Human Research Protection Program
Policies & Procedures
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1.0 Purpose
The purpose of this policy and procedure is to provide a basic description of the Organization’s Human Research Protection Program (HRPP) through: 1) the Organization’s stated mission, 2) application of ethical principles to guide all human subject research under the oversight of the Organization, and 3) regulatory compliance with all applicable federal, state and local laws.

2.0 Policy
It is the policy of the Organization to establish and maintain a progressive and up-to-date HRPP that is able to: 1) ensure the rights and welfare of human subjects are protected, 2) evaluate and continually improve the protection of human research subjects, and 3) foster important human subject research in accordance with its mission.

3.0 Organization
3.1 The Organization is comprised of the following:
   A. Nebraska Medicine consisting of:
      1) The Nebraska Medical Center (TNMC)
      2) UNMC Physicians
      3) Village Pointe
      4) Bellevue Medical Center (BMC)
   B. University of Nebraska Medical Center (UNMC)
   C. Children’s Hospital & Medical Center (CHMC)
   D. University of Nebraska at Omaha (UNO)

3.2 As specified in HRPP policy #1.2 and the associated IRB authorization agreements, these legally affiliated entities have granted authority to the IRBs operating within the HRPP for oversight of human subject research under its jurisdiction.

3.3 These HRPP policies and procedures serve as the governing procedures for the conduct and review of all human subject research conducted under the auspices of this Organization.

3.4 All HRPP policies and procedures are made available to all investigators and research staff and are posted on the IRB website at http://unmc.edu/irb.

4.0 HRPP Mission
4.1 The mission of the HRPP is to:
   A. Safeguard and promote the health and welfare of human research subjects by ensuring that their rights, safety and well-being are fully protected.
   B. Facilitate excellence in human subject research in accordance with the highest ethical standards in full compliance with all applicable regulatory and organizational requirements.
   C. Provide research personnel with high quality education on the ethics and regulation of human subjects research.
   D. Engage in continual quality improvement, including timely response to new ethical and regulatory challenges in order to ensure the highest possible degree of protection of human subjects.
E. Engage in community outreach activities designed to educate the public about research.

4.2 To ensure compliance with the stated mission, the HRPP will:
A. Exercise oversight of research protection through the Office of Regulatory Affairs (ORA).

B. Establish a formal process to monitor, evaluate and continually improve the protection of human research subjects.

C. Educate the research personnel about their ethical responsibility and regulatory requirements to protect human research subjects.

D. Assure investigators and other research personnel have the appropriate expertise and training in the protection of human research subjects to responsibly conduct their research with integrity.

E. Assure investigators and other research personnel display the highest possible degree of technical skill and care during the conduct of research.

F. When appropriate, intervene as necessary in ongoing research and respond directly to the concerns of research subjects.

G. Assure investigators and other research personnel adhere to the highest possible standards of research ethics, comply with all applicable federal, state, and local laws and regulations, and always place the rights and welfare of research subjects first.

H. Assure investigators and other research personnel respect all ethnic groups, cultures, and socioeconomic strata of the community served by this Organization.

I. Assure all IRB members and ORA staff keep abreast of the latest developments in the ethics and regulation of human subject research and perform thorough and consistent review of research proposals.

J. Receive from the Organization sufficient resources to support the mission of the HRPP.

5.0 Ethical Principles
5.1 All levels of the Organization consider protection of the rights and welfare of human subjects to be of the highest priority. The HRPP will uphold the cardinal principles for the ethical conduct of research (respect for persons, justice, and beneficence) described in the Belmont Report. In addition, due consideration will be given to the principles of the Nuremberg Code, the World Medical Association Declaration of Helsinki (2013) and the ethical guidelines put forth by CIOMS.

5.2 The HRPP, in partnership with the Organization’s research community, is responsible for ensuring the ethical and equitable treatment of all human subjects in research conducted under its auspices.

6.0 Regulatory Compliance
6.1 The HRPP will ensure compliance with 1) HHS regulations for the Protection of Human Subjects at 45 CFR 46, including Subparts A, B, C, D and Subpart E as required by
federal funding agencies; 2) FDA regulations for Protection of Human Subjects at 21 CFR 50 including Subpart D (as required); 3) 21 CFR 56 and other FDA regulations (as required); 4) the regulations and requirements of the other Common Rule agencies (as required); 5) the HIPAA Privacy and Security Rules at 45 CFR 160, 164 (as required); 6) other federal, state and local laws (as required); and 7) HRPP policies.

6.2 If a conflict arises between federal, state, and local law, the IRB will consult the University of Nebraska’s General Counsel Office, UNMC Chief Compliance Officer, and the General Counsel for CHMC as appropriate.

6.3 The Organization has “unchecked the box” on FWA00002939. However, the HRPP will apply equivalent protections to non-federally funded research.

   A. These protections will be based upon the ethical principles in the Belmont Report. In addition, the requirements in 45 CFR 46, Subpart A, B, C, and D will be applied to the greatest extent possible in consideration of the nature of the research. When an exception is made, it must not reflect a lower standard of human subject protection.

   B. The Organization will normally extend the length of continuing review to two years for medical records research which meets the following criteria:

   1) The research is not federally funded.
   2) The research is minimal risk.
   3) The research is not FDA regulated.

   C. The Organization will normally extend the length of continuing review to two years for research in standard follow-up (i.e., no research interventions are performed) and if the research was never FDA regulated when it was active.

6.4 The Organization applies the ICH-Good Clinical Practice (GCP) E-6 Guidelines to clinical trials when the sponsored agreement specifies compliance with ICH GCP in accordance with HRPP policy #1.12.

7.0 Federalwide Assurance (FWA)

7.1 The HRPP operates under the authority of its current Federal Wide Assurance (FWA00002939).

7.2 The Organization will apply the Common Rule (Subpart A) and HHS regulations at 45 CFR 46, Subparts B, C, D and E to federally funded research as required.

7.3 All FDA-regulated research will comply with 21 CFR 50, 56 and other FDA regulations as applicable.

7.4 The HRPP has designated four IRBs to review all human research protocols:

   A. IRB-01: IRB00000670
   B. IRB-02: IRB00000671
   C. IRB-03 (Rapid Response): IRB00002686
   D. IRB-04 (Joint Pediatric IRB): IRB00007222

   Note: In all of the HRPP policies hereafter, IRB-01, IRB-02, IRB-03, and IRB-04 will be referred to as “the IRB”, unless otherwise indicated for purposes of clarity.

8.0 Written Policies and Procedures

The HRPP Policies and Procedures detail the policies of the Organization and regulations governing conduct of research involving human subjects under the auspices of the
Organization. This is not a static document. Review and revision of these policies and procedures will be conducted in accordance with HRPP policy #1.15. Policies and procedures are available on the IRB website at http://unmc.edu/irb or copies are available upon request.

9.0 Description of the HRPP
The HRPP is a comprehensive system to ensure the protection of human subjects participating in research. The HRPP consists of the four IRBs, other review committees, administrative offices, and administrative officials as described in this policy.

9.1 Institutional Official
The ultimate responsibility of the HRPP resides with the Associate Vice Chancellor for Academic Affairs who serves as the Institutional Official (IO). The IO is legally authorized to represent the Organization. The IO is the signatory of the FWA and assumes the obligations specified in the FWA.

The IO is ultimately responsible for the following:

A. Foster, support and maintain an institutional culture supporting the ethical conduct of all research involving human subjects in full compliance with applicable Organizational and regulatory requirements as specified in Sections 5.0-7.0 of this policy.

B. Ensure the HRPP has the resources and support necessary to comply with all Organizational policies and with federal regulations and guidelines that govern human subject research, including:

1) Ensure HRPP and IRB staffing is commensurate with the size and complexity of the research enterprise.

2) Ensure there is adequate HRPP and IRB space, equipment, materials, and technology.

3) Ensure there are sufficient resources for the production, maintenance and secure storage of HRPP and IRB records,

4) Ensure there are sufficient resources for auditing and other compliance activities and investigation of noncompliance.

5) Ensure there is access to legal counsel.

6) Ensure there are sufficient resources for the identification and management of conflict of interest involving the HRPP (including IRB members, Office of Regulatory Affairs (ORA) staff, Principal Investigators and research staff, and the Organization).

7) Ensure there are sufficient resources to support the HRPP Quality Improvement Assessment (QIA) program.

8) Ensure there are adequate resources to support community outreach programs related to human research protections.

9) Support educational opportunities related to human research protections for IRB members, ORA staff, research personnel, and other members of the research community.
C. Oversight of the four IRBs within the Organization and ensuring the IRBs function independently.

D. Appointment and oversight of the IRB Executive Chair.

E. Exert ultimate oversight over the conduct of research conducted by all investigators and other research personnel within the Organization.

F. Ensure investigators and other research personnel fulfill their responsibilities to protect the welfare of human subjects in accordance with HRPP policies.

G. Ensure the IO is kept informed of the activities and decisions of the IRBs by the following:
   1) The IO receives copies of the IRB minutes.
   2) The IO meets with the IRB Executive Chair on a regular basis.
   3) The IO attends IRB staff meetings on a regular basis.
   4) The IO periodically attends IRB meetings.
   5) The IO is immediately advised of all compliance problems, complaints, or any other significant concerns regarding human subject protection.

H. The IO has the authority to further review and approve or disapprove research, but cannot approve research that has not been approved or has been disapproved by the IRBs.

I. Advise Organizational officials on key matters regarding research conducted within the Organization.

J. Oversight of the development and implementation of an educational plan for IRB members, staff, and investigators.

K. Completion of the following education requirements:
   1) OHRP Human Subject Assurance Training: (http://www.hhs.gov/ohrp/education-and-outreach/human-research-protection-program-fundamentals/index.html)

L. Maintain current CITI certification and participate in other training in human subject protections (e.g., PRIM&R and AAHRPP conferences).

M. Assure all IRB members are CITI certified and are appropriately knowledgeable to review research in accordance with ethical standards and applicable regulations.

N. Assure all investigators are CITI certified and are appropriately knowledgeable to conduct research in accordance with ethical standards and applicable regulations.

O. Work with the IRB Executive Chair to develop, manage, and evaluate policies and procedures that ensure compliance with all state, local and federal regulations governing research. This includes monitoring changes in regulations and policies that relate to human research protection and overseeing all aspects of the HRPP program.
P. Ensure that any investigator, research personnel, or IRB member has free and direct access to the IO in order to express any concerns.

Q. Implement the Organization’s HRPP policies and procedures.

R. Submit, implement, and maintain an approved FWA through the DHHS Office of Human Research Protections (OHRP).

S. Oversees the finances of the HRPP.

T. Direct day-to-day operation of the Office of Regulatory Affairs (ORA) office, including supervision of ORA staff.

U. Perform an annual evaluation of the HRPP in accordance with HRPP policy #1.19.

9.2 Institutional Review Boards:
   A. There are four fully constituted IRBs registered with DHHS OHRP and the FDA. The IRB prospectively reviews and makes decisions concerning all human subject research conducted by faculty, staff and students or others (e.g., visiting professor) within the Organization’s facilities or under auspices of the Organization.

   B. The IRB is responsible for the protection of the rights and welfare of human research subjects through assuring compliance with HRPP policies and Sections 5.0, 6.0, 7.0 of this policy. A description of the IRB membership and qualifications is found in HRPP policy #1.5.

   C. The HRPP utilizes the NCI Central IRBs for review and approval of applicable cooperative oncology group protocols involving adult and pediatric subjects in accordance with HRPP policy #1.3.

   D. The HRPP may utilize selected independent commercial IRBs or other IRBs associated with AMCs, universities, academic medical centers or hospitals for review and approval of applicable protocols in accordance with HRPP policy #1.3.

   E. The IRB may serve as the IRB of record for external organizations in accordance with HRPP policy #1.3.

9.3 Legal Counsel:
The Organization relies on Legal Counsel for interpretations and applications of law, as described in HRPP policy #1.10.

9.4 Departmental Chairperson or Authorized Delegate
Departmental chairs or authorized delegates are responsible for ensuring Principal Investigators (PIs) are qualified by training and experience to conduct the proposed research and have sufficient resources and facilities to conduct the research in a manner that fully protects the rights and welfare of subjects (HRPP policy #1.9).

9.5 Principal Investigator
The PI holds primary responsibility for the proper conduct of research in accordance with the approved research protocol. The specific responsibilities of the PI are defined in HRPP policy #3.13.
9.6 Other Review Committees
A. Other Organizational review committees have defined responsibilities to review proposed or continuing research, as follows: 1) Fred & Pamela Buffett Cancer Center Scientific Review Committee (SRC), 2) Pharmacy & Therapeutics Committee (P&TC), 3) Investigational Device Committee, 4) Institutional Biosafety Committee (IBC), 5) the Radioactive Drug Research Committee (RDRC), and 6) Conflict of Interest Committee (COIC). The responsibilities of these committees are described in HRPP policy #1.9.

B. Other review committees may not approve research to commence that has not been approved or has been disapproved by the IRB.

9.7 Other Related Units Within the HRPP
A. Sponsored Programs Administration
1) Sponsored Programs Administration (SPA) staff review all research agreements with federal, foundation, and commercial sponsors as specified in HRPP policy #1.11.

2) Only designated senior officials have the authority to execute the research agreements on behalf of the Organization.

3) UNO SPA reviews research agreements involving UNO.

4) UNMC SPA reviews research agreements involving UNMC, Nebraska Medicine and CHMC.

B. Research Subject Advocate
1) The purpose of this individual is to promote human subject protection in all clinical research conducted at UNMC and Nebraska Medicine through education, training, advocacy, and outreach.

2) The Research Subject Advocate is listed on all consent forms as another contact for research subjects or others.

3) The Research Subject Advocate is also a contact point for questions, comments, concerns, or complaints from individuals internal and external to the Organization.

4) The Research Subject Advocate works with the IRB and other Organizational Officials to resolve issues.

C. Pharmacy
1) *TNMC Pharmaceutical & Nutrition Care Department:*
   a) This department oversees the use of pharmaceutical and investigational agents in human subject research conducted at TNMC, UNMC, and BMC in compliance with hospital policy.

   b) This department will ensure compliance with all federal, state, and local regulations related to pharmaceutical and investigational agents used in clinical trials at Nebraska Medicine.
c) The Pharmacy & Therapeutics (P&T) Committee reviews all clinical protocols studying the effects of investigational or marketed drugs in accordance with HRPP policy #1.9.

d) The Investigational Drug Pharmacist is available to address questions or concerns. All investigational agents are ordered, dispensed, or administered only through the Investigational Drug Pharmacist and only after assurance of compliance with the regulations as reviewed by the P&T Committee and the IRB.

2) **CHMC Pharmacy Department:**
   a) This department oversees the use of pharmaceutical and investigational agents in human subject research conducted at CHMC in compliance with hospital policy.

   b) This department will ensure compliance with all federal, state, and local regulations related to pharmaceutical and investigational agents used in clinical trials at CHMC. The Pharmacy Manager is a member of the Joint Pediatric IRB and reviews all protocols to ensure compliance with all federal regulations.

   c) All investigational agents are ordered, dispensed, and administered through the pharmacy department only after assurance of compliance with the regulations as reviewed by the IRB.

D. **Medical Records**

   1) A legal medical record will be maintained for each individual who is evaluated as an inpatient, ambulatory care patient, or emergency patient per the specified hospital’s medical record policy.

   2) At several of the hospitals, medical records are systematically transitioning from patient information in multiple paper and electronic records to an integrated online medical record with a component for indicating when patients are also research subjects. This will assist with assurance of compliance with HRPP policies and procedures as well as research billing.

9.8 **Relationship Between Components**

   A. The IRB functions independently of, but in coordination, with other Organizational regulatory committees (see HRPP policy #1.9). The IRB, however, makes an independent determination whether to approve or disapprove a protocol based upon whether or not human subjects are adequately protected.

   B. As stated in HRPP policy #1.2, research that has been reviewed and approved by the IRB may be subject to review and disapproval by officials of the Organization. However, those officials may not approve human subject research that has not been approved by the IRB.

   C. The UNMC Compliance Committee meets to ensure dialogue is maintained between the various compliance entities within the Organization. Membership is comprised of representatives from the major components of the Organization with the Chief Compliance Officer as chair. The committee acts in an advisory capacity to the UNMC Chancellor/Vice Chancellor for Research, monitoring the effectiveness of existing compliance programs, developing new or revised policies as changes in
requirements occur, and disseminating updated compliance information to the research community.

9.9 HRPP Operations

A. The Office of Regulatory Affairs (ORA) is responsible for the day-to-day operations of the HRPP. All ORA staff must comply with all ethical standards and practices as well as local, state, and federal regulations in accordance with Sections 5.0-7.0 of this policy. The ORA reports to the IO and has a close working relationship with the IRB Executive Chair and the committees specified above in Section 9.6.

B. The ORA is located in the Academic Research Services Building at UNMC and is equipped with all necessary office space, file storage space, meeting space, and equipment to perform the functions required by the HRPP. The adequacy of the personnel and other resources required by the HRPP is assessed on an annual basis by the IO.

C. The Office is staffed by IRB Administrators and office support staff. The duties and responsibilities for all of the staff are found in their respective job descriptions on file with Human Resources and in the ORA. The performance of all Administrators and support staff is evaluated on an annual basis, in accordance with HRPP policy #1.19.

1) IRB Administrator Qualifications and Training
   a) IRB Administrators are hired by the IO. All IRB Administrators must have at least a Bachelor’s degree with advanced degrees preferred. In addition, they must have relevant previous experience in either the conduct or review of human subject research. The Administrators are expected to become Certified IRB Professionals (CIP) as soon as they are eligible and engage in on-going continuing education to enhance their knowledge and skill levels.

   b) IRB Administrators must complete, and keep current CITI certification in both the Biomedical and the Behavioral and Social Science tracts. IRB Administrators are expected to attend national or regional IRB conferences on a rotating basis.

   c) IRB Administrators are expected to keep abreast of new regulations and guidances issued by OHRP, FDA, and OCR as well as review of pertinent articles related to human subject protection.

2) IRB Staff Qualifications and Training
   a) The IRB staff are hired by the IO and supervised on a daily basis by an IRB Administrator. IRB staff must have relevant research and/or secretarial experience including computer word processing and data management skills. A Bachelor’s degree is preferred but not required.

   b) All IRB staff are encouraged to become Certified IRB Professionals (CIP) as soon as they are eligible and engage in on-going continuing education to enhance their knowledge and skill levels. IRB Administrator IIs are required to be a CIP. CIP certification must be kept current.

   c) IRB staff must complete the CITI training in both the Biomedical and the Behavioral and Social Science tracts.
D. Training Records
The IRB Education Coordinator is responsible for maintaining all initial and continuing education training records. The Education Coordinator will monitor the status of CITI certification for all IRB administrators and staff and notify them when it is time for renewal.

Administrative Approval:
Ernest D. Prentice, PhD.  Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD  IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the authority granted by the Organization for the IRBs operating within the HRPP.

2.0 Policy
2.1 It is the policy of the Organization that the rights and welfare of human subjects must be fully protected in accordance with the mission and expectations of the Organization described in HRPP policy #1.1.

2.2 The Organization will ensure compliance with the regulatory requirements as specified in HRPP policy #1.1, Section 6.0.

2.3 UNMC Associate Vice Chancellor for Academic Affairs serves as the Institutional Official (IO) in accordance with the provisions of the University of Nebraska Medical Center’s Federal Wide Assurance (FWA # 00002939). The IO is the Institution’s signatory official for the FWA and is responsible for allocation of necessary resources to fully support the HRPP.

2.4 UNMC Associate Vice Chancellor for Academic Affairs/IO is granted the authority and responsibility to carry out the daily operation of the HRPP and oversight of the UNMC Office of Regulatory Affairs (ORA) which provides administrative support to the HRPP.

2.5 The IO will interact with Organizational officials to ensure that there is effective ongoing interaction with other review committees which may impact the HRPP.

2.6 All research involving human subjects conducted at the Organization or conducted by employees or representatives of the Organization at external sites must receive approval by a designated IRB before the research may commence.

A. The IRB is authorized to independently review and approve all non-exempt human subject research conducted by the faculty, students, staff, or other representatives of the Organization, or by any non-affiliated investigators, when the research is conducted on the premises of any of the components of the Organization. The IRB may accept review and approval from external IRBs for any research conducted within the Organization on a case-by-case basis in accordance with HRPP policy #1.3.

B. The IRB is authorized to independently review and approve all non-exempt human subject research conducted by the faculty, students, staff, or other representatives of Organization, or by any non-affiliated investigators, when the research is conducted at an external institution. However, the Organization may accept external IRB approval in accordance with HRPP policy #1.3.

2.7 The IRB shall review and approve all non-exempt human subject research before such research is initiated, in full accordance with Sections 2.2 and 2.3 above.

A. Full IRB Review: The full IRB has the authority to approve, require modifications in (to secure approval), or disapprove any research activities conducted under the jurisdiction of the IRB in accordance with HRPP policy #2.2.
B. **Expedited Review:** When expedited review is used, in accordance with 45 CFR 46.110; 21 CFR 56.110, the expedited reviewer designated by the IRB Executive Chair has all the authority to approve or require modifications in (to secure approval) of research activities conducted under the jurisdiction of the IRB. The expedited reviewer is not authorized to suspend or disapprove research in accordance with **HRPP policy #2.3**.

2.8 All exempt research, which is conducted by faculty, students, staff, or other representatives of the Organization must be reviewed and approved by the UNMC Office of Regulatory Affairs (ORA) before it is initiated in accordance with **HRPP policy #2.6**. The ORA will accept approval of exempt research by an external institution on a case-by-case basis.

2.9 The IRB has the authority to observe or have a third party observe the informed consent process for ongoing research protocols.

2.10 The IRB has the authority to observe or have a third party observe the conduct of the research for ongoing protocols.

2.11 The IRB has the authority to review or have a third party review files related to the research under the jurisdiction of the IRB and when an external IRB serves as the IRB of record.

2.12 The IRB has the authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB’s requirements or that has been associated with unexpected serious harm to subjects. When subjects are judged to be at undue risk, or serious non-compliance has occurred, the IRB Executive Chair/designee, in consultation with the IO and others as necessary, is authorized to immediately halt the research.

2.13 The Organization acknowledges that research, approved by the IRB may be subject to further review by an authorized official (CEO/designee) of the involved component of the Organization in consultation with the IO. However, no authorized official may approve research if it has not been approved by the IRB.

2.14 Approval of research by the IRB can be overturned by an authorized official (CEO/designee) of the involved component of the Organization in consultation with the IO. The reason(s) for administrative disapproval of research by the authorized official shall be provided in writing to the PI and the IRB.

2.15 The PI may appeal the administrative decision to overturn IRB approval by submitting a written appeal to the authorized official who will review the appeal with the IO and make the final determination.

2.16 Any attempt to unduly influence the IRB from either within (including Organizational conflicts of interest) or outside the Organization is strictly prohibited and must be reported to the IO. The IO will take appropriate action by notifying the authorized official of the Organization and the supervisor of the individual who attempted to influence the IRB. Corrective action may include counseling or other disciplinary action as necessary.
ADMINISTRATIVE APPROVAL:
Ernest D. Prentice, PhD. Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for initiation of a reliance agreement, or other agreements, which cover research under the following circumstances:

1.1 The UNMC IRB serves as the IRB of record for research conducted at external sites.

1.2 An external IRB serves as the IRB of record for research conducted within the Organization (i.e., commercial IRB(s), NCI Central IRB (CIRB), and other external academic, research, or clinical center IRBs)

2.0 Policy
2.1 It is the policy of the Organization that the UNMC IRB may serve as the IRB of record for research conducted at external sites as permitted by HHS regulations at 45 CFR 46.114 and FDA regulations at 21 CFR 56.114 under the following conditions:

A. The Organization’s PI is conducting the research solely at the external site and either the external site has agreed to defer IRB review to the UNMC IRB or the external site does not have an IRB.

B. The Organization’s PI serves as the Lead PI for research that will also be conducted as an external site by a local investigator and the external site has agreed to defer IRB review to the UNMC IRB or the external site does not have an IRB.

C. For non-exempt research, the Organization requires execution of an IRB Reliance Agreement.

D. For exempt research, the Organization does not normally require execution of an IRB Reliance Agreement.

2.2 It is the policy of the Organization that PIs may utilize selected independent commercial IRBs as the IRB of record permitted by HHS regulations at 45 CFR 46.114 and FDA regulations at 21 CFR 56.114 for new Phase II, III, and IV commercially sponsored clinical trials, with the exceptions specified under Section 2.2D below.

A. The Organization must have an executed service agreement with the commercial IRB to provide this service.

B. The service agreement must specify that the commercial IRB may bill the sponsor directly for their services.

C. The Organization’s requires execution of an IRB Reliance Agreement.

D. Investigators are not permitted to utilize an independent commercial IRB for review of the following:
   1) Phase I commercially sponsored clinical trials.
   2) Research that is not commercially sponsored (e.g., NIH funded research).
   3) Investigator-initiated clinical trials.
4) Use of a Humanitarian Use Device (HUD) subject to 21 CFR 814.124(a)
5) Emergency research subject to FDA regulations at 21 CFR 50.24.
6) Research that involves the use of vaccines developed or manipulated at UNMC.
7) Gene transfer research.
8) Emergency use of a test article subject to FDA regulations at 21 CFR 56.102(d) and 21 CFR 56.104(c).
9) Research involving prisoners as subjects.
10) Research only involving medical records or data registries.
11) Research only involving human biological material.
12) Research involving fetal tissue or HESCs, or their derivatives

2.3 It is the policy of the Organization that PIs involved in research sponsored by the National Cancer Institute (NCI) National Cooperative Groups may utilize the NCI Central IRBs (CIRBs) as the IRB of record permitted by HHS regulations at 45 CFR 46.114 and FDA regulations at 21 CFR 56.114.

A. The Organization has chosen to utilize both the Adult and the Pediatric NCI CIRBs.

B. An IRB Reliance Agreement is on file with the NCI CIRB.

2.4 It is the policy of the Organization that IRBs at AMCs, universities, research centers, and hospitals may serve as the IRB of record permitted by HHS regulations at 45 CFR 46.114 and FDA regulations at 21 CFR 56.114. The acceptance of the external IRB of record will be based upon the following considerations:

A. The IRB of record is accredited by either AAHRRP or Alion.

B. The research is conducted in association with a consortium (e.g., Big 10 Cancer Consortium, PCORI Greater Plains Collaborative, StrokeNet).

C. The research is federally funded and requires the use of a single IRB.

D. The research involves minimal risk and qualifies for expedited review.

E. Other research on a case-by-case basis as determined by the IO in consultation with the IRB Executive Chair.

3.0 Procedures

3.1 UNMC IRB as the IRB of Record

A. The Principal Investigator (PI) who directs the research is a faculty member or other authorized individual within the Organization, and:
   1) The PI assumes overall responsibility for the safe and proper conduct of the research at the external site(s) in full compliance with all applicable regulations and UNMC HRPP policies.
   2) The external site(s) does not have an IRB or the site(s) agree to defer to the UNMC IRB as the IRB of record.

B. The PI must submit:
   1) A letter requesting UNMC IRB oversight of the research conducted at the external site(s).
2) Section I of the IRB application must identify the external site(s) requiring UNMC IRB oversight.
3) Consent form(s)/information sheet(s) must be developed for the external site(s) (as applicable).

C. The UNMC IRB Administrator will review the request and determine if it is appropriate for UNMC IRB oversight.

D. The Institutional Official (IO) must agree to allow the UNMC IRB to serve as IRB of record. The IRB Executive Chair and the full IRB will be consulted when warranted.

E. An IRB Reliance Agreement must be executed between the respective IRBs.

F. All external investigators must sign an External Investigator’s Assurance prior to activation of the research at the external site(s). The External Investigator’s Assurance (XIA) specifies the responsibilities of the external investigator(s) and serves as a certification of compliance with all applicable regulations and IRB requirements.

G. The external site must complete a Local Context Information Form.

H. The UNMC IRB will review the protocol and any associated documents in order to ensure that subjects will be adequately protected in accordance with HRPP policies #2.2 and #2.3.

3.2 External IRB as the IRB of Record

A. The PI who directs the research is a faculty member or other authorized individual within the Organization.

B. The PI assumes overall responsibility for the safe and proper conduct of the research in full compliance with all applicable regulations and applicable UNMC HRPP policies

C. The PI must submit:
   1) For biomedical research PIs should complete the CIRB for Review of Biomedical Research accessed online through RSS (https://net.unmc.edu/rss).
   2) For non-biomedical research, the PI should submit a letter requesting use of the external IRB.

3) All requests for external IRB review must be accompanied by:
   a) Identification of the external IRB.
   b) A copy of the protocol and any other relevant documents pertaining to the study
   c) The external IRB’s accreditation status
   d) The external institution’s FWA number (required for HHS funded research)
   e) The external institution’s IRB Registration number (required for FDA regulated research)
   f) A copy of the external IRB’s approval letter (when available)
   g) A copy of the informed consent form(s)/information sheet(s) approved by the external IRB (when available).
D. The UNMC IRB Administrator will review the request and determine if the protocol is eligible for review by the external IRB. The Administrator will also review informed consent form(s)/information sheet(s) to ensure compliance with applicable federal regulations.

E. The Institutional Official (IO) must agree to allow the UNMC IRB to serve as IRB of record. The IRB Executive Chair and the full IRB will be consulted when warranted.

F. An IRB Reliance Agreement must be executed between the respective IRBs.

G. Protocols determined to be eligible for review by the Central IRB will be accepted and assigned a protocol number ending with the suffix “CB” (Central Board). The IRB database will log which central IRB the study is assigned to.

H. The UNMC IRB Administrator will notify the PI and the Lead Coordinator of any of the following applicable Organizational requirements:
   1) Current CITI certification of all study personnel
   2) Pharmacy & Therapeutics (P&T) Committee approval
   3) Fred & Pamela Buffett Cancer Center Scientific Review Committee (SRC) approval
   4) Conflict of Interest Committee (COI) management plan
   5) Clinical Trial Master Matrix
   6) Coverage Analysis
   7) Executed sponsored agreement

I. When the Organization utilizes a commercial IRB or the NCI CIRB as the IRB of record, the UNMC IRB Administrator will provide that IRB with the required consent form letterhead, as well as the Organization's consent form language (e.g., compensation in case of injury, HIPAA, contraception, research subject advocate contact information).

J. The UNMC IRB Administrator will provide the external IRB with a copy of any COI management plan which impacts the protocol (e.g., prohibiting the PI from obtaining informed consent) or the disclosure in the informed consent form.

K. The UNMC IRB Administrator will review the completed Coverage Analysis. The external IRB will be notified of any findings of increased financial risk to the subject directly resulting from participation in the research.

L. The contract specialists will provide the UNMC IRB administrator with the subject injury language found in the sponsored agreement. As necessary, the external IRB will be notified of any discrepancies in the subject injury language found in the template consent form.

M. The UNMC IRB Administrator will provide the external IRB with any other additional information which should be considered by the external IRB.

N. Once all Organizational requirements have been met, the UNMC IRB Administrator will provide a letter of acceptance to the UNMC PI granting acceptance of IRB oversight by external IRB.
O. It is the PI's responsibility to complete all requirements for submission to the external IRB.

P. When the Organization accepts external IRB approval for research conducted at an external site, the external IRB must report the following to the UNMC IRB:

1) Any serious or continuing noncompliance.
2) Any FDA 483 or warning letter pertaining to the study or IRB review.

Q. The UNMC IRB will be notified of the acceptance of the external IRB(s) review and approval of the research as a special notification item in the IRB agenda and minutes.

R. The UNMC IRB Administrator must be notified by the PI when the external IRB has approved and released a study. The UNMC IRB administrator will enter the date of approval and release in the IRB database. Acceptance is valid for 5 years. At the end of 5 years, the PI will be contacted for an update on the study.

S. The UNMC IRB Administrator must be notified when a study is completed. The date of completion will be entered into the IRB database and the study will be reclassified as “completed”.

