk device (NSRD) is a device that does not meet the definition of an SRD.
  Note: NSR device studies must follow the abbreviated requirements at 21 CFR 812.2(b). These abbreviated requirements address labeling, IRB approval, informed consent, monitoring, records, reports, and prohibition against promotion. However, there is no need to make progress reports or final reports to FDA. NSR device studies do not have to have an IDE application approved by FDA.
  Note: FDA is the final arbiter as to whether a device study is SR or NSR and makes the determination when an IDE is submitted to FDA or if asked by the sponsor, clinical investigator, or IRB. See 21 CFR Â§ 812.2(b)(1).
- 3.7. Investigational New Device Exemption (IDE) is an application submitted to FDA to conduct a clinical investigation with an investigational device that is subject to 21 CFR 812.2 and is classified as an SRD. The IDE is submitted by the sponsor of the research. The FDA will provide a written authorization to conduct a clinical investigation within 30 days after receipt of the IDE. If the device is not an SRD, the investigation is considered by FDA to have an approved IDE unless FDA notifies the sponsor otherwise.
- 3.8. Marketed Device is a device approved by FDA for marketing and is generally in use for treatment or diagnostic purposes.
  Note: When a marketed device is used in a clinical investigation, it is subject to 21 CFR 812.2 unless it qualifies as an exempted investigation. IRB review and approval, however, is required.

- 3.9. Sponsor is the person who initiates, but does not actually conduct the investigation. The sponsor is responsible for complying with the requirements under FDA regulations at 21 CFR 812.40-47. The sponsor may be a device company, governmental agency, academic institution, private organization or an individual investigator.
- 3.10. Sponsor-Investigator is an individual that initiates and conducts an investigation, that is, under whose immediate direction the investigational device is administered, dispensed or used. An investigator who also serves as a sponsor must comply with all FDA requirements applicable to an investigator as well as a sponsor.
- 3.11. Treatment Use of an Investigational Device means use of a device that is not approved for marketing, but may be under clinical investigational, for a serious or immediately life-threatening disease or condition in patients for whom no comparable or satisfactory alternative device or other therapy is available. Under a treatment IDE, patients not in a clinical investigation may be treated utilizing the device in accordance with 21 CFR 812.36. IRB approval is required for treatment use of an investigational device.
- 3.12. Emergency Use means use of a test article on a human patient in a life-threatening or severely debilitating circumstance where no standard medically acceptable treatment is available and there is not sufficient time to obtain full IRB approval for use of the test article to treat the patient.
- 3.13. Unanticipated Adverse Device Effect (UADE) means an adverse effect caused by, or associated with, a device, if that effect was: 1) not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), and 2) the adverse effect relates to or impacts the rights, safety, or welfare of subjects.
- 3.14. A Custom Device (as defined in 21 CFR 812.3(b) and section 520(b) of the FFDA) means a device that meets all of the following criteria:
  It is necessarily different from generally available devices or performance standards to meet the order of an individual physician or dentist;
  (a) It is not generally available to, or used by, other physicians or dentists;
  (b) It is not generally available for purchase or dispensing upon prescription;
  (c) It is not offered for commercial distribution;
  (d) It is intended for use by an individual patient, or to meet the needs of the individual physician or dentist.

4.0 Requirements

- 4.1. All contracts between sponsors and UNMC, Nebraska Medicine, and BMC for investigational device studies must be reviewed and approved by UNMC Sponsored Programs Administration (SPA) or by UNeHealth, in compliance with HRPP policy 1.12 (Sponsored Research).
- 4.2. All contracts between sponsors and CHMC for investigational device studies must be reviewed and approved by UNMC Sponsored Programs Administration (SPA) or by

UNeHealth, or by CHMC Administration, in compliance with HRPP policy 1.12 (Sponsored Research). If the contract is reviewed and approved by CHMC Administration it will also be reviewed by UNMC SPA or UNeHealth to assure the requirements of HRPP policy 1.12, section 4.3 are met.

