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
It is the policy of the Organization that: a) 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; b) investigators will conduct such research in full accordance with the above cited regulations and applicable HRPP policies; and c) no research involving an investigational device can be approved by the IRB if it is unclear whether the device requires an IDE, or if the IDE status for an investigational device is unknown.

3.0 Definitions
3.1 Clinical Investigation: 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.

3.2 Investigator: The investigator is defined in 21 CFR 56.102(h) as the individual under which immediate direction the test article is administered or dispersed to a subject. Under HRPP policy #3.13, this individual is referred to as the Principal Investigator (PI).

3.3 Human Subject: 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.

3.4 Investigational Device: An 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.

3.5 Significant risk device (SRD): An SRD is defined as follows:
A. Intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject.
B. 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.
C. 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.
D. Otherwise presents a potential to the health, safety or welfare of a subject.

Note: SRDs are governed by the requirements of the IDE regulations. Examples of SRDs include pacemakers, IUDs, some laser systems, and some hemodialysis systems.
3.6 **Non-significant risk device (NSRD):** An NSRD is one that does not meet the definition of an SRD. 
*Note:* NSRDs are governed by abbreviated requirements at 21 CFR 812.2(b). Examples of NSRDs include: most daily wear contact lenses, lens solutions, heel cups, antibacterial surgical garments, incontinence devices, oral training splints, ultrasonic tooth cleaners and Foley catheters. It should be noted that an NSRD does not mean that the device presents minimal risk. Therefore, the IRB will also classify research involving NSRDs as minimal risk or greater than minimal risk.

3.7 **Investigational New Device Exemption (IDE):** An 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.

A sponsor must submit a separate IDE for any clinical investigation involving an exception from informed consent under the provisions of 21 CFR 50.24.

3.8 **Marketed Device:** A 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:** The sponsor is a 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 is usually a device company, but may be an academic institution, private organization, governmental agency or an individual investigator.

3.10 **Sponsor-Investigator:** A 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:** 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:** The 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. Refer to HRPP policy #6.4 for additional information.
3.13 **Humanitarian Use Devices (HUD):** HUDs are intended to benefit patients by treating or diagnosing a disease or condition that affects fewer than 4,000 individuals in the U.S. per year. Refer to [HRPP policy #6.3](#) for additional information.

3.14 **Unanticipated Adverse Device Effect (UADE):** 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.

*Note: The FDA regulations at 21 CFR 812.3(s) define an adverse device effect which is different than the definition of an adverse event in FDA IND regulations at 21 CFR 312. Refer to HRPP policy #8.2 for additional information.*

4.0 **Abbreviated Requirements**

4.1 The following categories of investigations are considered to have approved applications for IDE’s, unless the FDA notified a sponsor that approval of an application is required in accordance with 21 CFR 812.2(b):

**A.** An investigation of a device other than a significant risk device, if the device is not a banned device and the sponsor:

1) Labels the device.

2) Obtains IRB approval of the investigation after presenting the reviewing IRB with a brief explanation of why the device is not a significant risk device and maintains such approval.

3) Ensures that each investigator participating in an investigation of the device obtains from each subject under the investigator's care, informed consent and documents it, unless documentation is waived by the IRB under federal regulations.

4) Complies with the FDA requirements for monitoring investigations.

5) Complies with FDA requirements for maintaining records and filing the required reports.

6) Ensures that participating investigators comply with FDA requirements for maintaining records and filing the required reports.

7) Complies with the prohibitions against promotion and other practices.

**B.** An investigation of a device other than classified by the FDA as an investigation subject to an IND, if the investigation was begun on or before July 16, 1980 and to be completed, and is completed, on or before January 19, 1981.

5.0 **Exempted Investigations**

5.1 21 CFR 812.2(c) specifies categories of device investigations that qualify for an FDA exemption (i.e. the investigation need not comply with the IDE requirements.) The following categories of devices have been exempted by the FDA:

**A.** A device, other than a transition 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.
B. 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 808 in determining substantial equivalence.