T. Once it has been determined that an external IRB will serve as the IRB of record for any given study, all communications from the PI and other study personnel regarding IRB review of the study or its status must be sent to the external IRB. Since the UNMC IRB will not be the IRB of record, UNMC IRB staff have no authority or information to respond to questions or concerns.

U. All internal adverse events (AEs) and other events which qualify as an unanticipated problem (UP) involving risk to the subject or others must be reported promptly by the PI to the external IRB in accordance with their policies. The external IRB is responsible for review of the UP, any necessary action, and reporting as required to FDA, OHRP, and UNMC. Copies of all reports to the federal government will be provided to the UNMC IRB Administrator.

V. The UNMC ORA will promptly report to the external IRB any allegations of noncompliance which are received by the ORA. The external IRB, in conjunction with the UNMC ORA, will determine how best to handle the allegation in consideration of the need to maintain due process and protect the whistleblower.

W. Incidents of noncompliance (NC) must be reported promptly by the PI to the external IRB in accordance with their policies. The external IRB is responsible for review of the NC, the corrective action plan (in consultation with the UNMC IRB administrator as necessary), and reporting as required to FDA and OHRP. Copies of all reports to the federal government will be provided to the UNMC IRB administrator.

X. Protocol deviations must be promptly reported by the PI to the external IRB in accordance with their policies.

Y. Any complaints from subjects or others must be promptly reported by the PI to the external IRB in accordance with their policies. The external IRB will notify the UNMC IRB Administrator of any serious complaints which impact the rights and welfare of
research subjects and how the complaint was addressed. The Research Subject Advocate Office will assist in the resolution of the complaint as necessary.

Z. If the ORA receives a complaint directly from subjects or others, the ORA will notify the external IRB. The Research Subject Advocate Office will assist in the resolution of the complaint as necessary.

AA. The external IRB will provide the UNMC IRB Administrator with the results of any external audits conducted by FDA, OHRP, sponsors, and CROs.

**Administrative Approval:**

Ernest D. Prentice, PhD.  
Institutional Official and Associate Vice Chancellor for Academic Affairs

Bruce Gordon, M.D.  
IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for research conducted at an international site(s) under the following circumstances:

1.1 The PI is a faculty member, staff, student, or other representative of the Organization, and the research is conducted at the international site by the PI.

1.2 The PI is a faculty member, staff, student, or other representative of the Organization and the research is conducted under the direction of the PI by external investigators unaffiliated with the Organization.

2.0 Policy
2.1 The PI assumes overall responsibility for the safe and proper conduct of the research in full compliance with all applicable U.S. regulations, country specific laws/regulations, local IRB (e.g., IEC, REB, REC) requirements and UNMC HRPP policies.

2.2 When non-exempt research is conducted at an international site by the Organization’s faculty, staff, students, or other representative of the Organization, the following apply:

   A. Review and approval of the research will be required by both the: 1) UNMC IRB, and 2) any local IRB at the international site which has review and oversight jurisdiction over the research. If there is no local IRB, an exception may be granted by the Institutional Official upon recommendation by the IRB Executive Chair.

   B. Protections of human subjects at the international site must be at least equivalent to HHS regulations at 45 CFR 46.

   C. International research involving prisoners is not permitted.

2.3 When exempt research is conducted at an international site, the Organization requires review and approval by the: 1) ORA, and 2) local IRB or official which has review and oversight jurisdiction. The ORA may grant an exception on a case-by-case basis.

2.4 When reviewing research conducted entirely or in part in other countries, the IRB must have the appropriate knowledge concerning the laws, regulations, guidance, and customs in that country either through the expertise of IRB members or by the use of consultants. Note: The will utilize as a resource the latest edition of the “OHRP International Compilation of Human Research Standards” and required information as indicated in Section 3.1(A)(2) below.

2.5 When any collaborative research involves the shipment of human biological materials, hazardous materials, or dangerous goods, the PI must comply with UNMC policy #2002: Shipment of Hazardous Materials or Dangerous Good Policy. For more information contact, the UNMC Biosafety Officer, extension 559-7774 and/or UNMC Chemical and Radiation Safety 559-6356.

2.6 When any collaborative research is subject to US export control regulations, contact the UNMC Chief Compliance Officer at 559-6767.
2.7 It is the expectation of the Organization that the PI will comply with HRPP policy #3.13 which specifies the responsibilities of the PI.

3.0 Procedures

3.1 Non-Exempt International Research

A. In order for the Organization’s faculty, students, staff, or other representatives to conduct non-exempt research at an international site, the following must be submitted:

1) The appropriate IRB application

2) *Addendum T: International Research* which contains:
   a) Identification of the external site(s).
   b) Identification of the local IRB which has review and oversight jurisdiction.
   c) Contact information for the local IRB.
   d) Citation of country-specific laws, regulations and guidelines that govern the research. Include applicable website(s).
   e) Information about local customs, practices, language barriers, literacy issues, and standards of care.
   f) Identification of an independent expert(s) on local customs who can serve as a consultant, if necessary, to the UNMC IRB.
   g) The name and qualifications of any external investigators.
   h) The foreign institution’s FWA number (required for HHS funded research).

3) A copy of the approval letter from the local IRB as required.

4) A copy of the English version of the ICF

5) A copy of the ICF approved by the local IRB

6) An *IRB Reliance Agreement* which specifies the responsibilities of the local IRB which includes, but is not limited to, the following:
   a) Continuing review must be performed no less often than annually.

   b) Appropriate, ongoing post approval monitoring must be conducted at the site.

   c) Reports of complaints, serious or continuing noncompliance, protocol deviations, and unanticipated problems involving risk to the subject or others must be forwarded to the UNMC IRB.

   d) Reports of other serious problems in the conduct of the research must be forwarded to the UNMC IRB.

B. In addition to the requirements for IRB review specified in Section 3.1(B) above the IRB will also consider the following:

1) The qualifications of the PI and research personnel to conduct research in the specified country.
2) The consent process and consent documents are appropriate for the languages of the subjects and communication with the subject population. Arrangements are considered to communicate with the subjects throughout the research.

3) Verification that the PI has in place a process handling:
   a) Modifications to the research. The IRB and investigators should consider as many contingencies as possible when research is reviewed and approved.
   b) Complaints, noncompliance, protocol deviations, and unanticipated problems involving risk to subject or others.
   c) Post-approval monitoring of the research.

4) IRB mechanisms for communicating with the PI and research personnel when they are conducting the research in other countries.

C. The UNMC IRB will review the protocol and any additional pertinent documents in order to ensure that subjects will be adequately protected in accordance with *HRPP policies #2.2 and #2.3*.

D. If a conflict arises between country specific laws/regulations and applicable US regulations, the IRB will consult with international law firms, OHRP, and FDA as necessary.

### 3.2 Exempt International Research

A. In order for the Organization’s faculty, staff, students, staff, and other representatives to conduct exempt research at an international site(s), the following must be submitted to the ORA:

1) The appropriate IRB application
2) *Addendum T: International Research*
3) A copy of the approval letter from the local IRB or authorized official
4) A copy of the approval letter from the local IRB as required.
5) A copy of the English version of the ICF (if required)
6) A copy of the ICF approved by the local IRB (if required)

B. The above mentioned documents will be reviewed by the ORA utilizing exempt review in accordance with *HRPP policy #2.6*.

C. The PI must provide the following additional documents before final approval and release of the research:

1) A copy of the approval letter from the local IRB or authorized official.
2) A copy of the approved, translated ICF with verification of back translation (if applicable).

D. If a conflict arises between country specific laws/regulations and applicable US regulations, the IRB will consult with international law firms and OHRP, as necessary.

### 4.0 PI Responsibilities for Conducting International Research
4.1 To conduct international research, the PI must:

A. Ensure that they and their staff are qualified to conduct research in that country including knowledge of relevant laws, regulations, guidance, and customs.

B. Ensure that the consent process and consent document are appropriate for the languages of the subjects and communication with the subject population. Arrangements are considered to communicate with the subjects throughout the study.

C. Submit a plan to the IRB concerning how modifications to the research will be handled when the PI and research personnel are in the other country. The PI should consider as many contingencies as possible when research is reviewed at initial and continuing review.

D. Have a plan for communication to the IRB of the following: complaints, noncompliance, protocol deviations, and unanticipated problems involving risks to participants.

E. Submit to the IRB an appropriate plan for post-approval monitoring.

F. Obtain all appropriate host country permissions to conduct research (e.g., institutional, governmental or ministerial, IRB or EC, local or tribal).

G. Submit a plan for communicating with the IRB when conducting the research in other countries.

**Administrative Approval:**
Ernest D. Prentice, PhD.  Institutional Official and Associate Vice Chancellor for Academic Affairs
Bruce Gordon, M.D. IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for IRB composition, leadership, member qualifications, and responsibilities.

2.0 Policy
It is the policy of the Organization that the membership of its IRBs will include an appropriately diverse mixture of backgrounds, gender, and race/ethnicity in accordance with HHS regulations at 45 CFR 46.107 and FDA regulations at 21 CFR 56.107.

3.0 Number of IRBs
3.1 There are four duly constituted IRBs that are registered with DHHS OHRP and FDA:
   A. IRB-01 (IRB00000670): Primarily reviews research involving adult subjects
   B. IRB-02 (IRB00000671): Primarily reviews research involving adult subjects
   C. IRB-03 (IRB00002686): Utilized on an as-needed basis for research requiring expeditious IRB review.
   D. IRB-04 (IRB00007222): Primarily reviews research involving pediatric subjects.

4.0 Use of Central IRBs
4.1 The HRPP utilizes the NCI Central IRBs for review and approval of applicable cooperative oncology group protocols involving adult and pediatric subjects (HRPP policy #1.3).

4.2 The HRPP utilizes the selected external independent IRBs for review and approval of designated commercially sponsored clinical trials (HRPP policy #1.3).

4.3 IRB will accept central IRB for other collaborative multisite or NIH sponsored trials on a case by case basis in accordance with HRPP policy 1.3.

5.0 Composition of the IRBs
5.1 Each IRB will have at least five (5) members.

5.2 Each IRB will include members that are sufficiently qualified through experience and expertise, with appropriate ethnic and gender diversity to provide scientifically and ethically valid review of research, and ascertain the acceptability of the proposed research in terms of Organizational commitments and regulations, applicable law, and standards or professional conduct and practice.

5.3 Each IRB will include members representing the cultural and gender diversity of the community to provide guidance on issues pertinent to varying cultures, genders, and sensitivities.

5.4 Every effort will be made to ensure that the IRB does not consist entirely of men or entirely of women. No appointment will be made to the IRB on the basis of gender alone.

5.5 The IRB shall not consist entirely of members of one profession.
5.6 Each IRB will include at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in nonscientific areas. In order to qualify as a non-scientist member the individual must have little or no scientific training or experience.

5.7 Each IRB will include at least one member that is not affiliated with the Institution. This member must be able to adequately represent the community at large and will usually be a non-scientist.

A. The unaffiliated member should be able to represent the general perspective of research subjects. In general, such members will qualify based upon factors such as experience in counseling, patient and family advocacy, experience as a research subject, and experience on local committees, national committees or organizations devoted to various aspects of research, illnesses, or ethnic/cultural related concerns. These members should be particularly cognizant of the need to protect subjects vulnerable to coercion and undue influence.

B. The unaffiliated member must not have any professional relationship with the Institution as an employee, consultant, volunteer faculty, or student, or have a family member (first and second degree relative) who has such a professional relationship with the Institution. Before being appointed it will be determined through an interview that the individual qualifies as an unaffiliated IRB member.

C. An unaffiliated member is expected to attend at least 80% of the scheduled IRB meetings per year.

5.8 Each IRB will include at least one member who can represent the general perspectives of participants in research and is expected to attend at least 80% of the scheduled IRB meetings per year.

5.9 When the IRB reviews community-based participatory research, a consultant will provide education to the IRB and advise the Board on issues pertinent to the community and the nature of the research. The consultant will also assist researchers, as necessary, in the design, implementation of research and dissemination of results.

5.10 A member of the IRB may fill multiple membership position requirements if they qualify.

5.11 The IRBs will include one or more members who are knowledgeable about and experienced in working with the following vulnerable subjects: children, pregnant women, fetuses, neonates, and decisionally impaired individuals.

5.12 The IRB-04 will include a predominance of members who are knowledgeable about and experienced in working with children and neonates.

5.13 If any IRB encounters research involving a vulnerable population with which it has insufficient knowledge or experience, it will use the services of a consultant as described below in Section 5.17.

5.14 In situations where prisoners will be/are involved in research under IRB review: 1) the majority of the Board (exclusive of the prisoner member) will have no association with the prison(s) involved, apart from their membership on the IRB; and 2) the Board will include an ad-hoc prisoner representative with appropriate background and experience
to serve in that capacity. This individual must have a reasonable working knowledge, understanding, and appreciation of the prison conditions in the facility where the research will be conducted and be able to act in the best interests of the prisoners who will participate in the research.

5.15 Qualified IRB Administrators may serve as voting, or alternate voting, members of the IRBs. In order for an IRB Administrator to serve as a member of the IRB, they must have at least five years of experience in IRB Administration or equivalent experience (e.g., clinical coordinator, RN), and preferably be a Certified IRB Professional (CIP).

5.16 Any IRB member with a conflict of interest related to a specific study will be recused from participating in the discussion and vote except to offer information as requested by the IRB. This applies to both full board review and expedited review. A conflict of interest will be determined in accordance with HRPP policy #1.6.

5.17 When review of a proposal requires medical/scientific expertise or specific knowledge about vulnerable subjects that is not available on the Board, the IRB will request assistance from an expert consultant. Consultants will provide guidance/information in accordance with the following procedures:

A. Either before or during review of a protocol, the IRB Executive Chair/designee, assigned IRB reviewer, or the IRB itself may determine there is a need for appointment of an expert consultant, in accordance with the provisions of 45 CFR 46.107(f) and 21 CFR 56.107(f). Depending upon the nature and magnitude of the problem or concern, the IRB may seek more than one consultant.

B. Consultants will be selected from within the Organization, as well as from outside the Organization, based upon the required expertise.

C. Consultants will be officially appointed by the IRB Executive Chair/designee.

D. Consultants must certify in writing that they do not have any conflict of interest as described in HRPP policy #1.6.

E. Consultants will produce written reviews upon request which will be provided to IRB members.

F. Consultants may participate in the IRB’s discussion of the protocol but they may not vote and must be recused before a vote is taken.

5.18 IRB alternate members are appointed according to discipline and membership category. They may represent more than one named IRB member and may attend any IRB meeting. The alternate member’s professional specialty, qualifications, and experience must be comparable to those of the primary member to enable them to adequately fulfill the role of the member to be replaced. However, alternates are not permitted to vote unless the designated regular member is not present. All alternate members have access to IRB review materials regardless of whether or not they attend an IRB meeting.

5.19 The UNMC Chief Compliance Officer will regularly attend IRB meetings as a consultant, but will not vote.
5.20 Any Organizational representatives responsible for business development are prohibited from serving as an IRB member or in carrying out the day-to-day operations of the IRB review process. Organizational leadership may attend IRB meetings as necessary but will not vote.

5.21 When the IRB membership changes, the HHS/FDA IRB registration will be modified by the IRB Administrator responsible for membership documentation within sixty (60) business days.

5.22 A full listing of IRB members will be maintained by the ORA. This list will include for each IRB member:

A. Name

B. Earned degree(s)

C. Representative capacity

D. Scientific/nonscientific status

E. Affiliation status
   1) If the IRB member (or an immediate family member) is affiliated with the Organization.
   2) Any employment or other relationship between an affiliated IRB member and the Organization.

F. Indications of expertise sufficient to describe the IRB member’s chief anticipated contribution to IRB deliberations.

G. When applicable, identify alternate members and the IRB member or class of IRB member for whom the alternate member can substitute.

5.23 IRB members are expected to attend at least 80% of scheduled meetings. IRB member attendance records will be maintained by the ORA in accordance with HRPP policy #1.19.

5.24 The ORA will not release the names of any IRB members except as required by federal regulations or state law. The IRB will, however, provide a list of members by specialty and role.

6.0 IRB Leadership

6.1 IRB Executive Chair
The Organization currently has one IRB Executive Chair who serves as the Chair and voting member of the four UNMC IRBs

A. The IRB Executive Chair is a senior faculty member and preferably is a nationally recognized as an expert in the ethics and regulation of human subject research.

B. The IO will appoint an IRB Executive Chair to serve for renewable 3-5 year terms. Any change in appointment, including reappointment or removal, will require written notification.
C. The IRB Executive Chair reports directly to the IO on all matters pertaining to the IRB and related HRPP issues.

D. The IRB Executive Chair also has a direct line to the UNMC and UNO Chancellors, as well as Executive Leadership for Nebraska Medicine and CHMC on all matters as necessary concerning compliance with HRPP policies and procedures.

E. The IRB Executive Chair conducts the IRB meetings, performs expedited reviews, reviews adverse events, unanticipated problems involving risk to the subject or others, protocol deviations, noncompliance, reviews requests for emergency use of a test article under 21 CFR 56.104(c), provides continuing education of IRB members and investigators, and participates in the development of policies, procedures, IRB forms and checklists.

F. The IRB Executive Chair will consider special requests on behalf of the IRBs for visitors to attend IRB meetings on a case-by-case basis. 
*Note: The visitor will be required to sign the IRB Visitor Confidentiality Agreement a confidentiality statement and may be requested to leave the room during any discussion as necessary. Visitors will not be allowed to vote.*

G. The IRB Executive Chair is the Chair of the IRB Executive Committee, and serves as a member of the IRB Compliance Subcommittee and ad hoc IRB subcommittees.

H. The IRB Executive Chair is a signatory for correspondence in accordance with HRPP policy #1.16.

I. The IRB Executive Chair appoints qualified IRB members to perform expedited review, in accordance with HRPP policy #2.3.

J. The IRB Executive Chair advises the IO, on an on-going basis about performance and competence of the IRB Vice-Chair(s), IRB members and ORA staff.

K. The performance of the IRB Executive Chair will be reviewed in accordance with HRPP Policy #1.19.

L. The IRB Executive Chair must maintain current CITI certification in the Biomedical, Behavioral and Social Science, and Good Clinical Practice track.

M. The IRB Executive Chair must keep current with all updates in federal regulations and guidance, as well as attend regional and national conferences in human research subject protections.

### 6.2 IRB Vice Chairs

A. The IRB Vice-Chair(s) is appointed by the IO, in consultation with the IRB Executive Chair, for a renewable 2-4 year term. The Vice-Chair must:

1) Have at least two years of IRB experience.

2) Be knowledgeable about regulatory and institutional requirements for protection of human subjects.

3) Be committed to serving in a leadership role.
B. The IRB Vice-Chair(s) work closely with the IRB Executive Chair and serve in the absence of the IRB Executive Chair.

C. The IRB Vice-Chair(s) are also involved in the activities involved under Section 6.1E of this policy.

D. The IRB Vice-Chair(s) are members of the IRB Executive Committee, the IRB Compliance Subcommittee, and ad hoc IRB subcommittees.

E. The IRB Vice-Chair(s) must maintain current CITI certification in the Biomedical, Behavioral and Social Science, and Good Clinical Practice track.

F. The IRB Vice-Chair(s) should keep current with all updates in federal regulations and guidance, as well as attend regional and national conferences in human research subject protections.

G. The performance of the Vice-Chair(s) will be reviewed in accordance with HRPP policy #1.19.

6.3 IRB Executive Committee
A. The IRB Executive Committee is comprised of the IRB Executive Chair, the IRB Vice-Chair(s), and the UNMC Chief Compliance Officer.

B. The IRB Executive Committee meets quarterly or more often if needed.

C. IRB Administrators attend the IRB Executive Committee meetings as non-voting members on a rotating basis.

D. The purpose of the IRB Executive Committee is to:
   1) Perform ongoing assessment of the IRBs.
   2) Assist in the development of HRPP policies and procedures.
   3) Assist in the development of IRB forms.
   4) Address concerns of any nature which impact the effectiveness of the HRPP in assuring the protection of the rights and welfare of research subjects.

E. The IRB Executive Committee and the IO in accordance with HRPP policy #1.19 will meet on an annual basis with representatives of the components of the HRPP in order to facilitate the identification and resolution of problems and ensure continued evolution of the HRPP.

F. All four IRBs will be advised of Executive Committee deliberations that impact the HRPP.

7.0 IRB Members
7.1 IRB members will normally be identified and recruited by the IRB Executive Chair and the IRB Vice-Chairs. However, unsolicited nominations may be submitted to the IRB Executive Chair or the ORA at any time.
7.2 The IO will formally appoint all IRB members to a 1-3 year term.

7.3 Each IRB member is expected to be fully engaged in the HRPP and will be involved in carrying out the following responsibilities as assigned:

   A. Participate in all assigned IRB meetings and subcommittees with full voting privileges.
   
   B. Serve as a primary or secondary reviewer for new protocols.
   
   C. Serve as a primary reviewer for applications for continuing review.
   
   D. Serve as an expedited reviewer.
   
   E. Serve as a primary reviewer for internal unanticipated problems involving risk to the subject or others.
   
   F. Serve as a primary reviewer for changes in protocol and/or consent documents.
   
   G. Serve as a primary reviewer for incidents of noncompliance.
   
   H. Serve on IRB ad hoc subcommittees as needed.
   
   I. Serve on the IRB Compliance Subcommittee as needed.
   
   J. Serve on a quality improvement assessment team as needed.
   
   K. Attend an orientation for new IRB members conducted by the IRB Executive Chair/designee and IRB administrators.
   
   L. Participate in continuing education for IRB members.

7.4 The performance of all IRB members will be reviewed in accordance with HRPP policy #1.19.

8.0 IRB Alternate Members

8.1 The appointment and function of IRB alternate members is the same as that for regular IRB members.

   A. The alternate member must qualify in terms of expertise and role in order to serve in place of the regular member.
   
   B. The alternate member may serve as a voting member of the IRB when the regular member is unavailable to attend a convened meeting or perform expedited review.
   
   C. When an alternate member substitutes for a regular member, the alternate member will receive and review the same materials prior to the IRB meeting that the regular member received or would have received.

8.2 The IRB roster identifies the regular members(s) for whom each alternate member may substitute.

8.3 The alternate member will not be counted as a voting member unless the regular member is absent.
8.4 The IRB minutes will document when an alternate member replaces a regular member.

9.0 Attendance Requirements

9.1 IRB members should attend all meetings for which they are scheduled. If an IRB member is unable to attend a scheduled meeting, he/she should inform the designated IRB Administrator.

9.2 If an IRB member is to be absent for an extended period of time the IRB Executive Chair and/or designated IRB Administrator must be notified at least 30 days in advance so an appropriate replacement can be obtained. If the IRB member has a designated alternate, the alternate can serve during the regular member’s absence, provided the IRB Executive Chair and/or designated IRB Administrator have been notified in advance.

10.0 Training/Ongoing Education of IRB Members

10.1 Orientation

A. Prospective new IRB members, including alternate members, will meet with the IRB Executive Chair and designated IRB Administrator for an introductory session.

B. New IRB members will attend a 3 hour orientation covering:
   1) Evolution of research ethics
   2) Overview of HHS and FDA regulations
   3) HRPP overview
   4) Structure of IRB meetings
   5) Responsibilities of IRB members
   6) Overview of the Research Support System (RSS).

C. New IRB members are provided with an electronic link to the following:
   1) IRB meeting schedule
   2) Nuremberg Code
   3) Declaration of Helsinki
   4) Belmont Report
   5) HHS Regulations at 45 CFR 46
   6) FDA Regulations at 21 CFR 50, 56, 312, 812, 814
   7) Categories of Expedited Review
   8) HRPP policies and procedures
   9) UNMC IRB website: http://unmc.edu/irb/research-education/regulatory-sites.html

D. New IRB members are invited to attend an IRB meeting as a guest during the orientation period.

E. New IRB members must complete the CITI training in the Biomedical, Behavioral and Social Science, and Good Clinical Practice track.

F. Full orientation must be completed before the new IRB members may serve as a reviewer or count as a voting member.

G. New IRB members are assigned a mentor who is an experienced IRB member who will answer questions and provide assistance as necessary.

10.2 Continuing Education
A. Continuing education for IRB members is required throughout service on the IRB in order to ensure ethical oversight of human subject research and compliance with current regulatory and policy requirements.

B. IRB members are expected to participate in continuing education which may be obtained through the following mechanisms:
   1) In-service training at IRB meetings.
   2) Training workshops/webinars.
   3) Regional IRB conferences.
   4) Publications/journal articles distributed by the ORA via email.
   5) New information affecting the HRPP distributed by the ORA via email or at IRB meetings. This would include new laws and regulations, new OHRP/FDA guidance documents, new or revised HRPP policies, and emerging ethical and scientific issues.

C. IRB members are also required to complete CITI refresher course in the Biomedical, Behavioral and Social Science, and Good Clinical Practice track every three years as part of the continuing education requirements.

10.3 Training Records
The IRB Education Coordinator is responsible for maintaining all initial and continuing education training records. The Education Coordinator will monitor the status of CITI certification for all IRB members and notify them when it is time for renewal.

11.0 Liability Coverage for IRB Members
The Organization’s insurance coverage applies to employees and any other person authorized to act on behalf of the Organization within the scope of their employment or authorized activity.

12.0 Reporting and Investigation of Allegations of Undue Influence
If the IRB Executive Chair, IRB member, or staff person feels that the IRB has been unduly influenced by any party, they shall make a confidential report to the UNMC Chief Compliance Officer. A thorough investigation and corrective action will be taken to prevent additional occurrences.

**Administrative Approval:**
Ernest D. Prentice, PhD. Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for the identification and management of IRB member, IRB consultant, and IRB staff potential conflicts of interest.

2.0 Policy
It is the policy of the Organization that all potential financial and non-financial conflicts of interest that IRB members, IRB consultants, and IRB staff must be self-identified to the best of the individual’s knowledge and appropriately managed to prevent such conflicts from interfering with the objectivity and validity of the expedited or full board review process. The Organization does not require disclosure of the specifics of the conflict unless an exception is requested.

3.0 Definitions
3.1 Covered Persons: Covered persons are IRB members, IRB consultants, IRB staff and immediate family members of a Covered Person (spouse, dependent children, parents or anyone that a Covered Person may claim as a dependent under the Internal Revenue Code).

3.2 Potential Conflicts of Interest: The following are financial and non-financial conflicts of interest that exclude IRB members, IRB staff, and IRB consultants from participating in the IRB review of protocols, amendments, adverse event reports, unanticipated problems involving risk to the subject or others, noncompliance, complaints, or other problems that are related to the conduct of human subject research. In addition, IRB staff who have any of the conflicts listed below are excluded from serving as the key IRB administrator assigned to process the study in question.

A. The covered person serves as an investigator and is, accordingly, listed on the IRB application or is serving as a scientific/medical advisor to the PI.

B. The covered person is an advisor, or a direct supervisor, of a trainee’s (e.g., medical, graduate or undergraduate student) research.

C. The covered person has a financial interest (in any amount) defined as: 1) salary, royalties (or a commitment for future royalties), consulting fees, honoraria, gift(s), or other payments that has been received in the last twelve months, will be received while the research is being conducted or will be received within twelve months after the research is completed; or 2) an equity interest in the sponsor of the research. Mutual funds are excluded.

D. The covered person holds a position as director, officer, partner, trustee, or any other significant position in the company sponsoring the research or has held such a position in the past twelve months.

E. The covered person holds patent rights or royalties from such rights whose value may be affected by the outcome of the research, including royalties under any royalty-sharing agreements involving the Organization as described in HRPP policy #1.1, Section 3.1.
F. The covered person has a financial interest (as defined above) in a company which has a marketed product, or is in the process of developing a new product which is, or will be, in direct market competition with the product in the protocol under IRB review.

G. The covered person has a personal relationship, or a conflict, with any research personnel listed on the IRB application which would potentially cause the IRB member, in his/her opinion, to be less than objective in their review.

H. If a covered person is listed on the IRB application as a participating physician or other study personnel and will be involved in both obtaining and documenting informed consent as well as providing clinical care, that individual may serve as a primary or secondary IRB reviewer and participate in the discussion. Such IRB member reviewers, however, are required to abstain from voting.

Note: In the following instances the covered person does not have a conflict of interest:

1) The individual serves on the sponsor’s scientific advisory board for an area unrelated to the research under review.

2) The individual serves on an NIH study section or FDA advisory committee, where it has been determined by the NIH/FDA that a conflict does not exist.

3) The individual is listed on the IRB application as a participating physician or other study personnel and the only involvement in the protocol is in the context of providing clinical care to subjects. The individual will not obtain and document informed consent or be included as an author on any publications arising from the research.

4.0 Procedures for identification and management of conflict of interest

4.1 All IRB members must notify the IRB Executive Chair/designee of a potential conflict of interest in advance of the IRB meeting or upon assignment as an expedited reviewer for any action under review (i.e., review of new research, changes, continuing review, adverse events, unanticipated problems involving risk to subjects or others, and noncompliance). If the IRB member is uncertain if a potential conflict of interest exists, they are encouraged to consult with the IRB Executive Chair/designee.

4.2 Whenever a prospective consultant is asked to review a protocol, he/she will be provided with a copy of this policy and will be excluded from serving as a consultant if a conflict exists. Consultants must certify in writing that they do not have a conflict of interest.

4.3 Prior to the beginning of each meeting, IRB members will be asked to declare the existence of any undisclosed conflicts, but are not required to describe the nature of the conflict.

4.4 All IRB staff must immediately notify the IRB Executive Chair/designee if a conflict exists. The IRB Executive Chair/designee will determine what action is necessary.

4.5 When an IRB member has a conflict of interest, he/she must be absent from the meeting room during the discussion and voting phases of the review of the protocol in question. The IRB member may not vote on any protocol where he/she has a conflict of interest as defined above. Upon request of the IRB the member may provide information or respond to questions. The absent member is not counted towards determination of quorum during the vote on the protocol in question.
4.6 If an IRB member has a conflict of interest as defined by Section 3.2 of this policy, but in their opinion, the conflict will not interfere with the objectivity and validity of the review, the member may request approval of an exception to allow them to serve as a reviewer and be granted voting privileges. In such cases, the following procedure must be followed:

A. The IRB member must disclose the specifics of the conflict to the IRB Executive Chair/designee.

B. The IRB member must indicate whether they wish to serve as follows: (1) assignment as a primary or secondary reviewer with or without voting privileges; or (2) no assignment as a primary or secondary reviewer, but with voting privileges.

C. The IRB Executive Committee will review the conflict and determine whether or not the exception will be granted.

D. The full IRB will be notified that an exception has been granted and may request further details. The full IRB has the authority to overturn approval of an exception.

4.7 The IRB meeting minutes will specifically record that COI is the reason any IRB member is out of the room and did not vote.

**Administrative Approval:**
Ernest D. Prentice, PhD.  Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD  IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s policy and procedure for determining the investigational activities requiring IRB approval.

2.0 Policy
2.1 It is the policy of the Organization that UNMC IRB approval is required for research involving human subjects (as defined in Section 3.0 below) which is conducted under the jurisdiction and oversight of the IRB regardless of the funding source.

A. Research performed within the Organization (i.e., on the premises) by research personnel (faculty, students, staff or other representatives of the Organization.)

B. Research performed elsewhere by personnel specified in Section 2.1A above, as a part of their institutional responsibilities. However, with approval of the IO an external IRB may be accepted as the IRB of record in accordance with HRPP policies #1.3 and 1.4.

C. Research performed elsewhere by personnel specified in Section 2.1A above where the personnel are identified as being affiliated with the Organization (for example in research documents, publications, or clinical trial listings). However, with approval of the IO, an external IRB may be accepted as the IRB of record in accordance with HRPP policies #1.3 and 1.4.

2.2 IRB review will be performed in accordance with the authorities granted by institutions within the Organization in accordance with HRPP policy #1.2.

2.3 The IRB does not routinely review activities which do not meet the definition of human subject research, with the exception of research involving human fetal tissue and human embryonic stem cells.

3.0 Definitions
3.1 HHS Regulations
A. Research is defined at 45 CFR 46.102(d) as, “any systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge.” Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes.