- 4.3. Clinical investigations involving SR devices must be reviewed and approved by the full IRB in accordance with HRPP policy 2.2 (Full IRB Review). However, the IRB may determine select clinical investigations involving NSR devices and exempt devices that are no more than minimal risk may be eligible for expedited review in accordance with HRPP policy 2.3 (Expedited Review).
- 4.4. If the contract agreement requires compliance with ICH GCP, the IRB will review the submission in accordance with HRPP policy 1.13 (Compliance with ICH-GCP). The investigator will designate the need for ICH GCP compliance in the IRB application.
- 4.5. If a study involves an investigator-initiated IDE, it is the expectation of the Organization that the PI will also comply with the FDA-mandated sponsor requirements (21 CFR 812) and certify compliance by submitting Addendum P (Principal Investigator Responsibilities: Investigator-Initiated Device Trials) which specifies all of the responsibilities of the Sponsor-Investigator.
- 4.6. Any PI who has a study that is audited by the sponsor, a CRO or FDA must immediately notify the UNMC Chief Compliance Officer and provide the IRB with a copy of the report following the audit. When the study is audited by the Fred & Pamela Buffett Cancer Center Protocol Review Monitoring System (PRMS) Audit Committee, a copy of the report must be provided to the IRB.
- 4.7. If a study involves an investigator-initiated IDE, the PI must also comply with the FDA-mandated sponsor requirements.

5.0 IRB Procedures

- 5.1. The IRB will review information in the application to ensure that (1) the device has an IDE issued by the FDA, or satisfies the requirements for exemption from IDE; and (2) the device is not a banned device.
- 5.2. The IRB will review the information in the application to ensure that the PI has adequate controls in place for storage, security, and dispensing of investigational devices in accordance with 21 CFR 812.110. The IRB will assess whether:
  - 5.2.1. The device is stored and secured in a manner that restricts access to investigators. As appropriate this may be a cabinet that has a physical lock to which only an investigator has a key (physical or electronic), or some other equivalent process.
  - 5.2.2. The device is dispensed in a manner that assures that only subjects who have provided informed consent will be treated or tested/examined using the investigational device. This should involve marking the device in an easily visible manner that it is for investigational use only, and, as appropriate, include a

mechanism to have a second party review the signed consent form prior to dispensing the device from a storage location, or some other equivalent process.
    - 5.2.3. The investigator and the departments, sections, or operating rooms where device is used maintains records sufficient to document that the storage, security and dispensing of investigational devices has been in accordance with 21 CFR 812.110. These records may be physical or electronic, as long as they satisfy the requirements of 21 CFR 812.140, including, but limited to records of receipt, use or disposition of a device that relate to: (i) The type and quantity of the device, the dates of its receipt, and the batch number or code mark; (ii) The names of all persons who received, used, or disposed of each device, and (iii) Why and how many units of the device have been returned to the sponsor, repaired, or otherwise disposed of.
- 5.3. Unless the research is exempt from the FDA IDE regulations, the IRB will review the sponsor's determination of the risk classification of the device (SR or NSR) and make a determination of risk based upon the following:
    - 5.3.1. The potential harm associated with the device itself
    - 5.3.2. The proposed use of the device
    - 5.3.3. Any procedure necessary for implantation of the device
    - 5.3.4. A comparison of the risks of the device against the risks of alternative devices or procedures.
- 5.4. The IRBs determination of risk classification of the device and the rationale for the classification will be documented in the IRB minutes.
- 5.5. If the IRB has any question or concern about whether a study is SR and, therefore, requires an IDE, the PI will be instructed to contact the Food and Drug Administration (FDA) Center for Devices and Radiologic Health (CDRH) and obtain a written determination.
- 5.6. The IRB will notify the PI of the Board's SR/NSR determination. If the IRB disagrees with the sponsor or PI's determination that a device is NSR, the study can only be conducted within the Organization if an IDE is obtained. The PI is responsible for notifying the sponsor of the IRB's determination. The PI must provide the IRB with confirmation of this action.
  Note: In accordance with 21 CFR 812.150(b)(9), if the IRB determines that a device is SR and the sponsor had classified the device as NSR, the sponsor must submit to FDA a report of the IRB's determination within 5 work days after the sponsor first learns of the IRB determination. If FDA does not agree with the IRB's SR determination, the IRB will re-review the study. However, the IRB retains the ultimate authority in deciding whether or not to accept FDA's NSR classification.
- 5.7. NSR device studies do not require submission of an IDE application to the FDA before starting the study. The FDA considers an NSR device study to have an approved IDE application after obtaining and maintaining IRB approval. Sponsors and the PI must meet the abbreviated requirements at 21 CFR 812.2(b). These abbreviated requirements address labeling, IRB approval, informed consent, monitoring, records, reports, and prohibition against promotion.
- 5.8. If the IRB classifies a device as NSR, the IRB will continue to follow procedures in accordance with the IRB approval criteria HRPP policy 2.5 used in considering approval of any research involving an FDA-regulated product including all applicable local and regulatory requirements.
- 5.9. SR devices require submission of an IDE application to the FDA before starting the study. Final IRB approval and release of IDE studies is contingent upon the assigned IRB administrator's receipt of FDA notification approving the IDE. All protocol-related