C. A diagnostic device, if the sponsor complies with applicable FDA requirements in 21 CFR 809.10(c) and if the testing:
   1) Is noninvasive,
   2) Does not require an invasive sampling procedure that presents significant risk.
   3) Does not by design or intention introduce energy into a subject, and
   4) Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure.

D. 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.
   1) A device intended solely for veterinary use.
   2) A device shipped solely for research on or with laboratory animals and labeled in accordance with FDA requirements.
   3) A custom device as defined in 21 CFR 812.3(b), unless the device is being used to determine safety or effectiveness for commercial distribution.

E. Limit on certain exemptions: In the case of class II or class III device described in A(1) or 2 above, this part applies beginning on the date stipulated in an FDA regulation or order that calls for the submission of premarket approval applications for an unapproved class III device, or establishes a performance standard for a class II device.

   Note: 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.

6.0 Procedures

6.1 All contracts between sponsors and the Organization for investigational device studies must be reviewed and approved by UNMC Sponsored Programs Administration (SPA) in accordance with HRPP policy #1.11.

6.2 The Organization requires that 1) all investigational device studies (both SR and NSR), and 2) all studies of marketed devices be reviewed and approved by the full IRB in accordance with HRPP policy #2.2. Clinical investigations involving devices are not eligible for expedited review in accordance with HRPP policy #2.3.

6.3 In accordance with HRPP policy #2.1, the PI must submit the following for review by the full IRB: 1) Biomedical Research Application and 2) Addendum R: Investigational Devices. If the PI has an investigator-initiated IDE, Addendum P: Principal Investigator Responsibilities for Investigator Initiated Device Trials must also be submitted. For SR research, the PI must provide the IRB with a copy of the FDA’s approval of the IDE application.
6.4 It is the expectation of the Organization that investigators will fully comply with all of the FDA-mandated responsibilities in accordance with FDA regulations at 21 CFR 812.100, 110, 140, 145, 150 and ensure that the research is also conducted in full compliance with the requirements of 21 CFR 50,56 and 45 CFR 46.

6.5 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 (i.e., SR or NSR) and make a determination of risk based upon the following:
   A. The potential harm associated with the device itself
   B. The proposed use of the device
   C. Any procedure necessary for implantation of the device (e.g. surgery)
   D. A comparison of the risks of the device against the risks of alternative devices or procedures.

6.6 The IRB’s determination of risk classification of the device will be documented in the IRB minutes.

6.7 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.

6.8 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.

6.9 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.

6.10 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 requirement indicated above in Section 3.15. 

   Note: An NSR device study may represent greater than minimal risk depending on the research.

6.11 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.

6.12 The IRB will review the information in Addendum R 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:
A. 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.

B. 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.

C. 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.

6.13 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.

6.14 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.

6.15 It is the expectation of the Organization that sponsors and any CRO acting on behalf of the sponsor will fully comply with the FDA-mandated responsibilities in accordance with FDA regulations at 21 CFR 812.40-47. In addition, sponsor reports must be submitted to the IRB in accordance with 21 CFR 812.150(b)(1-3) and (5-7). The IRB will promptly review each report and take appropriate action to protect human subjects.

6.16 All unanticipated adverse device effects (UADEs) will be reported in accordance with HRPP policy #8.2.

6.17 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 Eppley Cancer Center Protocol Review Monitoring System (PRMS) Audit Committee, a copy of the report must be provided to the IRB.

6.18 If a study involves an investigator-initiated IDE, the PI must also comply with the FDA-mandated sponsor requirements. Such studies will be given priority for a Quality Improvement Assessment (QIA) audit as specified in HRPP policy #1.18.
ADMINISTRATIVE APPROVAL:
Ernest D. Prentice, PhD.  Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, M.D.  IRB Executive Chair