A systematic investigation means an activity described in a protocol which includes the following: a set of scientific aims or objectives, procedures to pursue the objectives (e.g., interventions), analysis of the data, and conclusions drawn based upon the analysis. The intent of the activity must be to develop or contribute to generalizable knowledge via publication or presentation of the results of the investigation.

The Belmont Report provides further clarification of “research” as follows: “… the term ‘research’ designates an activity designed to test a hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalizable knowledge (expressed, for example, in theories, principles, and statements of relationships).”
B. **Human Subject** is defined at 45 CFR 46.102(f) as, “a living individual about whom an investigator (whether professional or student) conducting research obtains: 1) Data through intervention or interaction with the individual, or 2) Identifiable private information”

1) **Intervention** means both physical procedures by which data are gathered and manipulations of the subject or the subject’s environment that are performed for research procedures. The intervention was carried out either solely or partially for the purposes of research.

2) **Interaction** means communication or interpersonal contact between the PI and other study personnel with the subject. The interaction was carried out either solely or partially for the purposes of research.

3) **Private information** means information about behavior(s) of the subject that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (e.g., medical record).

4) **Identifiable information** means information that is individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the PI or associated with the information.

C. **Investigator** is not specifically defined by HHS regulations. However, HHS guidance defines “investigator” as the individual performing various tasks related to the conduct of human subject research activities, such as obtaining informed consent from subjects, interacting with subjects, and communicating with the IRB. For the purposes of the HHS regulations, OHRP interprets an “investigator” to be any individual who is involved in conducting human subject research. Such involvement would include:

1) Obtaining information about living individuals by intervening or interacting with them for research purposes.

2) Obtaining identifiable private information about living individuals for research purposes.

3) Obtaining the voluntary informed consent of individuals to be subjects in research.

4) Studying, interpreting, or analyzing identifiable private information or data for research purposes.

Investigators can include physicians, scientists, nurses, administrative staff, teachers, and students about others.

The UNMC IRB broadly defines investigator as an individual who actually conducts human subject research as either a Principal Investigator (PI) or a Secondary Investigator (SI) (see HRPP policy #3.13 for UNMC definitions).

D. **Human subject research.** In order for an activity to constitute “human subject research, all of the following criteria must be met:
1) The primary intent is to conduct a systematic investigation, using an appropriate research design involving human subjects, in order to test a hypothesis.

2) There is an implicit or explicit data analysis plan which will permit scientifically valid conclusions to be drawn.

3) The intent of the activity is to develop or contribute to generalizable knowledge, with the expectation of publication or presentation of the results of the activity.

**E. Engagement in Human Subject Research.** The following is the interpretation (based on OHRP guidance, October 16, 2008) that the UNMC HRPP utilizes when determining whether an institution is engaged in human subject research.

In general, the Organization will be considered engaged in research when its employees (faculty, staff, students) or agents for the purposes of research obtain

1) Data about the human subjects of the research through intervention or interaction with them.

2) Identifiable private information about the human subjects of the research.

3) Informed consent of the human subjects of the research.

**3.2 FDA Regulations**

A. **Human Subject** is defined at 21 CFR 56.012(e) as “...an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy individual or a patient.”

Under FDA’s current regulations governing the conduct of in vitro diagnostic device (IVD) studies, the definition of human subject includes individuals on whose tissue specimens, an IVD is used [21 CFR 812.3(p)]. However, if the specimen is not individually identifiable by the investigator or any other individuals associated with the investigation, including the sponsor, the FDA will exercise enforcement discretion with regard to the requirements for informed consent in accordance with guidance issued April 25, 2006 titled “Guidance on Informed Consent for In Vitro Diagnostic Device Studies using Leftover Human Specimens That Are Not Individually Identifiable.” The UNMC IRB will determine whether subjects can be individually identified and apply 21 CFR 50, 56 accordingly.

B. **Clinical Investigation** is defined at 21 CFR 56.102(c) as, “…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 Food and Drug Administration under Section 505(i) or 520(g) of the Federal Food, Drug, and Cosmetic Act, or need not meet the requirements for prior submission to the Food and Drug Administration under these sections of the Federal Food, Drug, and Cosmetic Act, but the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration 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 for the purposes of FDA regulations.”

Experiments that must “meet the requirements for prior submission to the Food and Drug Administration under Section 505(i) of the Federal Food, Drug, and Cosmetic Act” means any use of a drug other than the use of an approved drug in the course of medical practice [21 CFR 312.3(b)].
Experiments that must “meet the requirements for prior submission to the Food and Drug Administration under Section 520(g) of the Federal, Food, Drug, and Cosmetic Act” means any activity that evaluates the safety or effectiveness of a device [21 CFR 812.2(a)].

Any activity in which results are being submitted to or held for inspection for FDA as part of an application for a research or marketing permit is considered to be FDA-regulated research [21 CFR 50.3(c), 21 CFR 56.102(c)].

C. Test Article is defined at 21 CFR 56.102(l) as, “any drug for human use, biological product for human use, medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the Act or under Sections 351 or 354-360F of the Public Health Service Act.”

1) **Human drugs:** The primary intended use of the product is achieved through chemical action or by being metabolized by the body.

   A *drug* is defined as a substance recognized by an official pharmacopoeia or formulary:
   a) A substance intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease.
   b) A substance (other than food) intended to affect the structure or any function of the body.
   c) A substance intended for use as a component of a medicine but not a device or a component, part or accessory of a device.

   *Note:* See [http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm](http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm) for further information.

2) **Investigational new drug:** An investigational new drug means a new drug or biological drug that is used in a clinical investigation.

3) **Medical devices:** A medical device is “an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is: recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them; 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, and which does not achieve any of 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 any of its primary intended purposes.”

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.

5) **Food additives:** *In its broadest sense, a food additive is any substance added to food.* Legally, the term refers to “any substance the intended use of which
results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of any food.” This definition includes any substance used in the production, processing, treatment, packaging, transportation or storage of food.

6) **Color additives**: A color additive is any dye, pigment or substance which when added or applied to a food, drug, or cosmetic, or to the human body, is capable (alone or through reactions with other substances of imparting color) ([http://www.fda.gov/Food/FoodIngredientsPackaging/ucm094211.htm#foodadd](http://www.fda.gov/Food/FoodIngredientsPackaging/ucm094211.htm#foodadd)).

7) **Foods**: Foods include dietary supplements that bear a nutrient content claim or a health claim.

8) **Infant formulas**: Infant formulas are liquid foods intended for infants which substitute for mother’s milk.

D. **Investigator** is defined 21 CFR 56.102(h) as, “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.”

### 4.0 HRPP Definitions of Research Personnel Classifications

#### 4.1 Principal Investigator (PI):

A. The PI assumes overall responsibility for:

1) Development and submission of the Application to the IRB.

2) Obtainment of legally effective informed consent and assent (as applicable) from prospective subjects by all authorized personnel listed on the Application.

3) Performance of research interventions.

4) Safe conduct of the research in full compliance with the protocol, IRB requirements, HHS regulations, applicable FDA regulations and state law, and 5) the presentation or publication of the data.

B. Only one PI can be named on the IRB application. Co-PIs (e.g., on NIH grants) must be listed as Secondary Investigators.

C. If the PI is a student (e.g., medical, dental, pharmacy, nursing, allied health, undergraduate, graduate), a faculty advisor must be listed and must sign the Principal Investigator’s Assurance. The faculty advisor assumes responsibility for overall supervision of the student’s research and must be listed as a Secondary Investigator.

*Note: PI qualifications and responsibilities are specified in greater detail in HRPP policy #3.13.*

#### 4.2 Secondary Investigator(s) (SI):

A. The SI may also be termed co-investigators and share responsibility with the PI for:

1) Development and submission of the Application to the IRB.

2) Obtainment of legally effective informed consent/assent from prospective subjects.
3) Performance of research interventions.

4) Safe conduct of the research in full compliance with the protocol, IRB requirements, HHS regulations, applicable FDA regulations and state law.

5) Presentation or publication of the data.

B. More than one SI may be named on the IRB application.

4.3 **Participating Personnel:**

A. Participating Personnel are *not* involved in the development and submission of the Application to the IRB.

B. Participating Personnel:
   1) Must have sufficient knowledge about the protocol, HRPP policies, HHS regulations, applicable FDA regulations, and state law to facilitate effective interaction with the subject and safe conduct of the research.
   2) Interact with subjects of the research through performance of research interventions.
   3) May be authorized by the PI to obtain informed consent or assent in accordance with *HRPP policy #5.1*.

4.4 **Lead Coordinator:**

A. The Lead Coordinator is directly involved with working with the PI in the submission of all applications and reports to the IRB.

B. The Lead Coordinator serves as the primary contact point for the ORA. All correspondence from the IRB will be directed to both the PI and Lead Coordinator.

C. The Lead Coordinator may be authorized by the IRB to obtain informed consent/assent in accordance with *HRPP policy #5.1*.

D. Only one Lead Coordinator may be named in a study.

E. A Lead Coordinator is not required for all research. The PI will serve as the single contact when a Lead Coordinator is not identified.

4.5 **Administrative and Data Management Personnel:**

A. Administrative and Data Management Personnel generally handle the data collected during the course of the research.

B. Administrative and Data Management Personnel may be involved in preparation of IRB applications and required paperwork under the direction of the Lead Coordinator and PI.

C. Administrative and Data Management Personnel do not have direct subject contact, but may have access to subject's *identifiable* protected health information (PHI).
5.0 **HRPP Classifications of Human Subject Research**

5.1 **Biomedical Research:** Biomedical Research includes all human subject research performed with intent to develop or contribute to generalizable knowledge (i.e., test a hypothesis and draw conclusions) about human biological systems and processes, including efficacy and safety of preventative, diagnostic or therapeutic methods. Subjects may be suffering from a condition or illness or may be healthy, and may or may not be seeking or expecting a health benefit.

5.2 **Human Biological Material Research:** Human Biological Material (HBM) research utilizes human biological specimens obtained directly from human subjects or from other sources such as a biorepository (tissue bank) for purposes of research. The full range of human biological specimens includes sub-cellular structures (e.g., DNA); cells; tissues (e.g., blood, bone, muscle, connective tissue, teeth, and skin); organs (e.g., liver, bladder, heart, kidney, and placenta); gametes (e.g., sperm and ova); and waste (e.g., hair, nail clippings, urine, feces, saliva, and sweat, which often contains shed skin cells).

5.3 **Medical Records Research:** Medical Records Research utilizes individual medical or clinical records with subject identifiers for both retrospective and prospective studies.

5.4 **Behavioral and Social Science Research:** Behavioral and social science research includes all research performed with intent to develop or contribute to generalizable knowledge (i.e., test a hypothesis and draw conclusions) about behaviors, attitudes and interactions among and between individuals, groups, and cultures. Generally this category of research has no intent of producing a diagnostic, preventive, or therapeutic benefit to the subject who is not seeking nor expecting a health benefit from the research. There may, or may not, be any prospect of direct subject benefit associated with this category of research.

6.0 **Activities Which Are Not Human Subject Research**

6.1 **Systematic investigation involving data or human biological materials (HBM) without investigator access to subject identifiers:** A systematic investigation involving data or HBM obtained from living individuals where there are no identifiers which would allow the investigator to readily identify the individual does not require IRB approval (except as described in example 5 below per this policy). Required de-identification (i.e., the number of identifiers which must be removed) before the data or HBM is given to the investigator depends on whether or not the research is subject to HIPAA.

*Example 1:* The research involves the use of existing clinical outcome data on patients with lymphoma treated at UNMC from 1990-2000. Before the data are given to the investigator by the clinic all eighteen HIPAA identifiers are stripped from the data (i.e., the data is de-identified). This is necessary because the outcome data contains protected health information (PHI) and HIPAA requires de-identification or authorization unless the IRB grants a waiver. This is not considered human subject research under HHS regulations at 45 CFR 46. Note: If, however, the data will be given to the investigator with the identifiers and the investigator then de-identifies the data, it would be considered human subject research classified as exempt and subject to ORA review and approval.

*Example 2:* The research involves the use of existing data on use of the institution’s daycare facilities, cost of care, and consumer satisfaction. The data are given to the investigator by the daycare facility with age of the children, dates of service by year, and
the classification of the employee as faculty, staff or student. This research is not subject to HIPAA. In this case, the demographic information associated with the data would not allow the investigator to readily identify the participants. This is not considered human subject research under HHS regulations at 45 CFR 46.

Example 3: The research involves lymphoma tissue obtained from a cooperative group tissue bank. The tissue is provided to the investigator with diagnostic data but there are no identifiers. This is not human subject research under HHS regulations at 45 CFR 46.

Example 4: The research involves breast cancer tissue obtained from the UNMC Tissue Bank. The tissue is given to the investigator with a code. The tissue bank has access to the linked code and can, therefore, identify the donors. The investigator, however, will not have access to the linked code and cannot identify the donor. An agreement is in place which prohibits release of the key to the investigator. This is not human subject research under HHS regulations at 45 CFR 46.

Example 5: An investigator wants to obtain ten samples of breast cancer tissue immediately after the pathology examination is complete. The tissue is excess HBM. The investigator contacts the surgeon and the pathology department who agree to provide the investigator with the ten samples without any subject identifiers. This is not considered human subject research under HHS regulations at 45 CFR 46. However, there is an ethical obligation for the surgeon providing the tissue to obtain informed consent from these patients. Therefore, this is considered human subject research under this policy.

6.2 Innovative Therapy: Physicians and other health care professionals are free to engage in innovative therapy if the innovative procedure is applied solely to enhance the well-being of their patient and is based upon sound clinical judgment. However, when innovative therapy differs significantly from routine practice it should be viewed and treated as such with appropriate safeguards in place to protect the rights and welfare of the patients through formal IRB review of a promising therapy in the context of a clinical trial. Therefore, in order to validate innovative therapy, the innovative procedure should be subjected early on to IRB review as a formal research protocol.

6.3 Quality Improvement Assessment: Quality improvement projects are not considered research if all of the following criteria are met:

A. The primary intent of the project is to:
   1) Improve the quality of patient care or efficiency of a healthcare operation, or
   2) Improve the quality or efficiency of a non-health care operation.

B. The project design uses established quality improvement methods.

C. The project does not impose any increased physical or psychological risk or burden on patients or other participants.

Note: Publishing or presenting the results of a quality improvement project does not necessarily mean the activity is research. Descriptions of non-research activities (e.g., an account of the quality improvement project) are often an expected outcome of the project. On the other hand, re-analysis of the data derived from the quality improvement project in order to prove or disprove a hypothesis is research. Depending on whether or not subject identifiers are maintained, it may qualify as exempt research.

Example 1: As a matter of policy, the hospital surgery suites introduce a validated surgical checklist which has been shown to reduce surgical errors and actual and “near
miss” adverse events. After some period, the hospital QI team is engaged to assess whether this change had a positive impact on surgical mishaps. This is a quality improvement project (not research), and nothing precludes the presenting or publishing of the results found.

Example 2: A surgical fellow develops a UNMC-based surgical checklist that she thinks might lead to a reduction in surgical mishaps. She recruits several surgeons who agree to use the checklist routinely during their surgeries and the plan is to compare surgical mishaps for the “checklist surgeons” and “non-checklist surgeons” during a 6 month period prior to and following the introduction of the checklist”. This is a systematic investigation to test a hypothesis with a data analysis plan conducted with the intent to develop or contribute to generalizable knowledge and would NOT qualify as a quality improvement project.

Example 3: The UNMC Center for Healthy Living designs a project to assess the quality and usage of their services. Over the next 30 days all users will be asked to complete a survey which rates the quality and frequency of use of services offered by the Center and identification of any services that are desirable, but not currently offered. This is a quality improvement project (not research) and nothing precludes the presenting or publishing of the results found.

6.4 Case Histories: Descriptive case histories which are published and/or presented at national or regional meetings are not considered research if: 1) the case is limited solely to a description of the clinical features and/or outcome of individual patients, and 2) the project does not satisfy all the criteria specified in Section 3.1(a) above.

Note: When a physician or other health care professional authors a case history that is not research, the following ethical guidelines should, nevertheless, be taken into consideration: 1) Informed consent should be obtained from the patient; and 2) Appropriate safeguards to protect confidentiality should be in place.

Note: If a case history involves multiple patients with concomitant analysis and correlation of data as part of a systematic investigation, it is considered research. Depending on whether or not subject identifiers are maintained, it may qualify as exempt research.

6.5 Oral Histories: Oral histories are not considered research when there is a simple recording of information with no attempt to perform a systematic analysis of the data in order to draw conclusions or test a hypothesis for the purpose of developing or contributing to generalizable knowledge. The collection of oral history information, like journalism, is generally considered to be a biography, documentary, or a historical record of the individual’s life and experience or of historical events.

Example: An oral historian conducts biographical interviews with a group of Vietnam veterans. The oral histories are conducted with the intent to provide a basis for a better understanding of the myriad ways in which the Vietnam War has influenced American culture. This project is not human subject research.

Example: A psychiatrist works with an oral historian to gain insight into the impact of the Vietnam War on veteran’s lives. The oral historian conducts biographical interviews and a psychiatrist administers PTSD scales to the participants. Based on the answers and the evaluation of the oral history, the psychiatrist develops generalizations about
how future veterans might respond in similar situations in order to better define treatment protocols for veterans. This project is considered human subject research.

6.6 **Student Projects:** A systematic investigation conducted by a student that involves living individuals, but is performed solely to meet educational requirements of a single academic course is not considered human subject research providing the results of the investigation are presented only within the confines of the classroom or similar forum and to the students, their instructors, parents/family members, or other invited guests. However, it is recommended that the students’ supervisor and/or department exert appropriate review and oversight of the project, including, for example, completion of an IRB application without submission to the IRB.

Note: *If a student conducts a systematic investigation with intent to present the results of the investigation outside of the confines of the institution (e.g., national research conference/forum) this does constitute human subject research.*

Note: *If a student initially conducts a systematic investigation to meet educational requirements with no intent to present the results of the investigation outside of the organization, but then re-analyses the data derived from the project in order to prove or disprove a hypothesis is research. Depending upon whether the subject identifiers are stripped from the data at the time of re-analysis, the project may be exempt.*

7.0 **Determination of When an Activity Constitutes Human Subject Research**

7.1 Individuals should contact the ORA for guidance in determining whether or not a proposed activity constitutes “research”. An IRB Administrator, in consultation with the IRB Executive Chair/designee as necessary, will determine whether or not the planned activities constitute human subject research.

7.2 The IRB Administrators and the IRB Executive Chair/designee will use a) the OHRP Human Subject Decision Charts (September 24, 2004), and b) the criteria in section 3.1(a) and 3.1(b) of this policy.

7.3 If a determination is made that the activity constitutes human subject research, the PI will be advised to submit the appropriate IRB application for review and approval.

7.4 When there is any question concerning whether or not an investigator will be engaged in human subject research, the IRB Administrators and/or the IRB Executive Chair/designee will consult with OHRP.

7.5 If a determination is made that the activity clearly does not constitute human subject research (e.g. use of immortalized cell lines with no subject identifiers), the investigator will be informed. All decisions will be explained fully in order to ensure the Organization’s faculty, staff, and students understand the criteria used in making the determination.

7.6 If an investigator submits an IRB application and it is determined in accordance with the above-described procedure that the activity does not constitute human subject research, the decision will be documented and the PI will be notified of this determination. All correspondence related to this determination will be maintained on file. However, the research will not be entered into the IRB database.
8.0 Type of Review

8.1 The type of IRB review required depends upon the proposal classification:
   
   A. Full Board (FB) research will be reviewed by the IRB in accordance with *HRPP policy #2.2*.

   B. Expedited (EP) studies will be reviewed by the IRB in accordance with *HRPP policy #2.3*.

   C. Exempt (EX) research will be reviewed by the ORA in accordance with *HRPP policy #2.6*.

8.2 The IRB Administrators and/or the IRB Executive Chair/designee will use the *OHRP Human Subject Decision Charts* as necessary in determination of the type of review.

**Administrative Approval:**
Ernest D. Prentice, PhD  Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD  IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for resources that are necessary for human subject protection, care of research participants, and safety during the conduct of research.

2.0 Policy
It is the policy of the Organization that during the conduct of research there must be the resources necessary to protect human subjects, including:

2.1 The PI is qualified to conduct and complete the research.

2.2 There is an adequate number of qualified, licensed and credentialed research personnel and facilities/equipment to complete the research.

2.3 There is adequate time for the PI to conduct and complete the research.

2.4 There is ethical access to the appropriate subject population for the purposes of the research.

2.5 There is adequate availability of medical or psychosocial resources in consideration of the nature of the research (e.g., availability of medical services or counseling, availability of social support services) and other resources necessary to facilitate communication with individuals who do not speak English, or have other impairments (e.g., visual, auditory).

3.0 Procedures
3.1 PI Assurance: The Organization holds the PI responsible for ensuring the necessary resources are in place to protect the rights and welfare of human subjects. The PI is required to sign an assurance that is part of the IRB application.

3.2 Resource Review Certification: The Departmental Chairperson/authorized delegate or appointed review committee of the PI’s school, department or division is responsible for certifying that the necessary resources are available to conduct and complete the study in a manner which fully protects the rights and welfare of research subjects.

3.3 IRB Review of Resources
A. The IRB will review the IRB applications with consideration given to resources necessary to fully protect research subjects based upon the nature of the research, the associated risk, and other factors which dictate resource requirements. If any questions arise concerning resources, the PI will be asked to respond.

B. The PI is required to notify the IRB if the necessary resources are no longer available. The IRB will review the problem and determine what action should be taken. If the necessary resources cannot be obtained and adequate protection of human subjects may be compromised, the PI will be required to close the study.

Administrative Approval:
Ernest D. Prentice, PhD  Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD  IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for scientific, scholarly merit, resource and other adjunct review of all human subject research protocols.

2.0 Policy
It is the policy of the Organization that all human subject research must undergo a substantive scientific, scholarly merit and resource review during the course of the research.

3.0 New Protocols
3.1 The Chairperson, Vice Chair, Section Chief, Director, or the Chair of an appointed review committee in the PI’s school, department, or division is responsible for review of the research proposal prior to submission to the IRB. This review must determine the following:

A. The research has an acceptable level of scientific/scholarly merit.

B. The research has a sound scientific design in consideration of the stated objectives.

C. The PI has the necessary qualifications, experience and credentials to conduct the research.

D. The PI has, or will have, the necessary funding to support the research.

E. There is adequate physical space, laboratory equipment, clerical support, data storage capability, and other resources necessary to complete the research.

F. There is appropriate emergency equipment, personnel, or services necessary to respond promptly to adverse events or unanticipated problems involving risk to the subject or others.

3.2 If the aforementioned reviewer determines that the above criteria (Section 3.1 A-F) have been met, the reviewer signs an attestation (certification) statement in the IRB application that all of the criteria have been met. In addition, the IRB application provides an opportunity for the reviewer to specify any additional comments which may be pertinent to human subjects protection.

3.3 The online IRB application system will not allow submission of a new protocol without this attestation.

3.4 The IRB will also evaluate the scientific and scholarly merit of all proposed studies. All of the IRBs have the appropriate disciplinary expertise for review of the majority of protocols submitted. When the IRB does not have sufficient expertise the Board will utilize a consultant. In judging the scientific and scholarly merit of the protocol, the IRB will utilize the following criteria:

A. The research uses procedures consistent with sound research design.
B. The research design will allow the proposed research questions to be answered with scientific validity.

C. The knowledge to be gained from the research is sufficiently important.

D. The risk/benefit relationship of the research is acceptable.

3.5 The IRB will evaluate the adequacy of available resources to conduct the research and fully protect the rights and welfare of the subjects. In assessing resources the IRB requires the following:

A. The IRB application must include the signed attestation certifying availability of the necessary resources per Section 3.1 above.

B. The investigator must satisfactorily complete the section of the IRB application that describes the resources available to safely conduct the research at each study site.

4.0 Continuing Review

4.1 During the process of Continuing Review, the IRB will evaluate the Continuing Review Application, the initial IRB application, and related documents (e.g., DSMB reports) to determine if the scientific and scholarly merit of the study continues to be acceptable as well as available resources. As indicated above in Section 3.3, the IRB will utilize a consultant when necessary. In judging the scientific and scholarly merit of the protocol, as well as available resources, the IRB will utilize the following criteria:

A. The research uses procedures consistent with sound research design.

B. The research design allows the proposed research questions to be answered with scientific validity.

C. The knowledge to be gained from the research continues to be important.

D. The risk/benefit relationship of the research continues to be acceptable.

E. The necessary resources continue to be available in order to safely carry out and complete the research.

5.0 Request for Change

5.1 During the review of modifications to active research, the IRB will evaluate the modifications to determine if the science and scholarly merit continue to be acceptable. As indicated above in Section 3.3, the IRB will utilize a consultant when necessary. In judging the continuing scientific and scholarly merit of the protocol, the IRB will utilize the following criteria:

A. The modified research continues to use procedures consistent with sound research design.

B. If the research design has been modified, it continues to allow the proposed research questions to be answered with scientific validity.

C. The knowledge to be gained from the research remains sufficiently important.
D. The risk/benefit relationship of the research continues to be acceptable.

6.0 Adjunct Reviews
Depending upon the nature of the research, proposals may be subject to additional review and approval by one or more of the following groups:

6.1 Fred & Pamela Buffett Cancer Center Scientific Review Committee (SRC):
A. The Fred & Pamela Buffett Cancer Center is a National Cancer Institute (NCI) designated cancer center. As such, a mandatory element of the cancer center is a functioning Scientific Review Committee (SRC).

B. The SRC oversees the scientific aspects of all cancer-related research involving human subjects conducted by members of the UNMC faculty and students and members of the Fred & Pamela Buffett Cancer Center.

C. The SRC is responsible for:
1) Evaluating all new and amended clinical research protocols for scientific merit and to ensure that there are adequate resources available to successfully complete the proposed research.

2) Monitoring accrual to active protocols to ensure that studies meet their accrual goals and to require a reassessment of recruitment strategies and/or accrual goals when necessary.

3) Ensuring that there are no competing studies with overlapping eligibility criteria for a specific disease indication.

4) Establishing each protocol's priority based on NCI guidelines and institutional priorities. The SRC is also responsible for the ongoing annual scientific review of cancer center protocols.

D. Changes to NCI National Cooperative Group trials do not require SRC review or approval.

E. A designated IRB Administrator attends every SRC meeting as the IRB representative.

F. SRC review may precede or follow IRB review depending upon the investigator's response to submission deadlines.

G. The ORA will be provided a copy of all SRC review letters. The letters are uploaded to the study file in RSS (https://net.unmc.edu/rss). The SRC is provided a copy of all IRB review letters for inclusion in the appropriate study files.

H. If SRC review precedes IRB review, the assigned IRB reviewers are notified by the designated IRB Administrator of any concerns expressed by the SRC.

I. If SRC review follows IRB review, the designated IRB Administrator will refer the protocol for re-review by the full IRB if the SRC required modifications are more than minor in nature.
J. If the SRC tables a study, IRB review will be held pending resolution of the SRC concerns. A revised protocol must be provided to the IRB for review.

K. The IRB will not issue full approval for any cancer-related study involving human subjects without first receiving written notice of approval from the SRC, stating that all scientific requirements for the study have been met.

L. The SRC may not approve human subject research to commence that has not yet been approved or has been disapproved by the IRB.

6.2 **Pharmacy and Therapeutics Committee (P&T Committee):**

A. The purpose of the P&T Committee review is to ensure safety, accurate dispensing and control of both investigational and marketed drugs used in research conducted at UNMC/Nebraska Medicine. In addition, upon request of the IRB, the P&T Committee will also review research involving the administration of agents such as vitamins or other chemicals not classified as drugs.

*Note: P&T Committee does not cover research involving both investigational and marketed drugs conducted at CHMC. CHMC utilizes the review of a designated pharmacist from the Pharmacy department who sits on IRB-04.*

B. P&T Committee review may precede or follow IRB review depending upon the investigator's response to submission deadlines.

C. The P&T Committee reviews are posted directly into the study file in RSS. The ORA is sent an email from RSS when the review is complete.

D. If the P&T Committee review precedes IRB review, the assigned IRB reviewers are notified by ORA staff of any concerns expressed by the P&T Committee.

E. If the P&T Committee review follows IRB review, the ORA staff will refer the protocol for re-review by the full IRB if the P&T Committee required modifications or concerns are more than minor in nature.

F. The IRB is responsible for assuring all issues identified by the P&T Committee are resolved. The IRB will not issue a full approval for any study involving drugs without resolution of all identified issues.

G. Investigational drugs shall be released for administration only after the P&T Committee has assurances of compliance with all state and federal statutes, and the IRB has formally approved and released the protocol to enrollment.

H. If a Request for Change involves a modification in dosing or route of administration of a study drug, P&T Committee review will be carried out in accordance with Section 6.2A above.

I. The P&T Committee may not approve human subject research to commence that has not yet been approved or has been disapproved by the IRB.

6.3 **TNMC Investigational Device Committee**

A. The Investigational Device Review Committee (IDRC) is an ad hoc review committee comprised of representatives from UNMC and Nebraska Medicine
ancillary department(s) that review the study requirements. The PI must provide the following information:

1) General study overview
2) Specific services requested
3) Cost, if any, to the ancillary department, along with the availability of grant funding to cover those costs
4) Logistical considerations, including inventory of device(s), confirmation of billing account number(s),
5) Services that are considered investigational, impact on workload when adding research patients to conventional care patient workload.

B. The purpose of the IDRC is to assure regulatory and operational compliance in efficient management and security of receiving, storing, dispensing, returning/destroying, and billing of investigational devices in accordance with Nebraska Medicine policy MI29 and Attachments 1-4.

C. A designated IRB Administrator will attend all IDRC meetings as the IRB representative.

D. The IDRC will send ORA the results of the review and final determinations. All letters will be uploaded to RSS in the study file.

6.4 **Clinical Trial Master Matrix and Coverage Analysis**

A. The Clinical Trial Master Matrix (CTMM) is an Excel spreadsheet workbook that records basic information about the clinical trial along with protocol specific scheduling of research related procedures/treatments and details how these procedures/treatments will be billed. The CTMM was designed to function as a “stand alone” document that serves as a resource for authorized personnel who do not have immediate access to the contract, budget, and/or protocol.

B. The Coverage Analysis (CA), using the CTMM, verifies conventional “standard” care vs. research only costs to identify what can or cannot be billed to a third party payer (either private insurance or Medicare).

C. The process also compares the matrix, ICF, and preliminary budget to ensure that all costs are covered, thereby assuring that the study budgets reflect the true cost of research.

D. A CTMM and CA is required of any study that includes clinical care activities conducted at Nebraska Medicine/UNMC/UNMC-Physicians clinics or facilities regardless of the funding source or lack of funding source. Examples may include but are not limited to:

1) Federal, state, foundation, external hospital, or university funding.

2) Investigator initiated research, cooperative group research, or collaborative group research that may or may not have funding provided.

3) Commercially funded clinical research.

4) CCTR Pilot Grant Program.
E. A CTMM and CA is not required for any study that does not include clinical care activities or has no potential to create a bill for technical fees and/or professional fees for Nebraska Medicine/UNMC/UNMC-Physicians clinics or facilities. Examples may include but are not limited to:

1) Retrospective studies that evaluate events that have already occurred including studies that rely exclusively on previously collected administrative records, medical data or other available data.

2) Laboratory analysis studies utilizing residual human tissue samples or human tissue samples obtained from another entity (non-clinical bio-banked materials).

3) Studies conducted at sites other than Nebraska Medicine/UNMC/UNMC-Physicians clinics or facilities.

4) Observational studies.

5) Survey studies.

F. The completed CTTM must be uploaded to RSS at the time of initial submission or at any time there are modifications associated with modifications in the protocol.

G. The IRB will not review a study if the matrix has not been provided.

H. The results of the CA are provided to ORA and will be uploaded into RSS in the study file. The full IRB will be notified if the study poses high financial risk to subjects.