documents, including FDA notification, must contain matching IDE numbers.
- 5.10. For studies involving marketed SR devices for potential new indications, the IRB may require submission of an IDE application to the FDA upon consultation with both the sponsor and the FDA.
- 5.11. All unanticipated adverse device effects (UADEs) will be reported in accordance with HRPP policy 8.1 (IRB Review of Adverse Events and Adverse Device Effects).

6.0 Exemptions from IDE Requirements

- 6.1. Any of the following types of clinical investigations are exempt from IDE requirements (21 CFR 812.2(c)):
  - 6.1.1. A clinical investigation with approved devices used in accordance with labeling. The device may have been approved for commercial distribution before May 28, 1976 or deemed substantially equivalent to a device commercially approved before May 28, 1976.
  - 6.1.2. A clinical investigation with in vitro diagnostic devices, if the sponsor complies with applicable labelling requirements in 21 CFR 809.10(c) and if the testing:
    - 6.1.2.1. Is noninvasive; and
    - 6.1.2.2. Does not require an invasive sampling procedure that presents significant risk; and
    - 6.1.2.3. Does not by design or intention introduce energy into a subject; and
    - 6.1.2.4. Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure.
  - 6.1.3. A clinical investigation with a marketed device undergoing consumer preference testing, testing of a modification, or testing of a combination of two or more devices in commercial distribution, unless testing is for determining safety and efficacy and/or puts subjects at risk.
  - 6.1.4. A custom device as defined in § 812.3(b), unless the device is being used to determine safety or effectiveness for commercial distribution.
- 6.2. Exemption from IDE regulations does not mean the study is exempt from IRB review and approval. If the study involves use of a device, whether or not the device has been approved by the FDA, the IRB's review and approval of the study must comply with all applicable local and federal regulations.

DOCUMENT HISTORY:

? Written: 1/12/2016 - original author not recorded

? Revised: 3/2/2018 - revision not documented

? Revised: 5/6/2022 (Approved: 5/6/2022) - revision not documented

? Revised: 9/29/2022 - corrected typographic errors in section 4.2 ? {Approved: Bruce Gordon (Assistant Vice Chancellor for Regulatory Affairs, Executive Chair)}

? Revised 1/23/2024 – clarified IRB procedures (section 5.1); added definition of custome device, and included such devices as exempt from IDE requirements (sections 3.1.4 and 6.1.4). {Approved Rusty McCulloh (Institutional Official), Bruce Gordon (Assistant Vice Chancellor for Regulatory Affairs, Executive Chair)}

Revision #7
Created 24 October 2019 21:41:19 by Autumn M Eberly
Updated 5 February 2024 15:17:16 by Robert A Lewis