6.5 UNMC Institutional Biosafety Committee (IBC):

A. The purpose of the Institutional Biosafety Committee (IBC) is to review research involving recombinant DNA molecules or human testing of materials containing recombinant DNA (including gene transfer and some vaccine trials.)

B. The IBC is administratively managed through the ORA. An assigned IRB/IBC Administrator attends every IBC meeting.

C. IBC review may precede or follow IRB review depending upon the investigator’s response to submission deadlines. The ORA will be given a copy of the IBC review.

D. If IBC review precedes IRB review, the assigned IRB reviewers are notified by ORA staff of any concerns expressed by the IBC.

E. If IBC review follows IRB review, the ORA staff will refer the protocol for re-review by the full IRB if the IBC required modifications or concerns are more than minor in nature.

F. The IRB will not issue a full approval for any study without first receiving written notice of approval from the IBC.

G. The IBC may not approve human subject research to commence that has not yet been approved or has been disapproved by the IRB.
H. A copy of the IBC review letters will be uploaded to RSS in the appropriate study file.

6.6 **Radioactive Drug Research Committee (RDRC):** The RDRC is currently registered with the FDA as inactive. However, should a human subject protocol involve research with radioactive drugs, the RDRC would be activated and IRB approval contingent upon RDRC approval.

6.7 **Conflict of Interest Committee (COIC):** Refer to [HRPP policy #3.12](#).

6.8 **Sponsored Programs Administration (SPA):** Refer to [HRPP policy #1.11](#).

**Administrative Approval:**
Ernest D. Prentice, PhD.  Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD  IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for HRPP access to legal counsel for the purpose of interpreting federal, state, and local law as needed.

2.0 Policy
It is the policy of the Organization that the HRPP will have ready access to legal counsel in order to ensure the correct interpretation and application of federal, state, and local law. When laws or regulations are issued or amended, the appropriate component of the HRPP will be advised in a timely manner and any necessary actions taken in accordance with effective dates.

3.0 Procedures
3.1 The IRB and ORA have immediate access to legal counsel. Depending upon the issue, consultation will be obtained from one or more of the following individuals:
   A. UNMC Chief Compliance Officer
   B. UNMC Associate General Counsel
   C. UN Senior Associate General Counsel
   D. UN Associate General Counsel
   E. CHMC Director of Compliance

3.2 The UNMC Chief Compliance Officer regularly attends IRB meetings and is, therefore, available to address legal issues which arise during the meeting.

3.3 The IO and the UNMC Chief Compliance Officer are responsible for advising the IRB and other HRPP components of new applicable legislation, as well as changes in interpretation of laws that impact human subject protection.

ADMINISTRATIVE APPROVAL:
Ernest D. Prentice, PhD. Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for application of the human research protection program to sponsored research.

2.0 Policy
It is the policy of the Organization that in sponsored research, both the Sponsor and the Organization have obligations to protect research participants and ensure that the research is conducted in accordance with the Organization’s ethical standards in full compliance with all applicable HRPP policies, federal regulations for protection of human subjects, applicable state regulations, and University of Nebraska Board of Regents By-Laws.

3.0 Definitions
3.1 Sponsor is defined as the company (e.g., pharmaceutical, device or biotechnology), other non-federal agencies, or individual donors providing financial or other support for a research study. The term sponsor also includes agents of sponsors (e.g., contract research organizations).

3.2 Contract is defined as a study agreement executed between the Sponsor and the Organization and signed by authorized representatives of each of the parties.

4.0 Procedures
4.1 All Contracts are received and reviewed by UNeHealth, UNMC Sponsored Programs Administration (SPA) or UNO SPA.

4.2 SPA provides the appropriate excerpts from the Contract in order for ORA to review the detailed study protocol, the IRB application, consent documents and the Contractual language in order to ensure consistency and compliance with the Organization and HRPP policies.

4.3 The Contract between the Sponsor and the Organization must address the following obligations:

A. The Organization will comply with the detailed study protocol, HRPP policies, and all applicable federal regulations.

B. The Sponsor’s responsibility for the payment of medical care for research participants who experience a research related injury is clearly defined as follows: 1) non-exculpatory limitations the sponsor has imposed on the extent of payment for medical care, and 2) the location(s) where medical care can be obtained. This statement of responsibility must be consistent with the compensation in case of injury clause found in the ICF.

Note: The ICF is required to contain standard UNMC IRB approved language which describes the availability of care in case of injury.

C. All non-routine patient care costs which result from procedures performed solely for research purposes must be supported by the study budget and not charged to the subject and/or their third party payors.

D. Indemnification language must not compromise the rights and welfare of research subjects.
E. Contracts cannot include a financial bonus or financial penalty specifically linked to subject recruitment efforts *(HRPP policy #3.6)*

F. Direct personal payments or other form of compensation from the Sponsor to investigators and other study personnel is not permitted.

G. In accordance with requirements of FDA regulations for IND studies [21 CFR 312.32(c), 21 CFR 312.55(b)]; and IDE studies [21 CFR 812.40, 21 CFR 812.46(a)], the Sponsor or their agent of record (e.g., CRO) will promptly (no longer than within 30 days) report to the Organization and/or PI any findings that could affect the safety of subjects, the willingness of subjects to continue participation in the study (e.g., serious adverse events), influence the conduct of the study, noncompliance, or other information important to the IRB's continued approval of the study.

H. The PI must promptly report the above to the IRB in accordance with the requirements of FDA regulations at 21 CFR 56.108(b) and HHS regulations at 45 CFR 46.103(b)(5)(i), and HRPP policies #2.4, 8.2, 8.4, and 8.5.

I. The Sponsor, or their agent of record (e.g., CRO), will provide the Organization with data safety monitoring reports as well as other routine or urgent reports promptly as indicated in the data and safety monitoring plan approved by the IRB.

J. The Sponsor, or their agent of record (e.g., CRO), will report to the Organization and/or PI any results of on-site monitoring conducted by the Sponsor or their agent of record at UNMC or other sites under the jurisdiction of the UNMC IRB. Corrective action shall be initiated in accordance with the requirements of 21 CFR 312.56(b) for IND studies and 21 CFR 812.46(a) for IDE studies.

K. The PI must promptly report the above to the IRB in accordance with the requirements of FDA regulations at 21 CFR 56.108(b) and HHS regulations at 45 CFR 46.103(b)(5)(i), and HRPP policies #6.1 and 6.2.

L. The Sponsor, or their agent of record (e.g., CRO), will have a plan in place to notify the Organization/PI of the results upon completion of the study when the findings may directly affect the safety or medical care of subjects. The PI will, in turn, notify the subjects.

M. There are no requirements which would cause the Organization to violate the HIPAA Privacy Act. When PHI is provided to the Sponsor which could be used to identify specific subjects (e.g., names, telephone numbers, addresses), the Sponsor must:

1) Refrain from using PHI to recruit subjects or advertise additional studies to subjects.

2) Refrain from using the PHI for marketing or market research.

3) Place the same restrictions on any third party to whom the Sponsor discloses PHI.

N. There is no prohibition for retention of a copy of the data generated during the study at UNMC or other study sites under the jurisdiction of the UNMC IRB.
O. There are no restrictions on publication of the results of the research which violate the University of Nebraska, Board of Regents Policy.

P. All commercially sponsored research is assessed a one-time only IRB review fee which will include all subsequent amendments and continuing review.

1) The PI must complete the Charge for IRB Review of Commercially Sponsored Projects (Full Board and Expedited Review) forms.

2) Request for waiver of the IRB review fee must be in writing and may be granted by the IRB Executive Chair.

SPA Contract Specialists and the Clinical Research Financial Compliance Specialist interact with Sponsors, investigators, legal counsel, IRB Executive Chair/designee and the IRB administrators to resolve identified issues and concerns.

If the IRB has already reviewed the project and the Contract requires a major modification of the IRB application and/or ICFs, the IRB will re-review the study.

The IRB will not issue a final release of commercially sponsored research until SPA has a fully executed Contract.

The ORA will be notified by email (irbora@unmc.edu) when the Contract is fully executed.

The ORA will notify SPA when the IRB has issued final approval and release of the research.

When the grant or contract agreement includes human research activities that will be conducted by investigators who are not employees or agents of the Organization, a subcontract is executed between the Organization and the collaborating institution.

The subcontract will include the requirement for the collaborating institution to assure compliance with federal regulations for the protection of human subjects in research and to provide documentation of current and ongoing IRB approval.

The collaborating institution must also ensure that key personnel involved in human subject research are in compliance with the NIH policy on education in the protection of human research subjects and provide documentation of education of key personnel to the Organization.

Administrative Approval:
Ernest D. Prentice, PhD    Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD    IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for compliance with the ethical principles that have their origin in the Declaration of Helsinki as embedded in the requirements of the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) E6 Guidelines.

2.0 Policy
In addition to all applicable HRPP policies, the Organization applies ICH-GCP E6 guidelines to IRB review and the conduct of clinical research when the sponsored agreement specifies adherence to ICH GCP.

3.0 Procedures
3.1 Contract Specialists notify the IRB via IRBORA whether the trial is subject to ICH-GCP Guidelines. The assigned IRB administrator reviews the submission for compliance with ICH-GCP.

3.2 The PI must be qualified by education, training, and experience to assume responsibility for the proper conduct of the trial and should meet all the qualifications specified by the applicable regulatory requirement(s). (ICH-GCP 4.1.1)

3.3 The IRB relies upon the Organization’s credentialing process and the peer review certification. However, when any questions arise concerning qualifications the IRB may request an up-to-date Curriculum Vitae (CV) and additional documentation.

3.4 The PI must be thoroughly familiar with the appropriate use of the investigational products, as described in the protocol, in the current Investigator’s Brochure (IB), in the product information, and in other information sources provided by the sponsor. (ICH-GCP 4.1.2)

3.5 A qualified physician (or dentist, when appropriate), who is an investigator or a sub-investigator for the trial, provides the medical (or dental) care given to, and medical (or dental) decisions made on behalf of, subjects (ICH-GCP 4.3.1)

3.6 The PI provides evidence of such qualifications through an up-to-date CV or other relevant documentation requested by the sponsor, the IRB, or the regulatory authority(ies). (ICH GCP 8.2.10)

3.7 During the assessment of the risks and benefits of the proposed research, the IRB will consider the following:

A. Determine that the available nonclinical and clinical information of an investigational product is adequate to support the proposed clinical trial. For purposes of this requirement, “investigational product” means a pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorization when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved indication, or when used to gain further information about an approved use (ICH-GCP 1.33 and 2.4), and
B. Ensure that clinical trials are scientifically sound and described in a clear, detailed protocol (ICH GCP 2.5).

3.8 The PI, sub-investigators, and research staff will provide all the disclosures and follow the requirements pertaining to consent covered by ICH-GCP. To be valid under ICH-GCP requirements, consent disclosures must provide the following additional elements of information to potential subjects (in addition to the elements described in HRPP policy #5.1):

A. For alternative procedures or treatment that may be available to the subject, include the important potential benefits and risks of alternative procedures or treatments that may be available to the subject. (ICH-GCP 4.8.10(i)).

B. That the monitor, the auditor, the IRB, and the regulatory authority will be granted direct access to the subject’s original medical records for verification of clinical trial procedures or data, without violating the confidentiality of the subject, to the extent permitted by applicable laws and regulations and that, by signing a written consent form, the subject or the subject’s legally authorized representative is authorizing such access. (ICH GCP 4.8.10(n))

3.9 If there substantive additions to the informed consent document or IRB application and/or protocol after IRB approval has been granted, the document(s) must go back to the full Board for review and approval prior to full release of the study.

3.10 When adults are unable to consent, the IRB shall determine:

A. A non-therapeutic clinical trial (i.e., trial in which there is no anticipated direct clinical benefit to the subject) should be conducted in subjects who personally give consent and who sign and date the written consent document (ICH-GCP 4.8.13), except as specified in section 3.10B below.

B. Non-therapeutic clinical trials may be conducted in subjects with consent of a legally authorized representative (LAR) provided the following conditions are fulfilled (ICH-GCP 4.8.14):

1) The objectives of the clinical trial cannot be met by means of a trial in subjects who can give consent personally.

2) The foreseeable risks to the subjects are low.

3) The negative impact on the subject’s well-being is minimized and low.

4) The clinical trial is not prohibited by law.

5) The opinion of the IRBs is expressly sought on the inclusion of such subjects and the written opinion covers this aspect.

6) Such trials, unless an exception is justified, should be conducted inpatients having a disease or condition for which the investigational product is intended. Subjects in these trials should be particularly closely monitored and should be withdrawn if they appear to be unduly distressed.
C. In those situations where there is an exception for the requirements for informed consent for planned emergency research, the subject, or LAR, must be informed about the clinical trial as soon as possible and provide informed consent if the subject wishes to continue in the clinical trial. Note: Currently there is no planned emergency research conducted within the Organization.

3.11 In order to satisfy the ICH-GCP requirements, PIs who conduct research involving human subjects will satisfy the following (in addition to the requirements set forth in HRPP policy #2.5):

A. During and following a subject's participation in a trial, the PI will ensure that adequate medical care is provided to a subject for any adverse events, including clinically significant laboratory values, related to the clinical trial. (ICH-GCP 4.3.2)

B. The PI will inform a subject when medical care is needed for other illnesses of which the investigator becomes aware. (ICH-GCP 4.3.2)

C. The PI will follow the trial's randomization procedures, if any, and ensures that the code is broken only in accordance with the Protocol. If the trial is blinded, the PI will promptly document and explain to the sponsor any premature unblinding. (ICH-GCP 4.7)

D. When appropriate, the PI will inform the subject’s primary physician about the subject’s participation in the clinical trial if the subject has a primary physician and if the subject agrees to the primary physician being informed. (ICH-GCP 4.3.2)

E. Although a subject is not obliged to give his or her reasons for withdrawing prematurely from the clinical trial, the PI will make a reasonable effort to ascertain the reason, while fully respecting the subject’s rights. (ICH-GCP 4.3.4)

F. Where allowed or required, the PI may assign some or all duties for investigational articles accountability at the trial sites to an appropriate pharmacist or another appropriate individual who is under the supervision of the PI. (ICH-GCP 4.6.2)

G. The PI and the investigational pharmacist will, in accordance with hospital policy, maintain records of a drug or biological product delivery to the trial site, the inventory at the site, the use by each subject, and the return to the sponsor or alternative disposition of unused products. These records will include dates, quantities, batch/serial numbers, expiration dates (if applicable), and the unique code numbers assigned to the investigational products and trial subjects. The PI will maintain records that document adequately that the subjects are provided the doses specified by the protocol and reconcile all investigational products received from the sponsor. (ICH-GCP 4.6.3)

H. The PI, or other designated individual, will maintain records of an investigational device, delivery to the trial site, the inventory at the site, the use by each subject, and the return to the sponsor or alternative disposition of unused products. These records will include dates, quantities, serial numbers, expiration dates (if applicable), and the unique code numbers assigned to the investigational device and trial subjects. The PI will maintain records that document adequately that the investigational device has been used as specified by the protocol and reconcile all investigational products received from the sponsor. (ICH-GCP 4.6.3)
POLICY #1.12
REQUIREMENTS FOR COMPLIANCE WITH ICH-GCP GUIDELINES
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I. The PI will permit monitoring and auditing by the sponsor, and inspection by the appropriate regulatory authority. (ICH-GCP 4.1.4)

J. The PI will ensure the accuracy, completeness, legibility, and timeliness of the data reports to the sponsor. (ICH-GCP 4.9.1)

K. The PI will report all serious adverse events (SAEs) or abnormal laboratory findings identified in the protocol as critical to safety evaluations to the sponsor according to the reporting requirements and within the time period specified by the sponsor in the protocol. The PI will follow regulatory requirements related to the reporting of unexpected serious adverse drug reactions to the regulatory authority and the IRB. (ICH-GCP 4.11.1)

L. The PI will report to the sponsor, IRB, and, as applicable, the Organization (ICH GCP 4.10.2):
   1) Any new information that may adversely affect the safety of the subject or the conduct of a clinical trial.
   2) Any changes significantly affecting the conduct of the clinical trial, or increasing risk to subjects.

M. The PI will maintain the clinical trial documents as specified in Essential Documents for the Conduct of a Clinical Trial and as required by the applicable regulatory requirements. (ICH-GCP 4.9.4)

N. Essential documents will be retained until at least two years after the last approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications in an ICH region or at least two years have elapsed since the formal discontinuation of clinical development of the investigational product. (ICH-GCP 4.9.5)

O. If the PI terminates or suspends a clinical trial without prior agreement of the sponsor, the PI informs the Organization, sponsor and the IRB. (ICH-GCP 4.12.1)

P. If the IRB terminates or suspends its approval of the clinical trial, the PI will promptly notify the sponsor. (ICH-GCP 4.12.3)

Q. Upon completion of the trial, the PI will inform the IRB with a summary of the trial's outcome, and the regulatory authority with any reports required. (ICH-GCP 4.13)

R. The PI will maintain a list of appropriately qualified persons to whom the PI has delegated significant trial-related duties. (ICH-GCP 4.1.5)

S. For reports of deaths, the PI will supply the sponsor and the IRB with any additional requested information (e.g., autopsy reports and terminal medical reports). (ICH-GCP 4.11.3)

3.12 When the protocol requires ICH GCP compliance, the IRB Administrator will ensure that the submission includes all necessary information in accordance with this policy.

3.13 When the full IRB reviews research that requires ICH GCP compliance, the IRB will ensure that all requirements are met prior to final approval.
ADMINISTRATIVE APPROVAL:
Ernest D. Prentice, PhD.  Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD  IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to specify the Organization’s requirements for the review, approval, conduct and oversight of human subject research funded by or involving the U.S. Department of Defense (DoD) and the U.S. Department of the Navy (DoN).

2.0 Policy
2.1 It is the policy of the Organization that it will comply fully with all approval requirements of DoD and DoN when its IRBs review, approve and provide oversight of human subjects research funded by or otherwise contractually subject to DoD or DoN regulations and requirements or uses a DoD/DoN property, facility or asset.

2.2 The Organization requires that the research specified in Section 2.1 above will comply with the following DoD/DoN requirements as applicable:
   A. The Belmont Report
   D. Title 21 Code of Federal Regulations 50, 56, 312, and 812, Food and Drug Administration (FDA) Regulations
   E. DoDD 3216.02, “Protection of Human Subjects and Adherence to Ethical Standards in DoD-supported Research”
   F. Title 10 United States Code Section 980 (10 USC 980), “Limitation on Use of Humans as Experimental Subjects”
   G. DoDD 3210.7, “Research Integrity and Misconduct”
   H. DoDD 6200.2, “Use of Investigational New Drugs in Force Health Protection”
   I. Department of the Navy
      1) SECNAVINST 3900.39D of 6 November 2006
      2) SECNAVINST 5720.44B of 1 November 2005
      3) SECNAV M-5210.1 of 1 December 2005
      4) OPNAVINST 5300.8B of 23 April 1997

2.3 Education and Training [DoDD 3216.02, para.4.5]
A. For initial and continuing research ethics education for all personnel who conduct, review, approve, oversee, support, or manage human participant research, there may be specific DoD educational requirements or certification required. All research personnel must complete training in accordance with HRPP policy #3.11. In addition, any other specific training will be determined by the ORA.
B. If during the process of submission or during the course of IRB review it becomes apparent that the investigator does not understand DoD requirements one-on-one training will be provided by ORA staff. The DoD may have specific training requirements in consideration of the complexity and risk of the research.

2.4 Additional protections for pregnant women, prisoners, and children [(Subparts B, C and D) of 45 CFR 46] DoDD 3216.02, para. 4.4.1; SECNAVINST 3900.39D, para 6a(6)]
For purposes of this paragraph, actions authorizing or requiring any action by an official of the Department of Health and Human Services (“DHHS”) shall be under the authority of the Director, Defense Research and Engineering.

A. Subpart B
1) The applicability of Subpart B is limited to research involving pregnant women as subjects in research that is more than minimal risk and included interventions or invasive procedures to the woman or fetus or involving fetuses or neonates as subjects.

2) For the purpose of applying Subpart B, DoD replaces the phrase “biomedical knowledge” with “generalizable knowledge”.

3) Fetal research must comply with US Code Title 42, Chapter 6A, Subchapter 111, part H, 1289g.

B. Subpart C
Research involving prisoners cannot be reviewed by the expedited review procedure.

C. Subpart D
The DoD does not apply Subpart D to active duty personnel under the age of 18 years of age, as it considers all active duty military to be adults with legal capacity to consent to participate in DoD supported research. However, in the state of Nebraska, the age of majority is 19 years. Therefore, the Organization restricts participation in DoD research to 19 years of age or older.

D. Other Vulnerable Subjects
Refer to DoDD 3216.02 for specific requirements.

2.5 Additional Safeguards for Research Conducted with International Populations [DoDD 3216.02 para, 4.9; SECNAVINST 3900.39D, para 6i]
Research involving human subjects who are not U.S. citizens or DoD personnel, conducted outside the United States, and its territories and possessions requires permission of the host country. The laws, customs, and practices of the host country and those required by this policy will be followed. An ethics review by the host country, or local Naval IRB with host country representation, is required.

2.6 Limitation of Waivers and Exceptions from Informed Consent [DoDD 3216.02, para. 4.2; SECNAVINST 3900.39D, para. 6a(3) and 7a(1); 10 U.S.C. 980]
If the research participant meets the definition of "experimental subject," a waiver of informed consent is prohibited unless a waiver is obtained from the Assistant Secretary of Defense for Research and Engineering. Research involving a human being as an experimental subject is an activity, for research purposes, where there is an intervention or interaction with a human being for the primary purpose of obtaining data regarding
the effect of the intervention or interaction. If the research participant does not meet the definition of “experimental subject,” the IRB may waive the requirement to obtain informed consent.

**Note:** The Assistant Secretary of Defense for Research and Engineering may waive the requirements for consent when all of the following are met:

1. The research is necessary to advance the development of a medical product for the Military Services,
2. The research may directly benefit the individual subject,
3. The research is conducted in compliance with all other applicable laws and regulations.

**Note:** An exception from consent in emergency medicine research is prohibited unless a waiver is obtained by the Secretary of Defense.

Waivers of the requirement for informed consent and exceptions from informed consent requirements for emergency research must be approved by the Secretary of the Navy.

**Note:** The IRB cannot waive the requirement for informed consent or grant an exception from informed consent for emergency research unless it has documentation that the Secretary of the Navy has approved it.

### 2.7 Limitations on Compensation for U.S. Military Personnel [Dual Compensation Act and 24 U.S.C. 30]

**A.** The Dual Compensation Act prohibits an individual from receiving pay from more than one position for more than an aggregate of 40 hours of work in one calendar week. This prohibition applies to employees paid from either appropriated or non-appropriated funds, or a combination thereof, and includes temporary, part-time and intermittent appointments. This law is not applicable to enlisted off-duty military personnel in relation to their military duty.

**B.** Federal employees while on duty and non-Federal individuals may be compensated for blood draws for research for up to $50 for each blood draw.

**C.** Non-Federal persons may be compensated for research participation other than blood draws in a reasonable amount as approved by the IRB according to local prevailing rates and the nature of the research.

### 2.8 Provisions for Research with Human Subjects using Investigational Test Articles (Drugs, Device and Biologics) [DoDD 3216.02, para 4.9; DoDD 6200.2; SECNAVINST 3900.39D, para. 6h]

PIs may not be sponsors for INDs and IDEs.

### 2.9 Prohibition of Research with Prisoners of War (POW) and Detainees [DoDD 3216.02, para 4.4.2; SECNAVINST 3900.39D, para. 6a(8)]

Research involving any person captured, detained, held or otherwise under the control of DoD personnel (military and civilian, or contractor employee) is prohibited.

**Note:** The prohibition on research involving a detainee as a human subject does not apply to research involving investigational drugs and devices when the same products would be offered to U.S. Military personnel in the same location for the same condition.

### 2.10 Classified research [SECNAVINST 3900.39D, para 6j]

Classified research must receive prior approval from the Secretary of Defense and be conducted following the requirements of Instruction 3216.02 13. It is not eligible for review under expedited review procedures.
2.11 **Responsibilities**

It is the responsibility of the principal investigator to ensure compliance with all additional Department of Defense (DoD)-Department of the Navy (DoN) requirements for human subject protection. It also is the responsibility of the IRB to ensure that all additional Department of Defense (DoD)-Department of the Navy (DoN) requirements for human subject protection have been met before IRB approval of the research project.

2.12 **Undue Influence [DoDD 3216.02, para.4.4.4]**

For research involving more than minimal risk and also involving military personnel, unit officers and noncommissioned officers (NCOs) shall not influence the decisions of their subordinates to participate or not to participate as research subjects. Unit officers and senior NCOs in the chain of command shall not be present at the time of research subject solicitation and consent during any research recruitment sessions in which members of units under their command are afforded the opportunity to participate as research subjects. When applicable, officers and NCOs so excluded shall be afforded the opportunity to participate as research subjects in a separate recruitment session. During recruitment briefings to a unit where a percentage of the unit is being recruited to participate as a group, an ombudsman not connected in any way with the proposed research or the unit shall be present to monitor that the voluntary nature of individual participants is adequately stressed and that the information provided about the research is adequate and accurate.

3.0 Definitions

3.1 **Research Involving a Human Being as an Experimental Subject** is defined as an activity, for research purposes, where there is an intervention or interaction with a human being for the primary purpose of obtaining data regarding the effect of the intervention or interaction [32 CFR 2.19.102(f)]. Research involving a human being as an experimental subject is a subset of research involving human subjects. This definition does not include activities that are not considered research involving human subjects, activities that meet exemption criteria, and research involving the collection or study of existing data, documents, records, or specimens from living individuals. Examples include, but are not limited to, a physical procedure, a drug, a manipulation of the subject or subject’s environment, the withholding of an intervention that would have been undertaken if not for the research purpose.

3.2 **Minimal Risk:** The definition of the minimal risk based on the phrase “ordinarily encountered in daily life or during the performance of routine physical or physiological examinations or tests” must not be interpreted to include the inherent risks certain categories of human subjects face in their everyday life. For example, the risks imposed in research involving human subjects focused on a special population should not be evaluated against the inherent risks encountered in their work environment (e.g., emergency responder, pilot, soldier in a combat zone) or having a medical condition (e.g., frequent medical tests or constant pain).

3.3 **DoD Components:** The term refers collectively to the organizational entities within the DoD that are subject to the human subjects protections laid out in Department of Defense Directive 3216.02. These entities include the Office of the Secretary of Defense, the Military Departments, the Chairman of the Joint Chiefs of Staff, the Combatant Commands, the Office of the Inspector General of the Department of Defense, the Defense Agencies, the DoD Field Activities, and all other organizational entities within the DoD.
3.4 **Support** of a study generally means the provision of at least a portion of the funding, personnel, facilities, and all other resources. Under this definition, studies that may be wholly funded internally or by a non-DoD component, such as an agency within the Department of Health and Human Services, but focus, for example, on a health concern prevalent in military populations may still fall under DoD purview. Such studies may, for example, require the commitment of DoD personnel as subjects, access to or information about DoD personnel for Recruitment, identifiable data or specimens from living individuals, or the use of other DoD data resources.

3.5 **Research Monitor** refers to an individual designated to oversee a specific protocol that involves more than minimal risk, especially issues of individual subject/patient management and safety. The research monitor functions independently of the research team and shall possess expertise consistent with the nature of risk(s) identified within the research protocol, in order to protect the safety and well-being of human subjects.

3.6 **Detainee** is defined as any person captured, detained, held or otherwise under the control of DoD personnel (military, civilian, or contractor employee). It does not include persons being held primarily for law enforcement purpose, except where the United States is the occupying power.

3.7 **DoD Personnel** includes DoD civilian employees and members of the military services, unit officers, and noncommissioned officers (NCOs).

4.0 **Procedures**

4.1 The IRB will review the application and complete the *Department of Defense Checklist* and ensure compliance with all applicable DoD requirements, DoN requirements, and HRPP policies.

4.2 **Appointment of a Medical (Research) Monitor [DoDD 3216.02, para.4.43]**

A. For research involving more than minimal risk to subjects, an independent medical monitor(s) shall be appointed by name. Monitors shall be physicians, dentists, psychologists, nurses, or other healthcare providers capable of overseeing the progress of research protocols, especially issues of individual subject/patient management and safety. Monitors shall be independent of the investigative team and shall possess sufficient educational and professional experience to serve as the subject/patient advocate. More than one monitor may be appointed.

*Note: An individual(s) serving as an ombudsman or a member of the data safety monitoring board may also be appointed as a monitor.*

B. The IRB must approve the monitor(s) and a written summary of the monitor’s duties, authorities and responsibilities.

C. The IRB Executive Chair/designee will communicate and confirm to the monitor(s) their duties, authorities, and responsibilities.

D. The duties of a research monitor(s) will be determined on the basis of specific risks or concerns about the research. The monitor has the authority to:

1) Discuss the research study with researchers.
2) Observe subject recruitment and enrollment procedures.
3) Oversee study interventions and interactions.
4) Oversee data collection and analysis.
5) Interview human subjects.
6) Stop a research study in progress.
7) Remove subjects from a study.
8) Take any necessary steps to protect the safety and well-being of subjects until the IRB can assess the monitor’s report.
9) Consult with others outside of the research study.

E. The research monitor(s) will promptly report to the IRB any findings or concerns related to human subject protection.

4.3 When recruitment involves US military personnel the following requirements apply:
A. When recruitment involves a percentage of a unit an independent ombudsman is present.
B. Individuals are prohibited from receiving compensation for participating in research during duty hours.

4.4 **Waivers of consent**
A. Waivers of consent are prohibited for classified research.
B. Waivers of consent must meet the requirements of the Common Rule (HRPP policies #5.2 and #5.3) and DoD approval requirements.

4.5 **Navy-Wide Survey Research Requires Additional Review** [SECNAVINST 3900.39D, para 6e; OPNAVINST 5300.8B]
A Privacy Act Statement must be displayed prominently on all Navy personnel surveys without exception regardless of whether personal identifiers are requested. The statement will identify the authority for survey administration (including OPNAV RCS), advise respondents of the purpose and routine uses of the survey, indicate that the survey is voluntary, explain the intended use(s) of the data, and describe measures used to safeguard confidentiality.

*Note: There is the distinct possibility that Navy personnel may be limited in getting compensation as research subjects.*

4.6 **Requirement for Reporting Unanticipated Problems, Adverse Events, and Research Related Injury** [SECNAVINST 3900.39.D, para 8d(2), para., 8e(6), and para. 8g(6)]
The IO will report the following to the DoD and DoN Human Research Protections Officer and appropriate sponsor(s) within thirty (30) days the following:
A. All suspensions or terminations of previously approved DoD and DoN supported research protocols.
B. The initiation and results of investigations of alleged non-compliance with human subject protections.
C. Unanticipated problems involving risks to subjects or others, or serious adverse events in DoD and DoN supported research.
D. All audits, investigations, or inspections of DoD and DoN supported research protocols.
E. All audits, investigations, or inspections of the institution’s HRPP conducted by outside entities (e.g., the FDA or OHRP).
F. Significant communication between institutions conducting research and other federal departments and agencies regarding compliance and oversight.

G. All restrictions, suspensions, or terminations of institutions’ assurances.

4.7 Recordkeeping Requirements [DoDD 3216.02, para. 5.3.2; SECNAVINST 3900.39D, para. 8c(18)]
   A. Recordkeeping requirements for DoD/DoN-supported research with human subjects are longer than the Common Rule’s requirement. DOD may require submitting records to DOD for archiving. The ORA will advise investigators accordingly.
   
   B. Representatives of the DoD/DoN may inspect and copy records at reasonable times and in a reasonable manner.

4.8 Addressing and Reporting Allegations of Non-Compliance with Human Research Protections [DoDD 3216.02, para. 4.10; SECNAVINST 3900.39D, para. 8d(2) and 6k]
   The IO will report the initiation of all investigations and report results regardless of the findings within thirty (30) days to the DoD human protection officer, the Navy Secretary General, and appropriate sponsors.

4.9 Addressing and Reporting Allegations of Research Misconduct [DoDD 3216.02, para. 4.8; DODD 3210.7; SECNAVINST 3900.39D, 8d(2) para. 6l]
   All findings of serious research misconduct under this section shall be reported by the IO to the Director, Defense Research and Engineering.

4.10 Additional Requirements for DoD and DoN Sponsored Research
   A. New research and substantive scientific amendments to approved research shall undergo scientific review and that the review is considered by the IRB in accordance with HRPP policy #1.9.
   
   B. Disclosure regarding the provisions for research-related injury follows the requirements of the DoD/DoN component.
   
   C. Notification to the DoD/DoN Protection Officer of significant changes to the research approved by the IRB, results of IRB continuing review, and any part of the HRPP under investigation for cause involving a DoD/DoN supported research protocol.
   
   D. The DoD/DoN Protection Officer will be notified promptly (no longer than within 30 days) any change of reviewing IRB.
   
   E. Surveys performed on DoD/DoN personnel will be submitted, reviewed, and approved by the DoD/DoN after the research protocol is reviewed and approved by the IRB.
   
   F. When conducting multi-site research, a formal agreement between organizations will specify the roles and responsibilities of each party.

Administrative Approval:
Ernest D. Prentice, PhD.  Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD  IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization's requirements for IRB record keeping.

2.0 Policy
It is the policy of the Organization that the IRB will maintain documentation of all IRB activities in accordance with HHS regulations at 45 CFR 46.115 and FDA regulations at 21 CFR 56.115. IRB records for each protocol will be organized to allow a reconstruction of a complete history of all IRB actions related to the review and approval of the protocol.

3.0 Procedures
3.1 Format of Protocol Files: Protocol files may be either in paper or electronic format. The format is dependent upon the year of initial IRB review, the type of review, and the current status of the study.

A. All research initially reviewed after January 16, 2012 will be in electronic format accessed through RSS (https://net.unmc.edu/rss).

B. All research initially reviewed by the full IRB prior to January 16, 2012 will remain paper files.

C. All research initially reviewed by expedited review AND still actively recruiting subjects after January 16, 2012 are converted to the electronic system at the time of continuing review and the paper files are stored. If the research is closed to further accrual the protocol file will remain a paper file.

3.2 Requirements for maintenance of IRB protocol files: Each IRB protocol file will include in date order, with the most current records at the front of the file:

A. The submitted IRB application which must contain all information necessary for the Board to make all the determinations required by 45 CFR 46.111 and 21 CFR 56.111.

B. Detailed protocol (if required)

C. Investigators Brochure (if required)

D. Federal grant applications (if required)

E. ICF/information sheets (if required)
   Note: HIPAA authorizations are not separate documents. When the research involved the use of PHI, the HIPAA authorization is combined into the ICF.

F. Documentation of scientific and scholarly merit review and approval of proposals by the Fred & Pamela Buffett Cancer Center Scientific Review Committee (SRC) for cancer-related studies.

G. Documentation of review and approval of proposals by the Pharmacy and Therapeutics Committee (P&T Committee) (if required).
H. Documentation of review and approval by the Institutional Biosafety Committee (IBC) (if required).

I. Copies of Clinical Trial Master Matrix and Coverage Analysis findings (if required).

J. Copies of any written reviews from consultants.

K. IRB review letters to the PI will include determinations in accordance with HRPP policy that the research satisfies, as applicable, all requirements of the following:

1) Subparts of 45 CFR 46 (Subparts B, C, and D)
2) 21 CFR 50 (Subpart D)
3) Categories under which research is approved under expedited review
4) Waiver or alteration of informed consent under 45 CFR 46.116(d)
5) Waiver or alteration of HIPAA authorization under 45 CFR 164.512
6) Waiver of documentation of consent under 45 CFR 46.117(c)(1) and (2) and 21 CFR 56.109(c)(1).
7) The category of research approved as exempt in accordance with 45 CFR 46.101(b) and 21 CFR 56.104(d).

Note: The basis upon which the IRB determined that the specific findings required by applicable HHS and FDA regulations were met is found in the specific IRB application that was reviewed.

L. PI responses to IRB review letters and any other IRB correspondence to PIs.

M. IRB approval of recruitment materials and copies of the IRB approval materials.

N. All Requests for Change and the correspondence pertaining to the request. Copies of the modified IRB approved and stamped ICF(s)/information sheets and/or protocols associated with the request.

O. Copies of any new significant information provided to subjects.

P. All Applications for Continuing Review and the correspondence pertaining to the request. Copies of the ICF(s)/information sheets approved in conjunction with continuing review.

Q. All interim progress reports and Data Safety Monitoring Board (DSMB) reports.

R. Internal adverse event/adverse device effect reports.

S. Reports of any non-physical injury to a subject.

T. Reports of unanticipated problems involving risk to the subject or others

U. Significant new findings provided by the investigator or discovered through other means.

V. Single subject protocol deviations and violations.

W. Subject complaints
X. Incidents of noncompliance, including documentation of investigation, correspondence, and reports to institutional officials, OHRP, and FDA where appropriate.

Y. Results from Quality Assessment reviews and correspondence regarding the findings.

3.3 Long-Term Record Storage

A. Paper copies of the IRB protocol records are maintained in the Office of Regulatory Affairs (ORA) until the protocol is completed or terminated.

1) **CD-ROM**: Prior to 2012, completed and terminated protocol files were sent to Digital Information Management for conversion to CD-ROM. The CD-ROM discs are stored indefinitely for future reference or inspection by HHS, FDA or other sponsor representatives during auditing visits.

2) **Hard Copy Storage**: As of 2012, long term storage was transferred to hard copy storage. Once a year (or more often as necessary) completed and terminated protocol files are sent for storage off campus. The protocol records are stored indefinitely for future reference or inspection by HHS, FDA or other sponsor representatives during auditing visits.

B. All protocol submitted electronically through RSS (after 2012) are maintained indefinitely in RSS for future reference or inspection by HHS, FDA, or other sponsor representatives during auditing visits.

*Note: All protocols that are cancelled without participant enrollment are also maintained indefinitely.*

3.4 UNMC Research Administration Database:

A. The UNMC IRB maintains a password protected database with full access by all members of the ORA. The database includes the characteristics of the research including the classification of the research, the study population, the designated risk level, type of review, funding source, and all other information necessary to allow the IRB staff to track and monitor the status of protocols, (e.g., IRB approval periods), and perform database searches in order to produce reports.

B. The database is available in “view” mode to selected groups outside of the ORA, including Sponsored Programs Administration; Protocol Review and Monitoring System (PRMS) Office of the Fred & Pamela Buffett Cancer Center specifically in response to the needs of the SRC; the adult Hematology/Oncology regulatory personnel, and the P&T Committee regulatory personnel.

3.5 **IRB Agendas, Meeting Minutes, and Membership Rosters**: Copies of all IRB minutes and current IRB membership rosters are maintained electronically within the ORA.

3.6 **IRB Educational Items**: Copies of all educational items given to the IRB members and Office of Regulatory Staff are maintained in the ORA.

3.7 **HRPP Policies and Procedures**: Copies of HRPP policies and procedures as required by 45 CFR 46.115(a)(6) and 21 CFR 56.115(a)(6) are maintained on the IRB website and in hardcopy.
3.8 **Availability of IRB records**: All IRB records are accessible for inspection and copying at reasonable times and in a reasonable manner in accordance with 45 CFR 46.115(b) and 21 CFR 56.115(b).

**Administrative Approval:**
Ernest D. Prentice, PhD.  Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD   IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for the review and approval of HRPP policies and procedures.

2.0 Policy
It is the policy of the Organization to continually assess the adequacy of existent policies and procedures in consideration of new information and Organizational requirements that may affect the HRPP, including federal, state, and local laws, regulations, and guidance, with additional focus on emerging ethical and scientific issues.

2.1 Review of HRPP Policies and Procedures
A. The IRB Administrators, IRB Executive Chair, and IO will review, at least annually, all HRPP policies and procedures. However, anytime a policy requires revision due to new federal guidance, changes in Organizational requirements, or identification of deficiencies the policy will be revised accordingly.

B. New and revised (draft) HRPP policies and procedures which do not significantly impact the Organization will be provided to the IRB for their information, but do not require formal approval.

C. Draft HRPP policies and procedures which significantly impact the IRB review system, investigators, and the Organization will be reviewed and approved by the full IRB, the IO, and in select cases, other Organizational officials.

2.2 Full IRB Review of Draft HRPP Policies and Procedures
A. All draft HRPP policies and procedures requiring review by the full IRB will be discussed at all three regularly scheduled IRB meetings.

B. IRB members will be given a copy of the draft policy approximately one week in advance of the scheduled IRB meeting.

C. All IRB members have the right to cast their vote (for, against, abstain) either in person at the IRB meeting or via e-mail. IRB members may provide written statements in support of their vote or ask other IRB members to express their opinions at the meeting.

D. In instances where approval of a policy is necessary before the next regularly scheduled meeting, voting procedure by e-mail alone will be allowed for consideration of a policy.

E. In order for a policy to be approved or disapproved, two-thirds of the entire IRB membership must cast a vote, either in person or by e-mail, for the motion to carry.

F. If the motion to approve a policy fails to pass, the draft policy may be referred to the IRB Executive Chair or an IRB subcommittee for further discussion and revision before re-consideration.
2.3 Organizational Notification of Changes to HRPP Policies and Procedures

A. Changes to HRPP policies and procedures will be communicated to the Organization’s research community through a memorandum and/or notification on the IRB website at http://unmc.edu/irb.

B. All IRB staff will be officially notified at the next staff meeting.

C. All new and/or revised HRPP policies and procedures will be available on the IRB website at http://unmc.edu/irb and RSS at https://net.unmc.edu/rss.

ADMINISTRATIVE APPROVAL:
Ernest D. Prentice, PhD. Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe Organization’s requirements for granting signature authority to the IRB Executive Chair, IRB Vice-Chairs, and ORA staff.

2.0 Policy
It is the Organization’s policy that the IRB Executive Chair, the IRB Vice-Chairs and qualified IRB staff will have appropriate signature authority on behalf of the IRB in order to: 1) facilitate the processing of items requiring IRB review, 2) improve the IRB services for investigators, and 3) increase the overall administrative efficiency of the IRB.

3.0 Procedures
The following individuals have signature authority as indicated below:

A. IRB Executive Chair: The IRB Executive Chair has the authority to sign: 1) HRPP policies in conjunction with the IO, 2) IRB authorization agreements on behalf of the IO, 3) IRB review letters, 4) IRB approval letters, and 5) all other IRB correspondence as necessary.

B. IRB Vice-Chairs: The IRB Vice-Chairs have the authority to sign: 1) IRB review letters, 2) IRB approval letters, and 3) all other IRB correspondence as necessary.

C. IRB Expedited Reviewers: IRB Expedited Reviewers have the authority to sign: 1) IRB expedited review letters, and 2) other related IRB correspondence as necessary.

D. IRB Administrators: The IRB Administrators have the authority to sign: 1) IRB review letters, 2) IRB approval letters, and 2) other IRB correspondence as necessary. In exercising this authority, the IRB Administrators will consult the IRB Executive Chair/Vice-Chairs or other IRB members as necessary and may refer IRB review letters or other correspondence to the IRB Executive Chair/Vice-Chairs for signature.

E. Office Assistant: The Office Assistant has the authority to sign routine ORA correspondence. This individual does not have the authority to sign correspondence on behalf of the IRB (such as IRB review letters).

ADMINISTRATIVE APPROVAL:
Ernest D. Prentice, PhD.  Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD  IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s involvement of the community in the research process, as well as the community outreach activities in order to enhance the public’s understanding of research, obtain feedback about any community concerns and respond to questions from prospective subjects about specific research protocols available within the Organization.

2.0 Policy
2.1 It is the policy of the Organization, in accordance with its mission statement, that research be conducted which will advance knowledge for the benefit of the local community, the State of Nebraska, the United States and countries abroad from which patients come for treatment and students come to enhance their education.

2.2 The Organization is committed to involving the communities the Organization serves, as well as the members of those communities in the research process, including the design and implementation of studies, analysis of data and the dissemination of results.

2.3 The Organization is committed to designing and initiating outreach activities to enhance the understanding of research by both the communities the Organization serves, as well as the members of those communities.

3.0 Procedures
3.1 Involvement in Research Design, Implementation and Analysis of Research Results
   A. The Organization supports mechanisms that promote the involvement of members of communities the Organization serves, in the research process, including the design and implementation of research, when appropriate, and analysis of results.

   B. The Organization utilizes a variety of different outreach activities to educate the community about science, ongoing research, research needs and involvement of the community in opportunities to advise on the design and implementation of research.

3.2 Outreach Activities for Education of the Community
   The Organization utilizes the following outreach activities for educational purposes, as well as the dissemination of research results:

   A. Omaha Science Café: http://www.unmc.edu/sciencecafe/
The science cafes involve a face-to-face conversation between the public and scientists within the Organization about current science topics. The science cafes are held approximately six times per year at casual meeting places within the local community and out-state Nebraska. Each meeting begins with a brief didactic presentation, followed by a question and answer period. The science cafes are available via Podcast.

   B. Nebraska Science Festival: http://www.nescifest.com/
The Nebraska Science Festival is an initiative of UNMC, which continues to administer the festival with the assistance of a number of organizations and individuals interested in the advancement of science literacy. The Science Festival is designed to make science accessible, interactive, relevant and fun for kids and adults alike.
C. **Talks and seminars in community settings**
Faculty and administrators from the Organization give educational talks and seminars about research in local community settings (e.g. Rotary Club) and in out-state Nebraska. Results from completed research may also be presented in community forums.

D. **Newspaper articles about research projects**
Local Nebraska newspapers feature articles about research projects, which help educate and inform the community about general research topics, specific upcoming or active projects, as well as the results from completed research studies.

E. **Social Media**
1) University of Nebraska Medical Center: [http://www.facebook.com/unmcedu](http://www.facebook.com/unmcedu)
3) Children’s Hospital & Medical Center: [https://www.facebook.com/ChildrensOmaha/](https://www.facebook.com/ChildrensOmaha/)
5) University of Nebraska Omaha: [http://www.facebook.com/unomaha](http://www.facebook.com/unomaha)

F. **Websites**
The following websites within the Organization are available to the public and contain information about the Organization, including material pertinent to research.
1) University of Nebraska Medical Center:
   a) [http://www.unmc.edu/cctr/for-public/index.html](http://www.unmc.edu/cctr/for-public/index.html)
   b) [http://www.unmc.edu/cctr/community/cer/index.html](http://www.unmc.edu/cctr/community/cer/index.html)
   c) [https://www.unmc.edu/newsfeed/?f=community](https://www.unmc.edu/newsfeed/?f=community)
2) Nebraska Medicine: [www.nebraskamed.com](http://www.nebraskamed.com)
3) Children’s Hospital & Medical Center: [http://childrensomaha.org/body](http://childrensomaha.org/body)
4) Bellevue Medical Center: [http://www.bellevuemed.com/](http://www.bellevuemed.com/)
5) University of Nebraska Omaha: [http://www.unomaha.edu/spr](http://www.unomaha.edu/spr)

3.3 **UNMC/TNMC utilizes the following educational outreach activities:**
A. **IRB Brochure:**
   A brochure titled “Participating in Clinical Trials” is distributed. The brochure gives a basic description of clinical trials and human subject rights. The brochure also directs the reader to the IRB website ([http://www.unmc.edu/irb](http://www.unmc.edu/irb)), which contains information about human subject research and links to relevant websites.

B. **UNMC Clinical Trials Database:** [http://net.unmc.edu/ctsearch/index_unmc.php](http://net.unmc.edu/ctsearch/index_unmc.php)
The UNMC Center for Clinical and Translational Research maintains a clinical trial database where the public can find information about available clinical trials by medical area.

C. **Research Subject Advocate Office:** [http://unmc.edu/vcr/policies/regulation/rsao.html](http://unmc.edu/vcr/policies/regulation/rsao.html)
The Research Subject Advocate (RSA) Office was created in part to provide community education about processes in place to safeguard research subject safety within clinical and translational research trials and programs. The RSA Office gives presentations to community groups interested in learning more about research or who have concerns or questions about research subject safety. The RSA Office maintains a record of all RSA community outreach activities.
D. "The Week": The Marketing Department for the Nebraska Medical Center publishes “The Week” on a weekly basis which is available to the public by distribution in hard copy in public areas.

E. “Ask UNMC” on KETV Channel 7

F. “UNMC Discover”: The Department of Public Affairs publishes semi-annually “UNMC Discover”, focusing on research at UNMC, which is available to the public either by cumulative mailing lists or by distribution to public libraries throughout the state of Nebraska.

G. “UNMC Connect”: The Department of Public Affairs publishes semi-annually “UNMC Connect”, which is available to the UNMC campus and UNMC alumni either by cumulative mailing lists or by distribution.

H. Community outreach groups: The Organization has a number of outreach groups which provide the public with the opportunity to convey special needs of the community in terms of medical care and other services, which can translate into research.

3.4 CH&MC utilizes the following educational outreach activities:
A. IRB Brochure: A brochure titled “Participating in Clinical Trials” is provided to CH&MC for distribution. The brochure gives a basic description of clinical trials and human subject rights. The brochure also directs the reader to the IRB website (http://www.unmc.edu/irb), which contains information about human subject research and links to relevant websites.

B. “The Hero”: The Marketing Department at CH&MC publishes “The Hero” on a weekly basis, which is available to the employees of CH&MC and the public in hard copy via distribution to public areas.

C. “Just Kids”: The Marketing Department at CH&MC mails “Just KIDS” on a quarterly basis to targeted zip codes in the Omaha metropolitan area.

3.5 Evaluation of Outreach Activities
The IRB Education Coordinator, in conjunction with the IO, the Executive Chair of the IRB, the RSA and UNMC Public Affairs, performs an ongoing evaluation of community outreach activities in order to identify the needs of the community and any concerns.

ADMINISTRATIVE APPROVAL:
Ernest D. Prentice, PhD.  Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD  IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for the Quality Improvement Assessment (QIA) Program for the conduct of research.

2.0 Policy
It is the policy of the Organization that a QIA Program will be conducted on an on-going basis in order to measure, maintain, and improve human subject research protection effectiveness, quality and compliance with all applicable regulations and HRPP policies. The QIA Program focuses on the education of investigators, staff, and students about ethical and regulatory responsibilities in the conduct of human subject research, as well as the identification and correction of problems and deficiencies.

3.0 QIA Program Objectives
3.1 Determine if the PI and other study personnel adhere to the research protocol as approved by the IRB.

3.2 Determine if the PI has filed all required reports to the IRB.

3.3 Determine if the process of informed consent and the informed consent document(s) meet all federal, state, and local requirements, as well as HRPP policies.

3.4 Identify the educational and training needs of the research community and determine the best methods for meeting those needs through:
   A. Individualized training to meet the specialized needs of specific PIs and their research personnel.
   B. General education programs designed for the research community at the Organization.

3.5 Assess the completeness and accuracy of IRB files which are linked to studies selected for a QIA.

4.0 Procedures
4.1 Study Selection Criteria
   A. Not For Cause QIA of Non-Exempt Research
      1) Categories of non-exempt research that will be considered for QIA will be randomly selected, in order of priority listed below:
         a) Investigator-initiated research
         b) Significant risk research
         c) Research involving vulnerable populations (e.g., pregnant women, children, decisionally-impaired, and prisoner)
         d) Greater than minimal risk research
         e) Research conducted under emergency waiver of informed consent (FDA regulations at 21 CFR 50.24)
         f) Minimal risk research
      2) Selected research must be currently IRB-approved and normally have been actively accruing subjects for at least one (1) year.
3) Research undergoing a not-for-cause QIA will generally be performed by a designated IRB Administrator. Other IRB representatives may be included as necessary. At least one or more non-exempt studies will be selected for audit per month.

B. **Not For Cause QIA of Exempt Research**
   1) Categories of exempt research that will be considered for QIA will be randomly selected.
   2) Selected research must have been approved by the ORA within the last year and ongoing.
   3) Research undergoing a not-for-cause QIA will generally be performed by a designated IRB Administrator. Every quarter at least one or more exempt studies approved during that quarter will be randomly selected for audit.

C. **For-Cause QIA**
   1) A for-cause audit will generally be scheduled based upon recommendation by the IO, IRB Executive Chair, or the IRB. The following criteria will determine when a for-cause audit is necessary:
      a) Issues related to noncompliance.
      b) Problems with continuing review, informed consent, or other IRB review.
      c) Monitoring reports issued by outside agencies (pharmaceutical sponsors, FDA, OHRP or others) that revealed problems areas.
      d) Other non-specified issues.
   2) These QIA visits will normally be completed by the designated IRB Administrator. Other IRB representatives may included as necessary.

4.2 QIA Process
A. The QIA visit will be scheduled at a time mutually acceptable to the PI and the designated IRB Administrator. Unannounced visits will **not** occur.

B. Prior to the QIA visit, the PI will be informed, in writing, that a QIA visit has been scheduled, including the date, time, place, and protocol(s) selected for review. The PI will also be provided a description of the audit process and criteria, as well as a copy of the *Checklist for Quality Improvement Assessment of On-Going Research* to be completed by the designated IRB Administrator during the visit.

C. The PI will be asked to complete the *Investigator Assessment Checklist for Regulatory Documentation* and submit it to the ORA prior to conduct of the QIA visit. However, all PIs are encouraged to complete this checklist on a regular basis as a mechanism for an internal audit of their records. This form is available on the IRB website. PIs are reminded of the availability of this assessment document at the time of continuing review notification.

D. Once a research protocol has been chosen for QIA, the designated IRB Administrator will carefully review, in advance, the entire IRB file utilizing the *IRB File Review Form*.

E. After completion of the pre-review of IRB records, the designated IRB Administrator will carefully review the PI’s study records utilizing the *Checklist for Quality Improvement Assessment of On-Going Research*. 
F. If the assessment visit will include observation of the process of informed consent or interviews with subjects, the PI will be asked to arrange this in advance with one or more subjects.

G. All subjects who have agreed must give written informed consent in advance by signing the Consent for IRB Observation of the Informed Consent Process.

H. The designated IRB Representative, or other designated individual, will utilize the IRB Observation of Consent Process Form to evaluate the process of consent.

I. Upon conclusion of the QIA, the designated IRB Administrator will schedule an exit interview with the PI and other study personnel. The purpose of this exit interview will be to present preliminary findings, obtain additional clarifications and/or corrections, and provide education concerning IRB requirements as needed.

J. After the QIA is complete and all findings are analyzed and determined to be valid, a written report will be developed by the designated IRB Administrator.

K. The PI will be given a copy of the written report and asked to develop a corrective action plan if needed.

L. All reports, including the written report developed by the designated IRB Administrator and PI’s response and any requested corrective action plan, will be reviewed by the Institutional Official (IO) in consultation with the IRB Executive Chair. Reports which indicate serious noncompliance or other concerns will be referred to the IRB for review in accordance with HRPP policy #8.5. If the assessment indicates there are few or no deficiencies, and/or the use of “best practices” was observed, this will be communicated to both the PI and the IRB.

M. The QIA Program will include appropriate follow-up to ensure that deficiencies are corrected in a timely manner. This follow-up may include only a written report of corrective action(s) implemented by the PI, or it may require additional monitoring by the IRB. In some cases, the PI and/or other study personnel may be required to undergo specific training in order to assist in achieving the desired level of compliance.

**ADMINISTRATIVE APPROVAL:**
Ernest D. Prentice, PhD. Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for assessment of the quality, effectiveness, efficiency and support of the Organization’s HRPP in carrying out its mission to ensure protection of human subjects and compliance with all applicable federal, state and organizational requirements.

2.0 Policy
It is the policy of the Organization that there will be an ongoing assessment of the HRPP, as well as a comprehensive annual HRPP assessment. These assessments are designed to ensure: 1) that the HRPP is fully capable of protecting the rights and welfare of research subjects; and 2) the HRPP will continue to evolve and improve in its effectiveness and efficiency.

3.0 Procedures
3.1 On-going Assessment of the HRPP
A. HRPP policies and procedures will be assessed on an ongoing basis by the IO, IRB Executive Chair and IRB staff.

B. When senior administrators (e.g., Vice Chancellor for Research) identify a problem or a needed improvement, this will be brought to the attention of the IO and IRB Executive Chair for appropriate action.

C. The IO, IRB Executive Chair, and IRB staff will continually monitor the efficiency of the IRB review process, identify problems and seek timely resolutions.

D. Metric data on IRB efficiency will be discussed on an ongoing basis in the ORA as well as at IRB staff meetings. These data will be provided to the IO, IRB Executive Committee and other Organizational administrators as requested.

E. One set of IRB minutes for IRB-01, IRB-02, and IRB-04 will be randomly selected for audit quarterly. IRB minutes for IRB-03 (Rapid Response IRB) will be monitored no less often than annually if the IRB has met during the year. The IRB will utilize HRPP policy #2.2 and OHRP Draft Guidance titled “Minutes of Institutional Review Board (IRB) Meetings: Guidance for Institutions and IRBs” (dated November, 2015)

F. PIs and other study personnel are provided an on-going opportunity to assess the effectiveness of the HRPP, including policies, quality of IRB review, efficiency of IRB review, IRB staff support and other components of the HRPP through communication with the IRB Executive Chair, IO, IRB staff, senior administration and through various IRB educational activities.

1) The IRB staff participate in round table discussions at the department level, conduct training within departments and also one-on-one sessions.

2) PIs and other study personnel may utilize the Investigator Assessment of the IRB form, available on the IRB’s website at http://www.unmc.edu/irb. This form may be submitted anonymously or with contact information.

3) PIs and other study personnel may utilize the “Report a Problem or Complaint” tab on the UNMC IRB website that provides access to “Solv-Anon,” a commercial site providing anonymous comments to the IRB.
G. All information gathered during the HRPP assessment will be utilized to identify areas of concern as well as identify areas for growth and development.

3.2 Evaluation of the IRB Executive Chair
A. The IO will evaluate the performance of the IRB Executive Chair on an annual basis utilizing a discussion format. The focus of the discussion will be on IRB leadership, accomplishments during the past year and goals for the future.

B. The IO will obtain feedback submitted from the IRB Members and IRB administrators on the IRB Annual Assessment Form (available at https://www.surveymonkey.com/r/UNMCIRBANNUAL) prior to this evaluation.

C. If the IRB Executive Chair’s performance is judged to be deficient, the IO will discuss his or her concerns with the Executive Chair and seek a satisfactory resolution. If the IRB Executive Chair’s performance continues to be deficient, the IO may remove the individual as the Executive Chair, in consultation with the Vice Chancellor for Research, the Vice Chancellor for Academic Affairs, and the Department Head/Section Chief to whom the IRB Executive Chair reports.

3.3 Evaluation of the Vice-Chairs
A. The IRB Executive Chair will review the performance of the IRB Vice-Chairs on an annual basis utilizing the following criteria:
   1) Attendance at meetings
   2) Chairing IRB meetings
   3) Completeness of reviews
   4) Service on IRB subcommittees
   6) Creative recommendations which help improve the HRPP.

B. If an IRB Vice-Chair’s performance is judged to be deficient, the IRB Executive Chair will discuss his/her concerns with the Vice-Chair and seek a satisfactory resolution. Upon recommendation of the IRB Executive Chair, the IO at his/her discretion may remove the individual as an IRB Vice-Chair.

3.4 Evaluation of IRB Members
A. All IRB Members will be invited to complete and submit the IRB Annual Assessment Form (https://www.surveymonkey.com/r/UNMCIRBANNUAL) prior to this evaluation.

B. The IRB Executive Chair will convene a meeting with the IRB Administrators and staff to evaluate the IRB Members using the following:
   1) The aggregate data derived from the IRB Annual Assessment Forms.
   2) Metric data for individual IRB members based on the following criteria:
      a) Attendance at meetings (attendance expectation is 80% of scheduled meetings)
      b) Timeliness and completeness of IRB reviews
      c) Participation in IRB discussions
d) Service on IRB subcommittees

3.5 Aggregate Data Feedback to IRB Members
A. The IRB Executive Chair will provide verbal feedback based upon analysis of the aggregate data to the UNMC IRBs during a convened meeting. No data will be linked to an individual IRB Member at this meeting.

B. The IRB members will be invited to comment on the results of the aggregate data analysis and offer recommendations for improvement.

3.6 Individual Feedback to IRB Members
A. IRB members will be provided feedback regarding their service.

1) If an IRB member’s service is judged to be significantly deficient, the IRB Executive Chair will discuss the concerns with the member in a private setting and seek a satisfactory resolution.

2) If an IRB member’s service is judged to be satisfactory, the IRB Executive Chair will so inform the member.

3) If an IRB member’s service is judged to be exceptional, the IRB Executive Chair will so inform the member.

B. Any IRB member whose contribution to the IRB is judged to be continually deficient despite feedback, may have their appointment terminated by the IO upon recommendation of the IRB Executive Chair.

C. Upon request of individual IRB members, the IRB Executive Chair and/or the IO will write letters of recommendation which attest to the quality and value of the member’s service on the IRB.

3.7 Evaluation of IRB Administrators and Staff
A. The IO will evaluate the performance of the IRB Administrators utilizing the UNMC Employee Evaluation Form and the IRB Annual Assessment Form.

1) The IO will provide feedback verbally to each IRB Administrator during the annual review process, as well as written comments on the Academic Affairs Performance Evaluation Form.

2) The IO will also provide ongoing feedback about the performance of the IRB Administrators throughout the year.

B. The supervising IRB Administrator will evaluate the performance of the IRB staff utilizing the UNMC Employee Evaluation Form and the IRB Annual Assessment Form.

1) The supervising IRB Administrator will provide feedback verbally to each IRB staff during the annual review process, as well as written comments on the UNMC Employee Evaluation Form.

2) The supervising IRB Administrator will also provide on-going feedback about the performance of the IRB staff throughout the year.
3.8 Annual Evaluation of the HRPP

A. The IO will appoint an HRPP Annual Assessment Committee (HRPP-AAC). This committee will consist of:

1) IO, the IRB Executive Chair and one or more designated IRB Administrator(s)
2) UNMC Associate Vice Chancellor for Clinical Research,
3) UNMC Chief Compliance Officer,
4) Conflict of Interest Officer,
5) A representative(s) from the:
   a) Investigational Drug Pharmacy,
   b) Grants and Contracts,
   c) Radiation Safety Office,
   d) Fred & Pamela Buffett Cancer Center Scientific Review Committee,
   e) Institutional Biosafety Committee
   f) Investigational Device Review Committee
   g) Research Subject Advocate Office
   h) Additional members as necessary.

B. A meeting of the HRPP-AAC will be held annually in order to evaluate the HRPP utilizing the Annual HRPP Assessment Form.

C. The objectives of the HRPP-AAC will be to:

1) Determine which items on the Annual HRPP Assessment Form are judged to be:
   a) Satisfactory (S). The item does not require a corrective action plan, targeted or set goals.
   b) A Target for Improvement (TFI). A plan to achieve the targeted goal(s) for the item is dependent upon available staff and resources.
   c) Unsatisfactory (US). The item requires a corrective action plan with set goal(s) in a time frame based upon the seriousness of the deficiency.

2) Identify the criteria that must be met in order for goal(s) to be achieved.

D. Accomplishment of the goals arising out of the HRPP-AAC will be evaluated by the IO in conjunction with other administrators in accordance with the corrective action and specified time frame.

Administrative Approval:
Ernest D. Prentice, PhD. Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to specify the Organization’s requirements for the review, approval, conduct and oversight of human subject research funded by or involving the U.S. Department of Justice (DoJ) and the Federal Bureau of Prisons (BoP).

2.0 Policy
2.1 It is the policy of the Organization that it will comply fully with all approval requirements of DoJ and/or BoP when its IRBs review, approve and provide oversight of human subjects research funded by or otherwise contractually subject to DoJ regulations (28 CFR 46) and BoP regulations (28 CFR 512).

2.2 The Organization requires that the research specified in Section 2.1 above will comply with the following DoJ requirements as applicable:
   A. The Belmont Report.
   D. Title 28 Code of Federal Regulations Part 22 (28 CFR 22), Confidentiality of Identifiable Research and Statistical Information.

2.3 Education and Training
   A. All research personnel must complete training in accordance with HRPP policy #3.11.
   B. Any other specific training related to DOJ requirements will be provided as necessary by the ORA.

2.4 Responsibilities
   A. Research Funded by the Department of Justice [28 CFR 46]
      1) It is the responsibility of the PI to ensure compliance with all additional DoJ requirements for human subject protection.
      2) It is the responsibility of the IRB to ensure that all additional DoJ requirements for human subject protection have been met before IRB approval of the research project.

   B. Research Conducted Within the Bureau of Prisons
      1) Regulatory Compliance [28 CFR 512]
         a) It is the responsibility of the PI to ensure compliance with all additional BoP requirements for human subject protection.
         b) All research proposals must be reviewed and approved by the Bureau Research Review Board (BRRB).
         c) It is the position of the Organization that the IRB of record should, whenever possible, be the IRB appointed by the warden of the facility where the
research will be conducted in accordance with 28 CFR 512.14. When multiple facilities are involved, the UNMC IRB may accept IRB approvals from multiple facilities, as appropriate.

d) It is the responsibility of the IRB to ensure that all additional BoP requirements for human subject protection have been met before IRB approval of the research project.

2) **Limitations on Research Projects [28 CFR 512.11(a)(3)]**
Research involving human subjects conducted within the BoP must not involve medical experimentation, cosmetic research, or pharmaceutical testing.

3) **Academic Preparation or Experience [28 CFR 512.11(a)(6)]**
The PI must have academic preparation or experience in the area of study of the proposed research.

4) **Personnel [28 CFR 512.11(a)(7)]**
For all research conducted within the BoP, the PI assumes responsibility for actions of any person engaged to participate in the research study as an associate, assistant (i.e., personnel listed in Section I of the IRB application) or subcontractor(s).

5) **Limitations on Incentives for Inmate Subjects [28 CFR 512.11(a)(5)]**
   a) Incentives may not be offered to help persuade inmate subjects to participate in research. However, soft drinks and snacks to be consumed at the test setting may be offered.
   
   b) Reasonable accommodations such as a nominal monetary recompense for time and effort may be offered to non-confined research subjects who are both: 1) No longer in BoP custody and 2) participating in authorized research being conducted by BoP employees or contractors.

3.0 **Definitions [28 CFR 46.102]**

3.1 **Human subject** is defined a living individual about whom an investigator (whether professional or student) conducting research obtains:

   A. Data through intervention or interaction with the individual and/or

   B. Identifiable private information.

3.2 **Intervention** includes both physical procedures by which data are gathered (for example, venipuncture) and manipulation of the subject or the subject’s environment that are performed for research purposes.

3.3 **Interaction** includes communication or interpersonal contact between PI and contact.

3.4 **Private information** includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may be readily ascertained by the PI or associated with the
information) in order for obtaining the information to constitute research involving human subjects.

4.0 Procedures

4.1 Research funded by the Department of Justice

A. The IRB will review the application and complete the Department of Justice Checklist and ensure compliance with all applicable DoJ requirements, BoP requirements, and HRPP policies.

B. Requirement for Privacy and Confidentiality [28 CFR 22]

All research funded by the DoJ must maintain the following documents:

1) A privacy certificate approved by the National Institute of Justice (NIJ) Human Subjects Protection Officer. A Privacy Certificate Template and Privacy Certificate Guidance are available on the National Institutes of Justice Website.

2) Signed employee confidentiality statements for the PI and research staff, which are maintained by the PI. 
   Note: “Research staff” is defined as anyone listed in Section I of an approved IRB application.


Research involving human subjects funded by the DoJ must include the following information in the ICF:

1) The name(s) of the funding agency(ies)

2) A statement describing the extent to which confidentiality of records identifying the subject will be maintained. For studies sponsored by the NIJ, the subject should be informed that private, identifiable information will be kept confidential and will only be used for research and statistical purposes. If, due to sample size or some unique feature, the identity of the individual cannot be maintained, the subjects need to be explicitly notified. If the PI intends to disclose any information, the subject needs to be explicitly informed what information would be disclosed, under what circumstances, and to whom. The subject must be informed of any risks that might result from this disclosure and must explicitly provide written consent prior to participating in the research.

3) Under a privacy certificate, PIs and research personnel do not have to report child abuse unless the subject signs another ICF to allow child abuse reporting. 
   Note: It is the position of the University of Nebraska that child abuse must be reported in accordance with Nebraska State Law. Therefore, the ICF must disclose this obligation.

D. Requirement for Reporting

For research studies involving human subjects funded by the DoJ, a copy of all data must be de-identified and sent to the National Archive of Criminal Justice Data, including copies of the ICF, data collection instruments, surveys, or other relevant research materials.
4.2 Research conducted within the Bureau of Prisons

A. The IRB will review the application and complete the Department of Justice Checklist and ensure compliance with all applicable DoJ requirements, BoP requirements, and HRPP policies.

B. The research design must be compatible with both the operation of prison facilities and protection of human subjects. The PI must observe the rules of the institution or office in which the research is conducted.

C. The research must have an adequate research design and contribute to the advancement of knowledge about corrections.

D. The selection of subjects within in one organization must be equitable.

E. Any researcher who is a non-employee of the BoP must sign a statement in which the researcher agrees to adhere to the provisions of 28 CFR 512.

F. For research conducted within the Bureau of Prisons, the researcher must assume responsibility for actions of any person engaged to participate in the research project as an associate, assistant, or subcontractor to the researcher.

G. For all research conducted within the Bureau of Prison, the PI must provide the following information:

1) A summary statement, which includes:
   a) Names and current affiliations of the Researchers
   b) Title of the study
   c) Purpose of the study
   d) Location of the study
   e) Methods to be employed
   f) Anticipated results
   g) Duration of the study
   h) Number of participants (staff or inmates) required and amount of time required from each
   i) Indication of risk or discomfort involved as a result of participation

2) A comprehensive statement, which includes:
   a) Review of related literature.
   b) Detailed description of the research method.
   c) Significance of anticipated results and their contribution to the advancement of knowledge.
   d) Specific resources required from the BoP.
   e) Description of all possible risk, discomforts and benefits to individual participants or a class of participants, and a discussion of the likelihood that the risks or discomforts will actually occur.
   f) Description of steps taken to minimize any risks.
   g) Description of physical or administrative procedures to be followed to:
i) Ensure the security of any individually identifiable data that are being collected for the study.

ii) Destroy research records or remove individual identifiers from those records when the research has been completed.

h) Description of any anticipated effect of the research study in organizational programs and operations.

i) Relevant research materials such as vitae, endorsements, sample consent statements, questionnaires, and interview schedules.

j) A statement regarding assurance and certification required by 28 CFR 46, if applicable.

H. Requirement for Confidentiality [28 CFR 512.11, 12, 13, 15]
For all research conducted with the BoP:

1) A non-employee of the BoP may receive records in a form not individually identifiable when an advance adequate written assurance that the record will be used solely as a statistical research or reporting record.

2) Except as noted in the consent statement to the subject, the PI must not provide research data that identifies the subject to any person without that subject’s prior written consent to release the information.

For example, research information identifiable to a particular individual cannot be admitted as evidence or used for any purpose in any action, suit, or other judicial, administrative, or legislative proceeding without the written consent of the individual to whom the data pertains.

3) Except for computerized data records maintained at an official DoJ site, records that contain non-disclosable information directly traceable to a specific person may not be stored in, or introduced into, an electronic retrieval system.

4) If the PI is conducting a study of special interest to the Office of Research and Evaluation (ORE), but the study is not a joint project involving the ORE, the PI may be asked to provide ORE with the computerized research data, not identifiable to individual subjects, accompanied by detailed documentation. These arrangements must be negotiated prior to the beginning of the data collection phase of the study.

I. Requirement for Informed Consent [28 CFR 512.16]
Research involving human subjects conducted within the BoP, must include the following elements of disclosure in the ICF:

1) Identification of the PI and research personnel listed in Section I of the IRB application.

2) Anticipated uses of the results of the research.

3) A statement that participation is completely voluntary and that the subject may withdraw consent and end participation in the study at any time without penalty
or prejudice (the inmate will be returned to regular assignment or activity by staff as soon as practicable).

4) A statement regarding the confidentiality of the research information and exceptions to any guarantees of confidentiality required by federal or state law. For example, a PI may not guarantee confidentiality when the subject indicates intent to commit future criminal conduct or harm himself or herself or someone else, or, if the subject is an inmate, indicates intent to leave the facility without authorization.

5) A statement that participation in the study will have no effect on the inmate subject’s release date or parole eligibility.

J. Documentation and Waiver of Signed Informed Consent [28 CFR 512.16(a)(12)]

1) A PI who is a non-employee of the BoP, in addition to presenting the statement of informed consent to the subject, shall also obtain the subject’s signature on the statement of informed consent prior to initiating the research activity.

2) The PI may not be required to obtain the signature if the PI can demonstrate that:

   a) The only link to the subject’s identity is the signed statement of informed consent, or
   
   b) That there is significantly more risk to the subject if the statement is signed.

3) The signed statement shall be submitted to the chairperson of the IRB of record.

K. Request for Change [28 CFR 512.11(a)(14)]

The PI must submit planned methodological changes in a research study to the IRB for approval, and may be required to revise study procedures in accordance with the new methodology.

L. Requirement for Reporting [28 CFR 512.19]

For research studies involving human subjects conducted within the BoP, the PI is responsible for the submission of the following:

1) A progress report of the research at least once a year to the Chief and ORE.

2) A copy of any report of findings, including an abstract, must be provided at least 12 days working days before it is to be released to the chairperson of the BRRB, the regional director and the warden of each institution which provided data or assistance.

M. Requirement for Publication of Results [28 CFR 512.20]

1) For all research conducted within the BoP, the publication of results of any research studies involving human subjects is permitted in book form and professional journals. In any publication, the PI is responsible for the following:

   a) An acknowledgment of the BoP’s participation in the research study.
b) Expressly disclaiming approval or endorsement of the published material as an expression of the policies or views of the Bureau.

2) Prior to submitting for publication, the PI will provide two copies of the material, for informational purposes only, to the Chief, ORE, Central Office, Bureau of Prisons.

4.3 Additional Requirements

A. New research and substantive scientific amendments to approved research shall undergo scientific review and that the review is considered by the IRB in accordance with HRPP policy #1.9.

B. Disclosure regarding the provisions for research-related injury follows the requirements of the DoJ component.

ADMINISTRATIVE APPROVAL:
Ernest D. Prentice, PhD  Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD  IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe Organization’s requirements for submission and pre-review of: 1) new IRB applications (exempt and non-exempt); 2) continuing review (CR), 3) requests for change in protocol (RFC); 4) single subject protocol deviations (SSPD), 5) adverse events (AEs); 6) reports of potential unanticipated problems involving risks to subjects or others (UPs), 7) noncompliance reports (NCR), 8) complaints (C), and 9) study completion reports (SCR).

2.0 Policy
It is the policy of the Organization that all submissions will be processed efficiently by the Office of Regulatory Affairs (ORA) for review in accordance with applicable HRPP policies.

3.0 Submission Requirements

3.1 Research protocols submitted after January 16, 2012
The following are the submission requirements for research protocols and other items requiring IRB review as of January 16, 2012:

A. All new IRB applications after January 16, 2012 must be submitted using the online Research Support System (RSS) (https://net.unmc.edu/rss).

B. Once a new IRB application is accepted by the ORA, an email will be sent by the IRB staff to the PI and Lead Coordinator (LC) specifying the requirements for submission, as needed.

C. All CRs, RFCs, SSPD, NCRs, and SCRs are submitted through RSS. UPs and Cs are submitted by a variety of mechanisms specified in HRPP policies #8.3 and 8.4.

3.2 Research protocols submitted prior to January 16, 2012
The following are the submission requirements for research protocols and other items requiring IRB review prior to January 16, 2012:

A. Full IRB studies
   1) Full Board studies submitted prior to January 16, 2012 have not been required to transfer to RSS.
   2) All other forms and submissions (i.e., CRs, RFCs, SSPD, NCRs, and SCRs) will continue to be submitted on paper.
   3) All necessary forms are available on the UNMC IRB website (http://www.unmc.edu/irb).
   4) The IRB will maintain paper files for the duration of these studies.

B. Expedited studies
   1) Studies that qualified for expedited review prior to January 16, 2012 have been converted to RSS, unless the study is in follow-up.
   2) All other forms and submissions prior to the conversion are submitted using the paper format.
   3) Once the study has been converted to RSS, all future submissions will be completed using the electronic format.

C. Exempt studies
   1) Studies that were classified as exempt prior to January 16, 2012 have not been required to transfer to RSS.
2) If the study continues past the five year approval period, then the study must be re-submitted on the appropriate application through RSS.

3.3 All internal adverse events that meet the criteria specified in HRPP policy #8.2 will continue to be reported to the IRB through RSS system.

4.0 Deadlines for Submission

4.1 Full IRB Review

A. The deadlines for submission of any materials requiring review by the full IRB are published on the IRB website at http://unmc.edu/irb. The deadlines are set 2 weeks prior to each meeting.

B. Applications for initial review must be submitted to the ORA with sufficient time for the IRB staff to accept the submission and make the copies for inclusion in the IRB review packets. Incomplete submissions may result in delay of IRB review. Once accepted, an email will be sent to the PI and LC indicating the submission has been accepted and the date of IRB review. 

Note: Sponsors and other funding agency deadlines for obtainment of final IRB approval should be considered when determining when items are submitted to the IRB for review.

C. Applications for initial review automatically qualify for pre-review by an IRB Administrator if submitted at least three weeks prior to the scheduled meeting. Applications submitted after this deadline will be pre-reviewed as time permits.

D. Previously tabled applications should be submitted to the ORA as soon as possible after the revisions are complete.

E. RFCs should be submitted at least two weeks prior to the scheduled meeting to be considered for review at that meeting.

F. CRs and SCRs should be submitted to the ORA as soon as possible after the investigator receives the notice that the study is due for re-review. The PI and LC will receive two (2) courtesy IRB notifications. The first email is sent approximately 60 days prior to expiration of IRB approval and the second is sent 10 business days later if the application has not been received by the ORA. In order to be considered for review at the next month's IRB meeting in which CRs are reviewed, applications must be submitted no later than the last day of the previous month (e.g. a CR to be reviewed in April must be submitted to the ORA no later than March 31).

G. Reports of internal AEs, potential UPs, NCRs, and Cs should be submitted to the ORA as soon as possible after the event becomes known in compliance with HRPP policies #8.1, 8.2, 8.3, 8.4 and 8.5.

4.2 Expedited Review

A. Items that qualify for expedited review in accordance with HRPP policy #2.3 have no deadlines for submission.

Note: Sponsors and other funding agency deadlines for obtainment of final IRB approval should be considered when determining when items are submitted to the IRB for review.
4.3 **Exempt Studies**
   A. Items that qualify as exempt in accordance with *HRPP policy #2.6* have no deadlines for submission.
   
   Note: Sponsors and other funding agency deadlines for obtainment of final ORA approval should be considered when determining when items are submitted to the ORA for review.

5.0 **IRB Review Limits**
5.1 **Full IRB Review**
   A. The IRB will normally review no more than 15 protocols (i.e., new submissions and previously tabled protocols) at each full IRB meeting. Assignment to the IRB meeting are made on a first-come, first-served basis. Protocols in excess of 15 will be assigned to the following IRB meeting.

   B. The IRB will review reports of internal AEs, potential UPs, NCRs, Cs, and RFCs at the earliest possible full IRB meeting without review limits.

5.2 **Expeditied Review**
Items that qualify for expedited review in accordance with *HRPP policy #2.3* have no review limits.

5.3 **Exempt Studies**
Items that qualify as exempt in accordance with *HRPP policy #2.6* have no review limits.

6.0 **ORA Receipt and Processing of Items Submitted for IRB Review**
6.1 New applications and other action items for IRB review are received by the ORA and processed in accordance with ORA office procedure.

6.2 The action items will be triaged to the appropriate IRB administrator.

6.3 All items are screened by the IRB administrator in order to determine if all required applications, consent forms/information sheets, detailed protocol, and other required documents have been submitted in accordance with the submission instructions provided on each application.

7.0 **Determination of Required IRB Review**
7.1 The IRB Administrator, in consultation as necessary with the IRB Executive Chair, will determine whether or not a protocol or other action item requires review by the full IRB or qualifies for expedited review in accordance with *HRPP policies #2.2 and #2.3*.

7.2 The IRB Administrator will review the database for status of other current research listed for that PI. IRB review and approval of any new submission may be held pending resolution of the approval status of other research.

8.0 **Pre-Review of Applications**
8.1 **Initial IRB Submissions**
   A. If the application has been submitted with sufficient time for pre-review, the IRB administrator, in consultation with the IRB Executive Chair/IRB member, as necessary, will pre-review the IRB application and supporting documents to determine if the submission is sufficiently complete in order to facilitate IRB review.
B. The PI and LC will be contacted to address any problems or concerns identified during pre-review. If the number of problems in the application are of such magnitude that IRB review is not possible, the full application and supporting documents will be sent back to the PI for revision and resubmission of a revised application and/or consent document(s).

C. The pre-reviewer will inform the assigned IRB reviewers of any problems or concerns which have not been addressed by the PI if an item has been scheduled for review by the full IRB.

8.2 Continuing Review and Study Completion Reports

A. The assigned IRB Administrator, in consultation with the IRB Executive Chair/IRB member, as necessary, will pre-review the CR application or SCR and supporting documents.

B. The CR application or SCR will be reviewed to ensure that it contains information which is consistent with the IRB study file.

C. The pre-reviewer will inform the assigned IRB reviewer of all problems and concerns identified during the pre-review.

D. In situations of potential noncompliance discovered during the CR process, the designated IRB Administrator will be notified. The potential noncompliance will be handled in accordance with HRPP policy #8.5.

8.3 Other Action Items

A. Requests for changes will be handled in accordance with HRPP policy #2.4.

B. Single subject protocol deviations will be handled in accordance with HRPP policy #8.1.

C. Adverse events will be handled in accordance with HRPP policy #8.2.

D. Complaints will be handled in accordance with HRPP policy #8.3.

E. Potential unanticipated problems involving risk to the subjects and others will be handled in accordance with HRPP policy #8.4.

F. Noncompliance will be handled in accordance with HRPP policy #8.5.

Administrative Approval:

Ernest D. Prentice, PhD. Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for: 1) submission of items required for full IRB review; 2) organization, scheduling, and conduct of full IRB meetings; 3) IRB approval criteria; 4) IRB actions; and 5) IRB documentation of actions.

2.0 Policy
It is the policy of the Organization that the IRB will obtain and review sufficient information in order to permit the Board to determine and document that all items which require full IRB review meet all applicable requirements of the following:

2.1 HHS regulations for the Protection of Human Subjects at 45 CFR 46, including Subparts B, C, D (as applicable); FDA regulations for Protection of Human Subjects at 21 CFR 50 including Subpart D, 21 CFR 56, and other FDA regulations as applicable, the regulations and requirements of the other Common Rule agencies as applicable, the HIPAA Privacy and Security Rules at 45 CFR 160, 164, and all other applicable federal, state and local law.

2.2 The Organization has “unchecked the box” on FWA00002939. However, the HRPP will apply equivalent protections to non-federally funded research. These protections will be based upon the ethical principles in the Belmont Report. In addition, the requirements in 45 CFR 46, Subpart A, B, C, and D will be applied to the greatest extent possible in consideration of the nature of the research. When an exception is made, it must not reflect a lower standard of human subject protection.

2.3 The Organization applies the ICH-Good Clinical Practice (GCP) E-6 Guidelines to studies where the sponsored agreement requires compliance with ICH GCP for clinical trials conducted internationally in accordance with HRPP policy #1.12.

2.4 The IRB will conduct continuing review of research at intervals appropriate to the degree of risk, but not less than once per year.

3.0 Procedures
3.1 Submission of Items for Full IRB Review
Information concerning: 1) procedures for submission, 2) deadlines for submission, 3) ORA processing, 4) review limits, and 5) pre-review are described in HRPP policy #2.1.

3.2 IRB Meeting Schedule
A. The schedule of IRB submission deadlines is posted on the IRB website at http://unmc.edu/irb.

B. IRB–01 meets the first Thursday of every month, except in January and July when the meeting is cancelled due to Holiday schedules. IRB-02 meets the third Thursday of every month.

C. IRB-03 meetings are held on demand and convened as soon as possible.

D. IRB-04 meetings are held the fourth Tuesday of every month at the Children’s Hospital & Medical Center.

E. Any IRB member scheduled to attend an IRB meeting, who encounters a problem which precludes attendance must notify the ORA as soon as possible.
3.3 Quorum
A. A full IRB meeting cannot be convened without the presence of a quorum. A duly constituted quorum must include: a) simple majority of the voting membership, and b) at least one member whose is unaffiliated and qualifies as a non-scientist.

B. Some or all IRB members may participate in the meeting by conference call, videoconference or web meeting. However, utilization of video conferencing or teleconferencing technology in the conduct of an IRB meeting will only be done under extenuating circumstances (e.g. major snow storm). Any IRB member participating by conference call, videoconference or web meeting will receive all relevant materials prior to the meeting and must be able to participate actively and equally in all discussions. Voting IRB members cannot participate in the meeting discussions or voting by email.

C. IRB members who are knowledgeable about and experienced in working with vulnerable populations including populations vulnerable to coercion or undue influence (e.g., pregnant women, prisoners, children, decisionally impaired persons, social or economically disadvantaged) will be present during the review of research involving these populations (in accordance with HRPP policy #1.5).

D. When the IRB reviews any items involving prisoners, a prisoner representative must be present in accordance with HRPP policies #1.5 and #4.3.

E. Any IRB member who does not have a conflict of interest (COI), as identified in HRPP policy #1.6, but abstains from voting for other personal reasons are included in the quorum. This is recorded as an abstention in the minutes.

F. Any IRB member who has a COI will be recused in accordance with 45 CFR 45.107(e), 21 CFR 56.107(e), and HRPP policy #1.6. If a conflicted member is participating by conference call, videoconference, or web meeting the IRB member’s participation is terminated for discussion and voting. The name of the individual and a statement that the individual was recused due to COI will be recorded in the minutes.

G. A designated IRB Administrator is responsible for determining quorum requirements, monitoring attendance at the meeting to verify maintenance of quorum, and recording the actions taken on all protocols and other items under review.

H. If attendance at a convened full IRB meeting falls below quorum (i.e., losing a majority of members, the unaffiliated, non-scientific member, or another required member), the meeting will be immediately suspended and no official business will be conducted until a legal quorum is re-established. If it is not possible to re-establish the quorum, the meeting will be adjourned and the remaining reviews will be conducted at the next available full IRB meeting.

3.4 Assignment of Reviewers and Creation of the Agenda
A. Primary and secondary reviewers will be assigned by the IRB administrators with advice from the IRB Executive Chair/designee as necessary. At least one (1) of the assigned reviewers for the full board meeting must have the necessary scientific, medical, or other expertise in order to perform an in-depth review of the protocol.
When necessary, the services of an expert consultant will be used as described in HRPP policy #1.5, Section 5.16.

B. If there is not at least one IRB member available to be present at the IRB meeting with appropriate expertise as described above, review of the protocol will be deferred to the next IRB meeting.

C. A primary and secondary reviewer will be assigned to review new IRB applications and tabled IRB applications.

D. Only a primary reviewer will be assigned to applications for continuing review, internal adverse event reports, external adverse event reports, reports of potential unanticipated problems involving risk to the subject or others, requests for change in protocol and/or ICF, reports of noncompliance and complaints unless it is determined by the IRB Executive Chair/designee that more than one reviewer is necessary.

E. Two agendas will be created:
   1) An abbreviated agenda which lists the new items for review and assigned reviewers. This is attached to the review packet mailed to IRB members.
   2) A detailed agenda which is emailed to IRB members at least 2 days before the meeting. A copy is also distributed at the meeting. This agenda contains: 1) education, policy, and informational items; 2) a categorized list of review items; 3) IRB reviewer assignment for each of the items under review, 4) IRB approval criteria, and 5) IRB actions.

   Per the requirements of 45 CFR 46.110(c); 21 CFR 56.110(c) all IRB members are provided with notification of all items approved via expedited review in accordance with HRPP policy #2.3, Section 12.0.

3.5 Review Materials Distributed to IRB Members
A. At this time the IRB is a hybrid paper/electronic IRB, as indicated in HRPP policy #2.1. All IRB members, including those attending through videoconference or teleconference, will receive review materials in paper format, but will also have the ability to view electronically all actions related to protocols submitted after January 16, 2012 online through the RSS system at https://net.unmc.edu/rss.

B. At least one (1) week before the IRB meeting, packets for review will be sent to IRB members scheduled to attend the meeting. Packets will be individualized in accordance with assigned review responsibilities.

C. Primary and secondary reviewers (if required per Sections 3.4B, C, and D above) receive complete review packets which include the following in consideration of their specific review assignments:
   1) IRB minutes
   2) Education, policy and informational items
   3) IRB applications for initial review, including all study documents (e.g., ICF/information sheets, advertisements/other recruitment materials, instruments/questionnaires, Clinical Trial Master Matrix, Investigational Drug Study Registry Form or Drug Registry Form for Marketed Drugs, detailed
4) For DHHS approved research, the IRB reviewers will also receive the DHHS-approved sample consent form (when one exists), the complete DHHS-approved protocol (when one exists), and any relevant grant applications.

5) Modified IRB applications for tabled research, including the IRB review letter, the PI response to the IRBs review, all other forms indicated in Section 3.5C(3) above (including those modified as directed by the IRB).

6) Continuing review applications, including the last version of the IRB application approved by the IRB, the ICF/information sheets to be approved for the next year, current study progress report for multicenter research, current data safety monitoring report, and a Request for Change if modifications are required in the research (with all modified documents indicated below in Section 3.5(C)(6) of this policy).

   Note: All IRB members have complete access to RSS at any time to review the complete protocol, including any protocol amendments or modifications previously approved by the IRB.

7) Requests for change, including all modified documents (e.g., IRB application, ICF/information sheets, modified protocol, investigator brochure, sponsor listing of modifications, and grant application).

8) Single subject deviation, including all associated documentation.

9) Reports of adverse events, including the sponsor documentation, clinical documentation, and a copy of the current IRB approved ICF.

10) Reports of potential unanticipated problems involving risk to the subject or others, including all associated documentation.

11) Reports of noncompliance, including all associated documentation.

12) Reports of complaints, including all associated documentation.

13) Any other information which is relevant to their reviews.

D. All other IRB members who are not assigned as either a primary or secondary reviewer receive abbreviated submissions which include all of the above listed documents, with the exception of the: 1) detailed protocol, 2) investigator’s brochure, and 3) grant application.

   Note: All IRB documents are available for review in RSS by any IRB member at any time. In addition the documents indicated in 3.5 (C) and (D) above are accessible during the IRB meeting in order to facilitate resolution of questions that may arise during the IRB’s deliberations.

E. When a protocol lists a PI or other study personnel who have a COI, the COI management plan will be reviewed in accordance with HRPP policy #3.12.
3.6 IRB Member Review Procedures
   A. All IRB members must be satisfied that they have sufficient information to make the determinations required for IRB approval in accordance with 45 CFR 46.111; 21 CFR 56.111.

   B. IRB members are expected to consult the IRB study files in RSS (as necessary), applicable regulations, HRPP policies, and access the OHRP and FDA websites as necessary during their review of the protocol. Links for these and other information resources are available at the UNMC IRB website (http://unmc.edu/irb).

   C. IRB members are expected to submit written reviews. Written reviews should be submitted as early as possible to ORA: (1) by e-mail (irbora@unmc.edu) no later than the day before the full board meeting; (2) by fax (402-559-3300) no later than the morning of the full board meeting; or (3) in person to an IRB staff member at the beginning of the meeting. In the latter case, six copies must be provided.

   D. Deficiencies and/or major points of clarification which require revision of the IRB application or other review item should be described fully, sequentially, and referenced to sections of the submitted form. The detailed protocol or grant should be referenced as necessary.

   E. Deficiencies (i.e., absence of required element(s) of consent, errors, inadequate explanations, and excessively high readability level) should be described sequentially according to the section of the ICF.

3.7 IRB Meeting Procedures
   A. When a quorum of the Board is present (see Section 3.3 above), the IRB meeting is called to order by the IRB Executive Chair/Vice Chair or designee (subsequently referred to as “Chair” in this policy) and each item on the agenda is acted upon sequentially.

   B. The Primary Reviewer will present the review followed by the Secondary Reviewer (as applicable). The protocol is then open for discussion by all IRB members. When the discussion is completed, a separate vote will be taken on each application or other item under consideration.

   C. In order to assist IRB members in their deliberation, the IRB staff have on-line web access to project on a screen to facilitate discussion by the full IRB any portions of applications and associated documents, as well as all applicable federal, state, and local regulations, and HRPP policies. Placemats with the criteria for IRB approval, Subpart B, C, and D determinations and other relevant information are spread throughout the room on the tables.

   D. Whenever a controverted issue arises during an IRB meeting and there is either no resolution or the resolution remains contentious, members will be asked if they wish to submit a minority opinion. The minority opinion will be appended to the minutes of the meeting.

   E. IRB discussion of any one item on the agenda is limited to 20 minutes. If the discussion reaches the time limit, the Chair will call for a motion to extend discussion an additional 20 minutes. If the motion fails to pass by two-thirds vote of those present, the protocol or issue then under discussion shall automatically be deemed to have been tabled, and shall be referred as needed, to an IRB
subcommittee for further study.

3.8 Voting Requirements

A. The Primary Reviewer will recommend an action which must be seconded by another IRB member, normally the Secondary Reviewer.

B. IRB voting on each motion will be recorded as the number of members in favor, the number against, and the number of abstentions. Separate votes for each action will be recorded.

C. No motion shall pass unless two-thirds of the IRB members which constitute a quorum are present during the discussion and vote in favor of the motion.

D. If a member must leave the meeting temporarily (e.g., answer a page) before the vote is taken, the vote can be delayed. If the vote is not delayed, the name of the absent member will be recorded in the minutes.

E. Voting by absentee is not permitted.

F. If a motion fails to pass by a two-thirds vote, other motions will be entertained. If no further motions are made, the protocol or issue under discussion shall automatically be deemed to have been tabled and shall be referred, as needed, to an IRB subcommittee for further study.

G. If a protocol or issue has been referred to an IRB subcommittee, the Chair will present the results of the inquiry at any subsequent full Board meeting.

H. The Chair will abstain from voting, but may exercise his/her voting privilege in order to reach a two-thirds majority in accordance with the voting requirements described above.

3.9 Criteria for IRB Approval and Other Determinations

A. Criteria for IRB approval of all human subject research (e.g., initial, continuing review, Requests for Change, and all other actions) is contained in HRPP policy #2.5.

B. During the review, the IRB must also determine:

1) When continuing review is required more often than annually [as required at 45 CFR 46.109(e); 21 CFR 56.108(a)(2)]. This determination will be based upon: 1) the nature of the research, 2) any history of noncompliance, and 3) other factors which warrant review of the protocol more often than annually.

2) Which projects need verification from sources other than the PI that no material changes have occurred since the previous IRB review as required at 21 CFR 56.108(a)(2).

3) The ICF(s)/information sheets(s) are accurate and complete.

4) Which projects should have a third party observe the consent process in accordance with HRPP policy #3.12.

5) Which projects require an audit of research records in accordance with HRPP policies #1.18 and 8.5.
6) Any significant new findings that arise from the review process and that might relate to a subject’s willingness to continue participation in the study will be provided to subjects.

7) When the PI is the lead researcher of a multi-site trial, the IRB will evaluate whether the management of information to the protection of human subjects is adequate, such as reporting of unanticipated problems, interim results, and protocol modifications.

C. Documentation of the basis for determination that an investigation involves a significant risk device or non-significant risk device in accordance with 21 CFR 812.66 and HRPP policy #6.2.

D. The IRB may determine that some components of the research have met the IRB criteria for approval whereas other components require minor or substantive changes. In this case, the IRB may choose to issue final approval and full release (Section 3.10A below) for those components that satisfy the IRB approval criteria. For those components that do not meet the IRB approval criteria the IRB may issue conditional approval (Section 3.10B below), table that component (Section 3.10C below), or disapprove that component (Section 3.10D below).

3.10 IRB Actions

A. **Final Approval and full release; initiation of the research is authorized.**
   All of the criteria for IRB approval are satisfied and no changes are required.

B. **Conditional approval; final IRB approval and full release contingent upon IRB Executive Chair/designee review and acceptance of specified modifications and/or submission of additional documents**
   All of the criteria for IRB approval are satisfied. The IRB requirements for final approval and release are considered minor and not substantive in nature.

C. **Tabled, full IRB re-review required**
   The IRB requires additional information, more than minor modifications or clarifications, and/or the IRB had concerns which warrant re-review by the full IRB.

D. **Disapproved**
   Applications may be disapproved for the following reasons:
   1) The protocol has a serious design flaw
   2) Subjects will be placed at undue risk.
   3) The PI refuses to comply with requested modifications/clarifications
   4) The protocol does not meet institutional policy or requirements.

   The PI has the right to appeal to the IRB in accordance with HRPP policy #8.7.

E. **Decline to complete the review**
   Adequate review of the protocol could not take place because the application is significantly deficient in information and content. The PI will be advised to carefully review the IRB submission requirements and revise the application accordingly.

F. **Suspension of IRB approval**
   The IRB requires all research activities be halted immediately because of serious subject safety or noncompliance concerns. The research does not continue to
remain in compliance with the IRBs requirements.  
*Note: This action may be taken in relation to continuing review, complaints, noncompliance, adverse events, and unanticipated problems involving risk to the subject or others.*

G. **Termination of the research**
   The IRB requires the study be terminated because the subjects have been placed at undue risk and/or there are very serious concerns. The research is not in compliance with the requirements of the IRB.  
*Note: This action may be taken in relation to continuing review, complaints, noncompliance, adverse events, and unanticipated problems involving risk to the subject or others.*

3.11 Study Disapproval, Suspension and Termination
Refer to **HRPP policy #8.7** for a description of the IRB’s procedures to carry out study disapproval, suspension or termination.

3.12 IRB Review Letters
   A. IRB review letters, which reflect the deliberations and decisions of the Board, are developed by the IRB Administrators, in consultation with the IRB Executive Chair and reviewers.

   B. IRB review letters must be written in a clear, explanatory, and facilitative fashion in order to assist PIs in understanding the rationale for any IRB concerns, clarifications and mandated changes to the IRB application, ICF(s)/information sheet(s) and/or other associated documents.

   C. The IRB review letters will clearly document the determinations of the Board, as referenced above in Sections 3.9-3.11 of this policy, including:
      1) The decision to approve, disapprove, or requirement modifications.
      2) A list of any modifications/clarifications required by the Board.
      3) If the IRB disapproves the action, a statement is given for the decision and the investigator is given the opportunity to respond in person or in writing in accordance with **HRPP policy #8.7, Section 4.0.**

   D. Signature authority is granted to the IRB Executive Chair, IRB Vice-Chairs, and IRB Administrators in accordance with **HRPP policy #1.16.**

3.13 IRB Meeting Minutes
   A. **Basic Information**
      1) The format of the IRB minutes reflects the standardized IRB minutes template which is consistent with the IRB agenda template.

      2) The IRB minutes are based upon the actions of the IRB recorded in detail by the assigned IRB Administrator. The minutes are then developed after the meeting by the IRB Administrators in consultation with the IRB Executive Chair/designee.

      3) The IRB minutes include the following components: core minutes, and addenda which contain the detailed review letters provided to PIs that reflect the IRBs requirements, as well as required documentation.

      4) Copies of the core IRB minutes are provided via e-mail to: a) IRB members before the next IRB meeting, and b) the IO, as well as other administrative
officials as appropriate within the Organization after the meeting.

5) Complete copies of the IRB minutes including: a) the core minutes, and b) the appended IRB review letters (the IRB minutes addendum) are distributed by email to IRB members and the IO three workdays prior to the date of the next IRB meeting. All IRB members, including alternates, receive a copy of all IRB minutes. In addition, all IRB members have access to the complete on-line protocol file which includes documents reviewed and review letters.

6) Each IRB will review the minutes for the preceding meeting of that IRB (e.g., IRB-01 will review the minutes of the preceding IRB-01 meeting). Any corrections are duly noted and the minutes are accepted. All IRB members, however, have access to the complete minutes for all IRB meetings.

7) The complete IRB minutes will be provided to OHRP, FDA, auditing groups, and other entities in accordance with all applicable federal, state, and Organizational requirements.

B. Core IRB Minutes:
   1) Identification of the individuals present at the meeting: IRB members, non-voting IRB member alternates, consultants, IRB administrative staff, and guests.

   2) Identification of IRB members, non-voting IRB member alternates and consultants who attended the IRB meeting via videoconferencing or teleconferencing.

   3) Identification of alternate IRB members and the IRB member for whom they are substituting.

   4) The names of IRB members who have a COI and are recused at the time of the discussion and vote on each board action.

   5) The names of IRB members who do not have a COI, but are absent from the room for other reasons at the time of the vote on each board action.

   6) IRB special notification items (e.g., items approved by expedited review) per IRB minutes template).

   7) Documentation of quorum for each separate vote count for all board actions (i.e., in favor, against, and abstentions) in the following categories per the IRB minutes template:
      a) IRB special review items (e.g., single subject protocol deviations requiring review by the full IRB; re-review of a protocol that was conditionally approved but now requires reconsideration by the IRB; unanticipated problem involving risk to the subject or others that is not an adverse event).

      b) Reports of noncompliance

      c) Internal adverse event reports that may be unanticipated problems involving risk to the subject or others

      d) Requests for change in approved research protocols
e) Continuing review of research proposals

f) Previously approved research proposals

g) Initial review of research proposals

8) Document the presence of a non-scientist member (i.e. a voting IRB member whose primary concern is in a non-scientific area) for each vote count.

9) Verification that all IRB members who attended through videoconferencing or teleconferencing were able to actively participate in all discussions and votes.

10) A written summary of the discussion and resolution of controverted issues which is generally no longer than a quarter to half page of text. A controverted issue is clarified for the purposes of this policy as one which generated a contentious discussion among members of the IRB over a human subject protection issue. Examples include, but are not limited to: a) concerns over the acceptability of the risk-benefit relationship of the research; b) concerns over additional protections for a vulnerable subject population and whether the protocol meets the requirements of Subpart B, C, or D; c) concerns over PI’s qualifications; and 4) concerns related to noncompliance.

11) A written summary of the discussion and resolution of actions taken with regard to significant new findings either provided by the investigator or provided by other sources, which may relate to the subject’s willingness to continue participation in the research.

12) The reason(s) for disapproval of research.

13) A determination of when continuing review is required more often than annually.

14) A determination of which projects need verification from sources other than the PI that no material changes have occurred since the previous IRB review.

15) A determination of which projects should have a third party observe the consent process.

16) A determination of which projects require an audit of research records.

17) Documentation of the basis for determination that an investigation involves a significant risk device or non-significant risk device.

C. Addenda

1) The IRB minutes addendum (detailed written review letters to PIs) are developed by the IRB Administrators and Continuing Review Coordinator based on written comments from reviewers, and discussions at the meeting, in consultation with the IRB Executive Chair/designee and IRB reviewers as necessary.

2) The IRB review letters for initial submission will include some or all of the following IRB requirements which require a written response from the PI:

   a) IRB Requirements:
(1) IRB Application

(2) Addendum

(3) Adult ICF

(4) Youth/Child Information Sheet(s)

(5) Advertisement

b) Additional Documentation:

(1) Documentation of the approval period for research granted full approval and release at the time of initial and continuing review.

Note: If the IRB conditionally approves a study at initial or continuing review, the IRB review letter generated from the meeting will not contain the “valid until date”. This documentation will appear in the final approval letter (see Section 6.2 below).

(2) Documentation of: a) the level of risk (i.e., minimal risk, greater than minimal risk, significant risk), and b) the rationale supporting this classification.

(3) Documentation that the IRB determined that the research satisfies the requirements of 45 CFR 46, Subpart B and the designated category (46.204; 46.205; 46.206). Per Section 2.2 of this policy the IRB will apply Subpart B as required for federally funded research and for non-federally funded research to the greatest extent possible. Any alteration of Subpart B requirements as applied to non-federally funded research will be documented.

(4) Documentation that the IRB determined that the research satisfies the requirements of 45 CFR 46, Subpart C (46.305) and is appropriately classified under the designated category [46.306(2)(i); 46.306(2)(ii); 46.306(2)(iii); 46.306(2)(iv)], as applicable. Per Section 2.2 of this policy the IRB will apply Subpart C as required for federally funded research and for non-federally funded research to the greatest extent possible. Any alteration of Subpart C requirements as applied to non-federally funded research will be documented.

(5) Documentation that the IRB determined that the research satisfies the requirements of 45 CFR 46, Subpart D and has met all the requirements for the designated category (46.404; 46.405; 46.406; 46.407), as applicable. Per Section 2.2 of this policy the IRB will apply Subpart D as required for federally funded research and for non-federally funded research to the greatest extent possible. Any alteration of Subpart D requirements as applied to non-federally funded research will be documented.

(6) Documentation that the IRB considered protocol specific findings for research involving decisionally impaired subjects.

(7) Documentation of the IRB rationale for nonsignificant/significant risk device determinations.

(8) Documentation that the IRB determined that the research satisfies the requirements of 21 CFR 50, Subpart D and has met all the requirements for the designated category (50.51, 50.52, 50.53, 50.54), as applicable.
(9) Documentation that the IRB determined that the research satisfies the requirements for waiver of informed consent/ HIPAA authorization under the federal regulations at 1) 46.116(c); or 2) 46 CFR 46.116(d) and 45 CFR 164.512(i)(2)(ii) or 3) 46.408(c), as applicable.

(10) Documentation that the IRB determined that the research satisfies the requirements for waiver of child assent under the applicable federal regulations at 1) 45 CFR 46.408(a) and 21 CFR 50.55(c)(1); or 2) 45 CFR 46.408(a) and 21 CFR 50.55(c)(2); or 3) 45 CFR 46.116(d) applied under 45 CFR 46.408(a) and 21 CFR 50.55(d).

(11) Documentation that the IRB determined that the research satisfies the requirements for waiver of signed consent under the applicable federal regulations at 1) 45 CFR 46.117(c)(1); or 2) 45 CFR 46.117(c)(2) and 21 CFR 56.109(c).

3) IRB required modifications of amendments to the IRB application and ICF(s)/information sheet(s).

4) IRB required actions in response to adverse event reports.

5) IRB required actions in response to reports of potential unanticipated problems involving risk to the subject or others.

6) IRB required actions in response to non-compliance or complaints from subjects or others.

7) A statement providing rationale why the IRB disapproved a research activity and an indication the PI has the opportunity to respond to the IRB’s review.

4.0 Deadlines for PI Responses

4.1 The PI is given 45 days from the date of the IRB review letter to respond to the IRB’s review by submitting appropriately revised documents. If no response is received by the end of the 30-day period, the PI and Lead Coordinator (if applicable) are contacted by either phone or email to determine the status of their response.

4.2 Extensions are given for legitimate delays. Protocols or other items reviewed, but pending IRB approval, are not permitted to remain in a pending status indefinitely. On a case-by-case basis, PIs will be given an absolute deadline which, if not met, will require the study to be withdrawn or closed.

5.0 Review of PI Responses

5.1 The PI’s response is routed to the assigned IRB Administrator.

5.2 If the IRB required only minor, directed modifications, the IRB administrator serves as the designated reviewer and is authorized to review and determine the acceptability of the PI's response. The IRB Administrator will consult with the IRB Executive Chair/designee or IRB reviewers as necessary.

5.3 If the IRB required modifications/clarifications that are more than minor in nature (i.e., the submission was tabled), the PI’s response will be returned to the full IRB for re-review. If possible, the revised submission is assigned to both the IRB that performed
the initial review and the original primary and secondary reviewers.

5.4 If the IRB Executive Chair/designee determines that a PI’s response to the IRB review is inadequate, incomplete, or contains significant changes not initially reviewed by the IRB, he/she can refer the submission for review by the full IRB regardless of whether the initial submission was tabled.

6.0 IRB Approval Periods

6.1 IRB approval periods for protocols reviewed by the full IRB begin as of the date of the convened meeting (initial or continuing review). Approval periods cannot exceed one year, which is defined as 365 days from the date of IRB review or sooner if the IRB sets a more frequent continuing review date.

For example, if the IRB reviewed a study at the convened meeting on December 3, 2015 and the reviewer set an approval period of one year, IRB approval is valid until December 3, 2016. This means that IRB approval is in force until 11:59 p.m. December 2, 2016. As of midnight all research activity must cease unless IRB re-approval and full release has been granted or an exception is granted by the IRB Executive Chair/designee for currently enrolled subjects because it is in the best interest of those subjects.

6.2 IRB approval letters provided to PIs and the IRB database contain the following dates:
   A. Date of full Board review.
   B. Date all conditions set by the IRB were determined to be met and the study was granted final approval and release.
   C. Valid until date (i.e., 365 days or less from the date of full Board review).

6.3 If a PI fails to submit the Continuing Review application or respond to the IRB review letter in sufficient time to allow the IRB to complete its’ review and grant re-approval and full release before the end of the current IRB approval period, the protocol will be classified as “IRB approval expired”. The followings actions must follow:
   A. All research activities must stop all research activities involving human subjects, including enrollment of new subjects; continuation of research interventions, or interactions with currently participating subjects, and data analysis of identifiable private information.
   B. The IRB has the option to determine if it is in the best medical interest of currently enrolled subjects to continue participation in the trial. The IRB Executive Chair/designee has the authority to make this determination in behalf of the IRB.
   C. The IRB will notify the PI of this action by email.

7.0 Final IRB Approval Letter

7.1 The IRB final approval letter will document the following determinations:
   A. Compliance with applicable HHS and FDA regulations.
   B. Risk determination for the research
   C. Subpart B category for inclusion of pregnant women, neonates, and fetus: viable and non-viable (as applicable)
   D. Subpart C category for inclusion of prisoners (as applicable)
   E. Subpart D category for inclusion of children (as applicable)
   F. Waiver or alteration of the requirements for informed consent (as applicable)
   G. Waiver of the requirement for documentation of informed consent (as applicable)
8.0 Review by Other Organizational Committees

8.1 Before the IRB will grant final approval and release, the Organization has determined that the ORA must receive verification of approval or completion of review by the following committees/offices as applicable:

A. Pharmacy & Therapeutics Committee
B. Fred & Pamela Buffett Cancer Center Scientific Review Committee
C. Institutional Biosafety Committee
D. Radioactive Drug Research Committee
E. Conflict of Interest Committee
F. Sponsored Programs Administration/Contracts Office
G. Research Billing/Coverage Analysis Office

Administrative Approval:
Ernest D. Prentice, PhD. Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for using expedited review procedures for consideration of: 1) new research proposals, 2) continuing review of previously approved research, 3) minor changes in protocol, 4) minor complaints, and 5) non-serious noncompliance.

2.0 Policy

2.1 It is the policy of the Organization that expedited review will be conducted in accordance with HHS regulations at 45 CFR 46.110; FDA regulations at 21 CFR 56.110; and will satisfy the criteria for IRB approval described in HRPP policy #2.5. Expedited review will be conducted in accordance with the Common Rule for both federally and non-federally funded research with the exception of extended continuing review for non-federally funded research per HRPP policy #1.1, Sections 6.3B and C.

2.2 Protocols initially reviewed and approved by the expedited method must: 1) be no more than minimal risk; 2) involve only activities listed in one or more of the categories specified in the Federal Register (63 FR 60364-60367, November 9, 1998); and 3) meet all the criteria specified in HHS regulations 45 CFR 46.111, FDA regulations at 21 CFR 56.111 (as applicable), the HIPAA Privacy Rule (as applicable), and UNMC HRPP policies.

2.3 Expedited review will not be used for initial or continuing review of: 1) classified research, 2) research involving drugs or devices, 3) research involving prisoners, and 4) research where a breach of confidentiality would place subjects at legal, civil, financial, reputational, social, or other risk.

2.4 Minor changes in IRB-approved research during the period (of 1 year or less) for which approval is authorized qualify for expedited review in accordance with HRPP policy #2.4. Minor changes in the categories of research specified above in Section 2.3 may be reviewed on a case-by-case basis via expedited review.

2.5 Continuing review by the expedited method of previously approved protocols must: 1) qualify under 45 CFR 46.110; 21 CFR 56.110; and 2) be substantive and meaningful in accordance with OHRP guidance (November 10, 2010); and FDA guidance (1998 FDA Information Sheets).

2.6 Continuing review of research which has been previously approved by the full IRB is eligible for expedited review providing the research meets one of the 3 conditions specified in Category 8 (Federal Register, 63FR60364-60367, November 9, 1998). The IRB interprets the criteria in category 8 (condition c) that states “no subjects have been enrolled” to mean no subjects have ever been enrolled at any study site.

2.7 Continuing review of research permitted under category 9 will seldom be allowed by the IRB.

2.8 Expedited review of complaints which are considered minor, unexpected incidents involving no more than minimal risk to subjects or others, and noncompliance which is not serious will be reviewed in accordance with HRPP policies #8.3 and 8.5.
2.9 The standard requirements for informed consent will be applied to all studies undergoing expedited review.  

*Note:* See HRPP policies #5.1, 5.2, 5.3, 5.4, 5.5, and 5.6 for further information related to the requirements for informed consent.

### 3.0 Definitions

#### 3.1 Expedited Review:
Expedited review is a method of review of research involving human subjects by the IRB Executive Chair or by one or more experienced reviewers designated by the Chair from among members of the IRB in accordance with the requirements set forth in 46 CFR 46.110; 21 CFR 56.110.

#### 3.2 Minimal Risk:
Minimal risk is defined under HHS regulations at 45 CFR 46.102(i), and FDA regulations at 21 CFR 56.102(i) with the parenthetical Organizational clarifications added, as “… the probability (of occurrence) and magnitude (seriousness) of harm or discomfort (e.g., physical, psychological, social, economic, legal) anticipated in the research are not greater than those ordinarily encountered in daily life (of the average person in the general population) or during the performance of routine physical or psychological examinations or tests.”

### 4.0 Expedited Review Categories

The following categories of research may be eligible for review through the expedited review procedure when the proposed research involves no more than minimal risk to subjects. Inclusion of research activities on the list eligible for expedited review does not mean the activity is necessarily minimal risk.

*Note: The Organization has elected not to use expedited review for studies which involve drugs or devices. Therefore expedited categories 1a, 1b, and 9 below do not apply per HRPP policies #6.1 and #6.2.*

1. Clinical studies of drugs and medical devices only when condition (a) or (b) is met:
   (a) Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)

   (b) Research on medical devices for which:
   (i) An investigational device exemption application (21 CFR Part 812) is not required; or
   (ii) The medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:
   (a) From healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or

   (b) From other adults and children\(^2\), considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.
(3) Prospective collection of biological specimens for research purposes by noninvasive means.

*Examples:*
(a) Hair and nail clippings in a nondisfiguring manner;
(b) Deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction;
(c) Permanent teeth if routine patient care indicates a need for extraction;
(d) Excreta and external secretions (including sweat);
(e) Uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gum base or wax or by applying a dilute citric solution to the tongue;
(f) Placenta removed at delivery;
(g) Amniotic fluid obtained at the time of rupture of the membrane prior to or during labor;
(h) supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques;
(i) Mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings;
(j) Sputum collected after saline mist nebulization.

(4) Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.)

*Examples:*
(a) Physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject’s privacy;
(b) Weighing or testing sensory acuity; (c) magnetic resonance imaging;
(d) Electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, Doppler blood flow, and echocardiography;
(e) Moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

(5) Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis). (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(4). This listing refers only to research that is not exempt.)

(6) Collection of data from voice, video, digital, or image recordings made for research purposes.

(7) Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (NOTE: Some research in this category may be exempt from the HHS
regulations for the protection of human subjects. 45 CFR 46.101(b)(2) and (b)(3). This listing refers only to research that is not exempt.)

(8) Continuing review of research previously approved by the convened IRB as follows:
(a) Where: (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or
(b) Where no subjects have been enrolled and no additional risks have been identified; or
(c) Where the remaining research activities are limited to data analysis.

(9) Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) above do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified

5.0 Procedures

5.1 Appointment of Designated Expedited Reviewers
A. No IRB member is permitted to serve as an expedited reviewer until they have served on the IRB for at least 1 year and has been judged by the IRB Executive Chair to be sufficiently qualified and experienced to serve as an expedited reviewer, i.e., the reviewer must have:

1) An acceptable level of knowledge about the area of research being reviewed.
2) An understanding of the categories of research that qualify for expedited review.
3) The ability to apply the IRB approval criteria and determine conditions required for IRB approval.
4) An absence of a COI in accordance with HRPP policy #1.6 and verified on the IRB Review Checklist: Full and Conditional Approval.

B. The IRB Executive Chair will normally designate qualified IRB Administrators who are a voting member of the IRB to serve as expedited reviewers in their area of expertise and responsibility. The IRB Administrator must be experienced and preferably, be a Certified IRB Professional (CIP). The assigned IRB Administrator will consult the IRB Executive Chair and other IRB members as necessary.

C. The IRB Administrator, in consultation with the IRB Executive Chair will, as necessary, refer the expedited review to other experienced IRB members.

D. When more than one expedited reviewer has been appointed, they must agree on the review. If a disagreement arises which cannot be resolved, the proposal must be referred for full IRB review.

5.2 Expedited Review Procedures
A. All IRB applications are submitted to the ORA and processed in accordance with HRPP policy #2.1.
B. The designated Expedited Reviewer will receive and review all documentation that the full IRB would normally receive for an initial review, continuing review, Request for Changes, and other actions. The Expedited Reviewer will also have full access to view all documents (including any changes previously approved by the IRB) online through RSS (https://net.unmc.edu/rss), in accordance with HRPP policy #3.3, Section 3.5.

C. The Expedited Reviewer will use the IRB Review Checklist: Full and Conditional Approval to determine and document that the criteria for IRB approval of research specified in 45 CFR 46.111 and 21 CFR 56.111 and HRPP requirements have been or continue to be met (HRPP policy #2.5).

D. The Expedited Reviewer will conduct the review with the same depth as that which would occur if the research was referred to the full IRB.

E. The Expedited Reviewer will determine the IRB approval period based upon: 1) the nature of the research, 2) a history of noncompliance, and 3) or other factors which warrant review of the protocol more often than annually. The approval period will be documented in the IRB records and conveyed to the PI.

F. The Expedited Reviewer will determine which projects need verification from sources other than the PI that no material changes have occurred in the research since the previous IRB review.

G. The Expedited Reviewer will determine that the ICF(s)/information sheets(s) are accurate and complete.

H. When the PI is the lead researcher of a multi-site trial, the Expedited Reviewer will evaluate whether the management of information to the protection of human subjects is adequate, such as reporting of unanticipated problems, interim results, and protocol modifications.

I. The Expedited Reviewer, in consultation with the IRB Executive Chair, will determine which projects should have a third party observe the consent process.

J. Any significant new findings that arise from the review process and that might relate to a subject’s willingness to continue participation in the study will be reported to subjects.

K. The Expedited Reviewer, in consultation with the IRB Executive Chair, will determine which projects require an audit of research records.

L. The Expedited Reviewer retains the right to refer any protocol for review by the full IRB. However, it should be noted that the reviewers may not disapprove the research. A research activity may be disapproved only after full IRB review.

6.0 Expedited Review Actions
The actions that can be taken by the Expedited Reviewer for initial review, continuing review, Requests for Change, minor complaints, and non-serious noncompliance are described on the appropriate IRB Review Checklist: Full and Conditional Approval.

6.1 Final approval and full release; initiation of the research is authorized.
All of the criteria for IRB approval are satisfied and no changes are required.
6.2 **Conditional approval; final IRB approval and full release contingent upon IRB Expedited Reviewer/designee acceptance of specified modifications and/or submission of additional documents**

All of the criteria for IRB approval are satisfied. The IRB requirements for final approval and release are considered minor and not substantive in nature.

6.3 **Refer to full IRB for review**

The protocol contains significant scientific, regulatory, or ethical problems/concerns that warrant review by the full IRB.

7.0 **Development of IRB Expedited Review and Final Approval Letters**

7.1 Expedited IRB review letters (for initial, continuing review and Requests for Change) are developed by the IRB Administrators in consultation with the IRB Executive Chair (as necessary).

7.2 IRB review letters must be written in a clear, explanatory, and facilitative fashion in order to assist PIs in understanding the rationale for any IRB concerns, clarifications and mandated changes to the application and ICF(s)/information sheet(s).

7.3 The IRB review letters will clearly document the determinations of the Expedited Reviewer, as referenced above in Sections 5.2 of this policy, including:

A. The decision to approve, disapprove, or require modifications.
B. List any modifications/clarifications required by the Expedited Reviewer.

7.4 Signature authority is granted to the Expedited Reviewer in accordance with *HRPP policy #1.16*.

8.0 **Deadlines for PI Responses**

8.1 The PI is given 45 days from the date of the IRB review letter to respond to the IRB's review by submitting appropriately revised documents. If no response is received by the end of the 30-day period, the PI and Lead Coordinator (if applicable) are contacted by either phone or email to determine the status of their response.

8.2 Extensions are given for legitimate delays. Protocols or other items reviewed, but pending IRB approval, are not permitted to remain in a pending status indefinitely. On a case-by-case basis, PIs will be given an absolute deadline which, if not met, will require the study to be withdrawn or closed.

9.0 **Review of PI Responses**

9.1 The PI's response is routed to the assigned IRB Administrator.

9.2 The IRB Administrator will review and determine the acceptability of the PI's response, and will consult with the IRB Executive Chair as necessary.

10.0 **Final IRB Approval Letter**

10.1 The IRB final approval letter will document the following determinations:

A. Compliance with applicable HHS and FDA regulations
B. Verification that the research is classified as minimal risk
C. The applicable expedited review category
D. Subpart B category for inclusion of pregnant women
E. Subpart D category for inclusion of children (as applicable)
F. Waiver or alteration of the requirements for informed consent (as applicable)
G. Waiver of the requirement for documentation of informed consent. (as applicable)

11.0 IRB Approval Periods

11.1 IRB approval periods for protocols reviewed by the expedited method begin as of the date of completion of the review (initial or continuing), which is the date of the review letter. Approval periods cannot exceed one year which is defined as 365 days from the date of IRB review. IRB approval therefore expires on the 366th day or sooner if the expedited reviewer sets a more frequent continuing review date.

For example, if expedited review was completed on February 17, 2011, and the reviewer set an approval period of one year, IRB approval is valid until February 17, 2012. This means that IRB approval is in force until 11:59 pm February 16, 2012. As of midnight all research activity must cease unless IRB re-approval and full release has been granted. Approval of a Request for Change does not alter the IRB approval period.

11.2 If a PI fails to submit the Continuing Review application or respond to the IRB review letter in sufficient time to allow the IRB to complete its' review and grant re-approval and full release before the end of the current IRB approval period, the protocol will be classified as “IRB approval expired”.

12.0 Documentation of Expedited Review

12.1 The IRB Review Checklist: Full and Conditional Approval must be completed and maintained in the protocol file. This checklist will specify: a) the category of research under which the protocol qualifies, b) the risk level as being no more than minimal risk, and c) the IRB approval criteria are satisfied.

12.2 IRB members and the IO are advised via electronic distribution of the minutes of all actions reviewed and approved by the expedited review procedure.

12.3 Any IRB member can request access to the complete study file and can make any concerns known at the full IRB meeting. Even if a protocol, or an amendment, has been approved using the expedited review procedure, the full IRB can require modification of the protocol and/or ICF(s). Additionally, the full IRB can suspend the study or halt accrual if warranted.

13.0 Review by Other Organizational Committees

13.1 Before the IRB will grant final approval and release, the Organization has determined the ORA must receive verification of approval or completion of review by the following committees/offices as applicable:

A. Fred & Pamela Buffett Cancer Center Scientific Review Committee
B. Conflict of Interest Committee
C. Sponsored Programs Administration/Contracts Office
D. Research Billing/Coverage Analysis Office

ADMINISTRATIVE APPROVAL:
Ernest D. Prentice, PhD Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for IRB review of changes in previously approved research.

2.0 Policy
It is the policy of the Organization that any proposed major or minor change in a research activity must be reviewed and approved by the IRB prior to implementation in accordance with the requirements of 45 CFR 46.103(b)(4); 21 CFR 56.108(a)(4) except when: 1) a change is necessary to eliminate an apparent immediate hazard to the subject(s), or 2) a subject needs to be advised immediately of significant new information. Administrative changes do not require IRB review and can, accordingly, be approved by ORA.

3.0 Definitions
3.1 Major: A major change must be reviewed by the full IRB when the change meets one or more of the following criteria:
A. The change includes an intervention(s) which is classified as greater than minimal risk.
B. Multiple interventions are added to the protocol which increases the burden and/or time requirements imposed upon the subject.
C. A vulnerable subject population is added.
D. The eligibility criteria are either broadened or narrowed.
E. The ICF is modified to include substantive changes.
F. Any change determined by the IRB Executive Chair to warrant full Board review.

Examples of major changes include: a) adding a drug, changing dosages or frequency of drug administration, revising eligibility requirements, and b) substantive revisions of the ICF (e.g., addition of risks, revision of a risk statement, or inclusion of other information relevant to the subject’s willingness to continue participation in the research).

3.2 Minor: A minor change may be eligible for expedited review. The change must involve:
A. No more than minimal risk to the subject in accordance with the definition of minimal risk per HRPP policy #2.3, section 3.2, and/or
B. The proposed change falls into expedited review categories 1-7.

Examples of minor changes include: a) the addition of study personnel, b) blood draw where a small volume of blood is taken from a healthy subject, c) the addition of magnetic resonance imaging, electrocardiography, or standard psychological tests, and d) revisions of the ICF which are not substantive.

3.3 Administrative: To be classified as an administrative change, one of the following criteria must be met: 1) the proposed change has no impact on human subject protection, or 2) the proposed change is necessary to clarify or provide only editorial updates to the protocol and/or ICF. These changes can be reviewed and approved by IRB administrators/staff in consultation with the IRB Executive Chair as necessary.

Examples of administrative changes include: changes in telephone numbers, deletion of study personnel, correction of typographical errors, or minor administrative changes in the protocol by the sponsor.
4.0 Procedures

4.1 The PI must submit a Request for Change (RFC) in accordance with HRPP policy #2.1.

4.2 The RFC will be processed for review in accordance with HRPP policy #2.1.

4.3 Administrative changes are reviewed and processed by an IRB Administrator or ORA staff.

4.4 The procedure for review and approval via expedited review or full IRB review is in accordance with HRPP policies #2.2 and 2.3.

4.5 The date of continuing review is not changed based on the date of IRB approval of a RFC.

5.0 Changes in a research activity requiring immediate implementation

5.1 If the change is required to eliminate an apparent, immediate hazard to the subject(s), the PI is authorized to implement the change without IRB approval in accordance with 45 CFR 46.101(b)(4); 21 CFR 56.108(a)(4).

5.2 The ORA must be notified as soon as possible, but no later than two (2) business days from the time the change was initiated.

A. If the change was initiated for all subjects, the RFC, the revised IRB application and other required documents must be submitted in accordance with this policy.

B. If the change was initiated for a single subject, the Single Subject Protocol Deviation (SSD) must be completed and submitted in accordance with HRPP policy #8.1.

5.3 The full IRB will be notified of all changes implemented without prior IRB approval and will take any additional actions necessary to protect human subjects.

6.0 Provision of new information to subjects which requires immediate implementation

6.1 If a change involves immediate disclosure of significant new information (e.g., an important new risk) which is essential to a subject’s decision to continue participating in research, the investigator is authorized to implement the change without IRB approval in accordance with 45 CFR 46.101(b)(4); 21 CFR 56.108(a)(4) and HRPP policy #5.1, Section 12.3.

6.2 The ORA must be notified as soon as possible, but no later than two (2) business days from the time the change was initiated in accordance with HRPP policy #5.1, Section 12.4. No new subjects can be accrued without IRB approval of a revised ICF that includes the relevant information.

6.3 If a RFC is submitted to the ORA which includes a revised ICF or an addendum ICF containing significant new information involving risk which is germane to a subject’s decision to continue participating in the research and the change is not eligible for expedited review, the ORA will submit the RFC for review at the earliest possible full Board meeting.

6.4 The full IRB will be notified of all changes implemented without prior IRB approval and will take any additional actions necessary to protect human subjects.
POLICY #2.4
IRB REVIEW OF CHANGES IN PREVIOUSLY APPROVED RESEARCH
PAGE 3 OF 3

Ernest D. Prentice, PhD.  Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD    IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for the criteria for IRB approval for both expedited review and review by the full IRB.

2.0 Policy
It is the Organization’s policy that IRB review and approval of human subject research, both initially and on an on-going basis, will comply fully with the requirements contained in HRPP policy #1.1.

3.0 Criteria for IRB Approval
Each of the following criteria for IRB approval must be satisfied in full accordance with applicable federal regulations and HRPP policies which contain greater detail about how the IRB interprets and applies these criteria. The criteria must be met before the IRB can grant approval of any submission (e.g., Continuing Review, Request for Change, Adverse Event Report) by expedited review or full IRB review.

3.1 Risks to subjects are minimized: (i) By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and (ii) whenever appropriate, by using procedures, already being performed on the subjects for diagnostic or treatment purposes.

A. The IRB will:
   1) Ensure that the PI and other study personnel have the necessary qualifications, experience and medical licensure.
   2) Evaluate the research design in order to ensure that it is both sound and does not unnecessarily expose subjects to risk.
   3) Assess whether risks are minimized to the greatest extent possible by ensuring that the research uses procedures already being performed on the subjects for diagnostic or treatment purposes and/or alternative procedures are used that have less risk.

B. The IRB’s peer review requirements and hospital credentialing in advance of IRB review will facilitate IRB assessment that risks to subjects are minimized.

Note: Minimal risk means “The probability (of occurrence) and magnitude (seriousness) of harm or discomfort (e.g., psychological, social, legal, economic) associated with the research are not greater than those ordinarily encountered in daily life (of the average person in the general population) or during the performance of routine physical or psychological examinations or tests.”

Minimal risk is used to define a threshold of anticipated harm or discomfort associated with the research that is low. The evaluation of whether or not research involves minimal risk must take into consideration not only the risk associated with interventions (e.g., a blood draw), but also the risk of violating the privacy of subjects in the case of unauthorized use or disclosure of PHI. In this case, the determination of whether the research involves more than minimal risk is also based upon a) the adequacy of the plan to protect subject identifiers from improper use and disclosure and b) the adequacy of the plan to destroy the identifiers at the earliest opportunity.

If the research does not qualify as minimal risk, the IRB will determine whether the research should be classified as greater than minimal or significant. Any increase in
3.2 Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result. In evaluating the risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

A. The IRB will only consider those risks and benefits that may result from the research as distinguished from risks and benefits of therapies (or other interventions) the subjects would receive if not participating in the research.

B. The IRB will carefully evaluate the protocol in order to identify all risks. A risk is a potential harm (injury) associated with the research that a reasonable person in the subject position would likely consider significant. Risks can be generally categorized as physical, psychological, sociological, economic, and legal.

C. In evaluating the risk(s) of the research, the IRB will use the criteria that the risk(s) must be “reasonably foreseeable”. This means data exists which indicate there is a reasonable possibility that the subject could experience the harm described. It does not mean that every known risk associated with each research intervention must be addressed. It is also important to consider when a harm may be irreversible (i.e., not amenable to treatment).

D. The IRB will assess the anticipated benefits to subjects (if any) and the importance of the knowledge that may be reasonably expected to result from the research. In making this assessment, the IRB will consider the background section, the literature citations, and other sections of the IRB application and other related materials (e.g., detailed protocol) which support the PI’s statement of anticipated benefits. The IRB does not classify financial compensation to the subject as a “benefit”.

E. The IRB will assess the risk/benefit relationship of the research and ensure that it is both acceptable and that subjects are not disadvantaged by participating in research as opposed to choosing available alternatives which may be more advantageous.

3.3 Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.

A. The IRB will assess the IRB application and other related materials (e.g., recruitment advertisements) in order to ensure that the selection of subjects is equitable with respect to age, gender, reproductive status, ethnicity, inclusion of vulnerable populations and any other factors that affect the equitable selection of
subjects. No group should receive a disproportionate share of the benefits of the research or bear a disproportionate burden.

B. In making this assessment the IRB will evaluate the:
1) Purpose of the research.
2) Setting in which the research occurs
3) Whether prospective subjects will be vulnerable to coercion or undue influence
4) The selection (inclusion/exclusion) criteria
5) Scientific and ethical justification for inclusion of vulnerable populations
6) Scientific and ethical justification for excluding classes of persons who might benefit from the research.
7) Subject recruitment and enrollment procedures
8) The influence of compensation to participants

C. The IRB’s assessment of equitable subject selection will be made at the time of initial review, continuing review, and changes in protocol.

3.4 Informed consent will be sought from each prospective subject or the subject’s legally authorized representative, in accordance with, and to the extent required by the Federal Regulations.

A. The IRB will review the IRB application and ICFs in order to determine that legally effective informed consent will be sought from each prospective subject or the subject’s Legally Authorized Representative (LAR). In addition to ensuring that the ICF contains all required elements of informed consent, the Board must also determine there is an appropriate process of informed consent in consideration of the nature of the research, risks associated with the research, and the characteristics of the subject population.

B. The IRB will determine which projects should have a third party observe the consent process.

3.5 Informed consent will be appropriately documented, in accordance with, and to the extent required by the Federal Regulations.

A. The IRB will review the IRB application and ICFs in order to determine that all individuals involved in the obtainment and documentation of informed consent have the necessary expertise as well as sufficient knowledge about the protocol and IRB consent requirements.

B. Under certain circumstances, the IRB may determine that obtainment and documentation of informed consent by a physician or dentist will be required for some trials.

3.6 When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

A. The IRB will review the IRB application and other related materials (e.g., detailed protocol) in order to determine that the safety monitoring plan makes adequate provision for monitoring the involvement of subjects and the collection of data to ensure the safety of subjects.
B. The overall elements of the monitoring plan will vary depending on the potential risks, complexity, and nature of the research. These may vary from monitoring by the PI in a small, low risk study to the establishment of an independent data and safety monitoring board (DSMB).

C. The IRB will also determine whether the research requires review more often than annually based upon:
   1) The nature of the research.
   2) History of noncompliance.
   3) Other factors which warrant review of the protocol more often than annually.

D. The approval period will be documented in the IRB records and conveyed to the PI.

E. The IRB will determine which projects need verification from sources other than the PI that no material changes have occurred in the research since the previous IRB review.

F. The IRB will determine which projects require an audit of research records.

3.7 When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

A. Privacy refers to persons and their interest in controlling access to themselves. In order to ensure protection of subjects privacy, the IRB will apply the following criteria:
   1) The methods used to identify and contact prospective subjects is acceptable.
   2) The settings in which the individual will participate in the consent process as well as the research adequately protect privacy.
   3) The personnel involved in the research are appropriate in consideration of their responsibilities.
   4) All necessary procedures are in place during the research to protect privacy.

B. Confidentiality refers to protecting data. In order to ensure there is an appropriate plan to maintain confidentiality and minimize the possibility that information will be inappropriately disclosed, the IRB will apply the following criteria:
   1) The reason(s) for disclosing data to individuals, sponsors or other organizations is justified.
   2) The procedures for securing and transmitting data are acceptable.
   3) The potential harm that may result from inappropriate disclosure of research data is minimized.

3.8 When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.
A. The IRB will review the characteristics of the proposed subject population in consideration of:
1) The nature and risks of the research.
2) Whether the subjects are likely to be vulnerable to coercion, undue influence, or more susceptible to risk.

B. The IRB will ensure that additional safeguards are included in the protocol in order to fully protect the rights and welfare of vulnerable subjects in accordance with HRPP policy #1.1.

**Administrative Approval:**
Ernest D. Prentice, PhD.  Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD  IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for determining if a research proposal is eligible for exemption under 45 CFR 46.101(b) and 21 CFR 56.104(d), with appropriate protections in place for research subjects.

2.0 Policy
2.1 It is the policy of the Organization that all proposed exempt research must be independently reviewed and approved by the ORA prior to initiation.

2.2 Investigators are not permitted to make a final determination of the exempt status of research.

2.3 Exempt research must be conducted in accordance with sound ethical standards and all subjects must be provided with appropriate protection of their rights and welfare.

2.4 Exempt research is approved for a maximum of 5 years and continuing review is not required. Any changes in the research must be submitted to the ORA for review and approval.

3.0 Categories of exemption
3.1 Category 1: Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as 1) research on regular or special education instructional strategies; or 2) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods. (45 CFR 46.101(b)(1))

Per HRPP policy, all of the following requirements must be met to determine eligibility under Category 1:

a) The research is conducted in a commonly accepted educational setting (e.g., public or parochial schools, YMCA,YWCA, youth clubs).

b) The research involves normal educational practices (e.g., comparison of instructional techniques).

c) The study procedures do not represent a significant deviation in time or effort requirements from those educational practices already existent at the study site.

d) The study procedures involve no increase in the level of risk or discomfort attendant normal, routine educational practices.

e) The study procedures do not involve sensitive subjects (e.g., sex or substance abuse education).

f) Provisions are made to ensure the existence of a non-coercive environment for those students who choose not to participate.

g) The school or other institution grants written approval for the research to be conducted.

h) Informed consent is obtained from subjects or their LAR unless a waiver is granted by the IRB Executive Chair/designee.
Note: Educational projects that do not meet the above-listed conditions are not exempt and must undergo expedited or full board review.

3.2 **Category 2:** Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior, unless: (i) the information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and (ii) any disclosure of the human subjects’ responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects’ financial standing, employability, or reputation. (45 CFR 46.101(b)(2))

Note: Comprehensive cognitive or diagnostic tests that require significant effort on the part of the subject and/or are considered invasive are not exempt.

Note: Sensitive survey research involving sensitive or highly personal aspects of the subject’s behavior, life experiences or attitudes (e.g., chemical substance abuse; sexual activity or attitudes; sexual abuse; criminal behavior; sensitive demographic data; detailed health history) are not exempt regardless of whether or not there are any subject identifiers.

The principal determination for sensitivity is whether or not the survey research presents a potential risk to the subject in terms of possible precipitation of a negative emotional reaction. An additional risk consideration is whether or not there is a risk associated with a breach of confidentiality. With respect to potential psychological risk associated with a survey, the presence or absence of subject identifiers is not necessarily a consideration since the risk may be primarily associated with the sensitive nature of the survey as opposed to being dependent upon confidentiality. Subject identifiers do, however, become a factor when confidentiality is an issue.

Note: Survey procedures involving children is not exempt under category 2.

Note: Observation of public behavior under Category 2 applies only to behaviors that are widely available to normal observation by members of the general public and there in no expectation of privacy on the part of the subject. These behaviors would include for example, walking down a public street or attending a football game. Classroom behaviors are usually not public behavior since access to classrooms is usually restricted to teachers, students and staff.

Observation of public behavior which involves children is only exempt when the investigator(s) do not participate in the activities being observed.

3.3 **Category 3:** Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under # 2 above, if: (i) the human subjects are elected or appointed public officials or candidates for public office, or (ii) federal statute(s) require(s), without exception, that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter. (45 CFR 46.101(b)(3))

Note: Sensitive survey research involving sensitive or highly personal aspects of the subject’s behavior, life experiences or attitudes (e.g., chemical substance abuse; sexual activity or attitudes; sexual abuse; criminal behavior; sensitive demographic data;
detailed health history) and observational research are not exempt under category 3 regardless of whether or not there are any subject identifiers.

3.4 **Category 4:** Research involving the collection or study of existing data, documents, and records, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects. (45 CFR 46.101(b)(4))

Note: This category applies only to research involving existing non-medical data, documents, and records where the information recorded by the investigator for research purposes from the initial data set is de-identified (i.e., the identity of the subjects cannot be readily identified by the investigator). Existing means that all the information used in the research is “on the shelf” as of the date of ORA approval of the exemption and no additional information will be collected for research purposes.

Note: If, during the course of an exempt project under category 4, there is a need to utilize additional available resources specified above which did not exist as of the date of the initial IRB application, the amended protocol will no longer qualify for exemption. Use of the additional resources may be approved in accordance with 45 CFR 46.110, expedited category 5. In this case, informed consent is required unless waived by the IRB under 45 CFR 46.116(d).

Note: If the research involves the use of existing medical data (e.g., the medical record), the application for Medical Records Research must be completed.

3.5 **Category 5:** Research and demonstration projects which are conducted by or subject to the approval of department or agency heads, and which are designed to study, evaluate, or otherwise examine (i) public benefit or service, (ii) procedures for obtaining benefits or services under those programs, (iii) possible changes in, or alternatives to, those programs or procedures, or (iv) possible changes in methods or levels of payment for benefits or services under those programs, providing there is no statutory requirement that the project be reviewed by an Institutional Review Board (IRB) [Federal Register, 48 FR 9266-9270, March 4, 1983]. (45 CFR 46.101(b)(5))

Note: Research which is exempt under Category 5 must meet the following requirements:

a) The program under study must deliver a public benefit (e.g., financial or medical benefits as provided under the Social Security Act) or service (e.g., social, supportive, or nutrition services as provided under the Older Americans Act). State programs are not included in this exemption unless the Federal Government has contracted or otherwise entered into an agreement with the State to evaluate a program.

b) The research or demonstration project must be conducted pursuant to specific federal statutory authority.

c) There must be no statutory requirement that the project be reviewed by an Institutional Review Board (IRB).

d) The project must not involve significant physical invasions or intrusions upon the privacy of participants.

3.6 **Category 6:** Taste and food quality evaluation and consumer acceptance studies, i) if wholesome foods without additives are consumed, or ii) if a food is consumed that
contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe by the Food and Drug Administration, or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture. (45 CFR 46.101(b)(6))

Note: This category is generally restricted to research involving normal, wholesome foods where the source of the food and the volume of the food consumed are not unusual. This category may not apply to consumer evaluation or acceptance of high fat, high caloric fast foods which are consumed as part of a research project.

3.7 FDA Category (d): Taste and food quality evaluations and consumer acceptance studies, if wholesome foods without additives are consumed or if a food is consumed that contains a food ingredient at or below the level and for a use to be safe, or agricultural, chemical, or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture. (21 CFR 50.104(d))

Note: FDA ensures the safety and wholesomeness of almost 80% of the US food supply except meat, poultry and some egg products through field inspections monitoring and investigations of food borne illness. This category, like category 6 under 45 CFR 46.101(b) is generally restricted to research involving normal wholesome foods without additives such as chemical preservatives or food coloring.

4.0 Research that is not exempt

4.1 Research involving children where research involves survey or interview procedures or observation of public behavior that qualify under 45 CFR 46.101(b)(2) and the investigator(s) will participate in the activities being observed. Note: If the investigator(s) do not participate in the activities being observed then the research can be exempted from the requirements of the federal regulations.

4.2 Research involving prisoners or

4.3 Research which is FDA-regulated under 21 CFR 56.104 Note: Emergency use of a test article is exempt from the requirements of IRB review, provided that such emergency use is reported to the IRB within 5 working days. Any subsequent use of the test article at the Organization is subject to IRB review (see HRPP policy #6.4.

4.4 Research involving vulnerable populations as determined by the designated IRB Administrator.

4.5 Research involving sensitive behaviors or topics.

4.6 Research involving photographing, audiotaping or videotaping subjects during the research if the subject is placed at any risk.

4.7 Research involving deception or withholding of information from the subject which would be material to their decision to participate in research.

4.8 Research involving more than minimal risk to subjects.
4.9 Other research as determined by the designated IRB Administrator.

5.0 Procedures

5.1 The Organization utilizes the following applications for proposed exempt research:

A. **Exempt Educational, Behavioral, and Social Science Research**: This application is used for the following categories of research which qualify for exemption:
   1. Categories 1-3
   2. Category 4: Non-medical records research only
   3. Categories 5-6:
   4. 21 CFR 56.104(d)

B. **Human Biological Materials Research**: This application is used for the following category of research which qualifies for exemption under 45 CFR 46.101(b)(4) (research involving existing pathological specimens or diagnostic specimens). 
   *Note: This application is also used for research involving human biological material that is non-exempt.*

C. **Medical Records Research**: This application is used for the following category of research which qualifies for exemption under 45 CFR 46.101(b)(4), research involving existing medical records. 
   *Note: This application is also used for research involving medical records that is non-exempt.*

5.2 Protocols which appear to be eligible for exemption under the categories specified at 45 CFR 46.101(b); 21 CFR 56.104(d) (if applicable) are reviewed by a designated IRB Administrator. This individual will have no direct involvement in the activity he or she is reviewing or any other conflict of interest that would compromise objectivity.

5.3 The IRB Administrator, in consultation, as necessary, with the IRB Executive Chair/designee, will make the final determination of exempt status.

5.4 The IRB Administrator will determine whether appropriate protections of subjects are in place and obtain additional information and/or a revised application as necessary.

5.5 The IRB Administrator will complete the *Exempt Research Checklist* which includes the category under which the research qualifies for exemption. This checklist will be maintained in the electronic file.

5.6 The determination will be communicated to the PI and Coordinator(s) via letter, email and/or the electronic file.

5.7 Projects determined not to be exempt may be referred for expedited review provided the project qualifies under the categories specified at 45 CFR 46.110 or 21 CFR 56.110. 
   *Note: If the Exempt Educational, Behavioral, and Social Science Research Application was used, the PI will be instructed to fill out the Behavioral and Social Science Research Application in order to provide the IRB with the information needed to perform a thorough review to ensure that the IRB approval criteria at 45 CFR 46.111 have been satisfied.*

5.8 If *Behavioral and Social Science Research Application* is submitted and subsequently determined to be exempt, the PI is notified accordingly.
5.9 The Organization reserves the right to refer any research proposal which technically qualifies for exemption to the full IRB when there are concerns which merit consideration at a convened meeting. The full board, in turn, will determine whether the research should be exempted or not.

6.0 Criteria For Approval Of Exempt Research

6.1 The research must qualify for exemption under the categories specified at 45 CFR 46.101(b) or 21 CFR 56.104(d).

6.2 The research holds out no more than minimal risks to subjects.

6.3 Selection of subjects is equitable.

6.4 If there are recording of identifiable information, there are adequate provisions to maintain the confidentiality of the data.

6.5 The rights and welfare of research subjects are adequately protected.

6.6 If there are interactions with subjects, the IRB has determined there is a process of informed consent that will disclose such information as: 1) the activity involves research; 2) a description of the procedures; 3) a statement that participation is voluntary; 4) Name and contact information for the researcher; and there are adequate provisions to maintain the privacy interest of subjects.

7.0 Actions

7.1 Approval and full release; initiation of the research is authorized.
The IRB Administrator has not required modification or clarification in the protocol, IRB application, and/or other documents. The protocol qualifies for exemption under 45 CFR 46.101(b) or 21 CFR 56.104(d) and contains appropriate protections for the rights and welfare of research subjects. The investigator will be notified of the approval in writing and is authorized to start the study.

7.2 Conditional approval; final ORA approval and full release contingent upon IRB Administrator acceptance of specified modifications and/or submission of additional documents.
The investigator will be notified in writing as to the nature of the required modifications and/or submission of additional documents.

7.3 Referred for expedited review
The protocol is referred for expedited review in accordance with the requirements of 45 CFR 46.110; 21 CFR 56.110.

7.4 Referred for full board review
Concerns have been identified which warrant review of the protocol by the full IRB.

8.0 Review by Other Organizational Committees

8.1 Before the IRB will grant final approval and release, the ORA must receive verification of approval or completion of review by the following committees/offices as applicable:
A. Fred & Pamela Buffett Cancer Center Scientific Review Committee
B. Conflict of Interest Committee
C. Sponsored Programs Administration/executed contracts office
 ADMINISTRATIVE APPROVAL:
Ernest D. Prentice, PhD.   Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD   IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization's requirements for determining the need for: 1) IRB review more often than annually, 2) increased monitoring, and 3) verification from sources other than the PI that no material changes have occurred since previous IRB review.

2.0 Policy
It is the policy of the Organization that all non-exempt research will be assessed at both initial and continuing review in accordance with the requirements set forth by HHS regulations at 45 CFR 46.103(b)(4), FDA regulations at 21 CFR 56.108(a)(2), and all applicable state and local laws.

3.0 Increased Monitoring and/or Interim Continuing Review
3.1 The following categories of research may require increased monitoring and/or more frequent continuing review as determined by the IRB:
   A. Studies that utilize highly toxic or dangerous treatments.
   B. Studies where there is an expectation of high morbidity and mortality due to the medical condition of the subjects.
   C. Studies whose design includes the use of placebos where there is an active alternative treatment, sham surgeries, or withholding psychiatric drugs during some point in the study.
   D. Studies where the Fred & Pamela Buffett Scientific Review Committee (SRC), or other equivalent scientific review body, has indicated the need for interim review or additional monitoring.
   E. Studies submitted by research teams with a history of non-compliance that warrant additional monitoring.

3.2 When the IRB determines the need for increased monitoring this may be accomplished by either: 1) submission of interim reports by the PI, or 2) auditing of PI records by the IRB Administrator/Compliance Coordinator and/or an IRB member(s). The PI will be notified of these requirements in writing.

3.3 If the IRB determines the need for more frequent continuing review the PI will be notified in writing and the IRB approval period will be set accordingly.

4.0 Verification from Sources Other than the Investigator
4.1 The following circumstances may require verification from sources other than the PI that no material changes have occurred since the previous IRB review:
   A. History of noncompliance.
   B. Recurrent delays in submitting amendments.
   C. High number of IRB approval expirations.
   D. Failure to respond to IRB review letters or other correspondence in a timely manner.
E. Research conducted at external sites where the UNMC IRB is the IRB of record.

4.2 When the IRB determines that verification from sources other than the PI is necessary the designated IRB Administrator and/or IRB member(s) will perform the necessary verification by conducting an audit.

ADMINISTRATIVE APPROVAL:
Ernest D. Prentice, PhD. Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for minimization of risk and data safety monitoring for non-exempt research.

2.0 Policy
It is the policy of the Organization that an appropriate plan must be in place for minimization of risk and data safety monitoring in consideration of the nature and risk level of the research. Appropriate monitoring may include a data safety monitoring plan (DSMP), as well as a Data Safety Monitoring Board (DSMB).

2.1 Data and Safety Monitoring Plan
A. The DSMP must be developed to fit the design and risk profile of the research. It should include, as appropriate, elements such as scheduled follow-up visits with the investigator/study personnel, laboratory tests and radiographs to assess toxicity and efficacy, frequency of data collection, frequency of review of cumulative safety data, withdrawal criteria, and stopping rules.

B. If a DSMB is not being used, the protocol must define statistical tests for analyzing the safety data to determine whether harm is occurring.

C. There are provisions for oversight of the safety data by either a DSMB or other monitoring such as external review by a sponsor appointed medical monitor or a CRO.

D. The IRB will evaluate the DSMP in order to ensure that it meets the needs of safety monitoring.

E. The IRB will determine if increased monitoring, interim continuing review, and verification from sources other than the investigator is required to minimize risk to the subjects (see HRPP policy #2.2).

2.2 Data Safety Monitoring Board
A. The IRB may determine that research also requires a DSMB if:
   1) The research is a NIH funded phase III randomized clinical trial.

   2) The research is a commercially sponsored multi-center Phase III clinical trial.

   3) The research is a PI-initiated clinical trial.
      Note: The Fred & Pamela Buffett Cancer Center DSMC reviews all investigator-initiated clinical cancer studies.

   4) The research involves use of highly toxic therapies and/or high risk interventions.

   5) The trial is blinded, has multiple participating sites, and is expected to enroll vulnerable populations.

   6) There are expected high rates of morbidity and mortality in the study population (related to either the expected natural history of disease progression or an aging study population).
7) High probability of early termination of the study (related to safety, futility or efficacy issues).

B. If a DSMB has been established by the sponsor, the IRB will ensure that the application indicates the frequency of reports to be provided to the IRB and that this is acceptable.

C. If a DSMB has not been established by the sponsor, the IRB may: 1) request that the sponsor establish a DSMB, or 2) accept the sponsor’s monitoring plan in lieu of a DSMB.

D. For investigator-initiated studies, if a DSMB is not already in place, the IRB may require the creation of an internal DSMB and may offer to assist the investigator in establishing such a board.

E. The Sponsor, or their agent of record (e.g., CRO), must provide the PI with DSMB reports as well as other routine or urgent reports which impact subject safety within thirty (30) days.

F. The PI is responsible submitting copies of all DSMB reports must be submitted to the IRB within five (5) business from receipt of the report.

G. If a report received by the PI contains information about risk which represents a serious threat to subject safety, the report must be submitted to the IRB within 24 hours via email.

H. If the DSMB or other monitoring determines there is immediate risk to subjects, the IRB will take action in accordance with HRPP policy #8.7.

Administrative Approval:
Ernest D. Prentice, PhD. Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for: 1) protection of privacy interests of research subjects/registry participants (hereafter referred to as participants) and 2) maintenance of confidentiality of data.

2.0 Policy
It is the policy of the Organization that: 1) the privacy interests of participants must be protected; 2) the confidentiality of data involving Protected Health Information (PHI) must be protected in accordance with HRPP policy #3.4; and 3) other non-PHI data must also be appropriately protected.

Note: Data may be found in written and paper documents and other physical media (e.g., CDs, tapes).

3.0 Definitions
3.1 Privacy is defined as having control over the extent, timing and circumstances of sharing oneself (i.e. a participant’s interest in controlling access to themselves).

Note: Privacy and confidentiality are not the same, although there are overlapping elements.

3.2 Private information is defined as information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public. For example, a medical record contains private information.

3.3 Protected Health Information (PHI) is defined as individually identifiable health information, whether oral or recorded in any medium, that: 1) is created or received by the Organization; and 2) relates to the past, present, or future physical or mental health or condition of an individual; the provision of health care to an individual; or the past, present, or future payment for the provision of health care to an individual.

3.4 Confidentiality refers to protecting data in order to ensure that it is not improperly divulged.

3.5 Anonymity means that the participant cannot be identified and, therefore, their participation is anonymous.

Note: Confidentiality and anonymity are not the same.

4.0 Procedures
4.1 Protection of Privacy
The IRB will review all applications to determine whether there are adequate provisions to protect the privacy interests of the participants. The greater the risk to privacy, the greater the need to have more stringent protections in place. During the course of review, the IRB will consider the nature and degree of risk to the privacy interests of the participants, as well as the participants’ expectations of privacy and make the following determinations:

A. The PI and other research personnel have ethical access to the participant’s private, identifiable information in accordance with HRPP policy #3.4.

B. The methods used to identify and contact potential participants are designed to minimize the risk to privacy.
C. The location where informed consent will be obtained is conducive to thoughtful decision-making on the part of the participant and their privacy interests.

D. No other persons are present during the informed consent process or during research activities unless the individual(s) is listed by name on the IRB application or is involved in the clinical care of the participant or to provide technical assistance. Other individuals can only be present with the consent of the participant.

E. The research activities are performed in as private of a place as possible.

F. The minimum amount of PHI or other personal information necessary to complete the study will be maintained.

4.2 Protection of Confidentiality

A. The IRB will review all applications to determine whether there are adequate provisions to protect the confidentiality of data. The greater the risk (i.e. harm associated with a breach of confidentiality), the greater the need to have more stringent protections in place.

B. During the course of review, the IRB will consider the:
   1) type of data maintained
   2) justification for sharing data with subject identifiers
   3) nature and degree of risk
   4) participants’ expectations of confidentiality

C. The PI and all other research personnel must comply with the following requirements, as applicable:
   1) Research/registry data must be physically secured from intrusion and theft. Data stored on a departmental shared drive is considered physically secure.
   2) Unique user identification and passwords must be utilized to access confidential data.
   3) ITS must have the ability to determine the identity of individuals who access research/registry data.
   4) Passwords must be formulated in order to adequately protect against unauthorized access and must be changed periodically in accordance with ITS requirements.
   5) An information custodian and system administrator must be assigned to databases.
      a) The information custodian is responsible for the “data” being created and maintained. This role may be assigned to the PI, coordinator, or other administrative/data personnel involved in the conduct of the study.
      b) The system administrator is responsible for the operating system used to support the data collection.

D. The PI must verify on the IRB application that only those with a “need to know” have access to the research data. If an individual leaves the Institution or transfers to
another position, that individual’s access to the research data must be removed promptly.

**E.** When the research data is no longer required, the data must be appropriately archived or destroyed (see [HRPP policy #3.5](#) for the requirements for record retention).

*Note: Simply reformatting the hard drive will not meet the destruction criteria. With forensic tools, hard drive data can be retrieved after a reformatting of the drive.*

**F.** Secure methods must be in place to transfer data between networks in order to ensure protection against introduction of viruses and worms.

**G.** When extracting data from systems for use within the Organization, the data must be stored securely.

1) No data may be extracted and shared with people not listed on the IRB application without the express approval of the IRB.

2) If data is extracted and stored on a mobile device (i.e., flash drive; laptops; PDA’s), it must be stored in a physically secured manner and the user must take additional security precautions such as encryption or password protection.

**H.** When research data containing confidential information is available via the internet, access must be granted through a secure technical method set in place by ITS.

*Note: Research data containing PHI cannot be placed on a public website as it is in violation of HIPAA Privacy Laws.*

**I.** A contingency plan for accessing data must be in place for those situations where physical problems prevent admittance to the building where the research computer is housed.

*For example, noxious fumes are found in the building and entrance is forbidden or a natural disaster has caused extensive damage to the building.*

**J.** If remote access to the research database is required by a sponsor or others not associated with the Organization, access must be accomplished by establishment of a Virtual Private Network (VPN) or secure web access. Direct inbound modems should never be used as they provide unsecured access to the network.

**K.** Transfers of information (files) outside of the Organization must meet information security guidelines. When files need to be transferred outside of the campus network, a secure file transfer methodology (as determined by the type of equipment and operating system used) must be used.

**L.** Workstations must have current operating system patches, Microsoft Office patches, and current anti-virus installed.

**M.** All operating and application software must be appropriately licensed thereby ensuring compliance with all copyright laws.

**N.** The IRB has the option to require the PI obtain a Certificate of Confidentiality when additional protections are required to guard disclosure of sensitive data.
ADMINISTRATIVE APPROVAL:
Ernest D. Prentice, PhD.  Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD    IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for ensuring the appropriate protections for use of Protected Health Information (PHI) in the following instances: 1) research preparation; 2) recruitment of subjects; 3) IRB-approved research protocol requiring the use of PHI; 4) IRB-approved data registries, and 5) research involving decedent’s PHI.

2.0 Policy
2.1 It is the policy of the Organization that investigator access to records containing PHI will comply with: 1) HHS regulations at 45 CFR 46.111(a)(7) and 45 CFR 164.512(i) (HIPAA Privacy and Security Act); 2) 21 CFR 11 (as applicable), 3) UNMC policies #6045, 6057, 6059, 6061, 6071; 4) UNMC Board of Regents Executive Memorandum No. 27 (HIPAA Compliance Policy), and 4) the need to ensure that the individual who will use the records has permitted access for research purposes.

2.2 All patients have a right to privacy which precludes the use of their records containing any PHI by an individual who does not have permitted access as defined in this policy.

2.3 Records containing PHI, in any form, are the property of the Organization. The PHI contained in the record is the property of the individual who is the subject of the record.

2.4 When using or disclosing PHI or when requesting PHI from another covered entity, the Organization must make reasonable efforts to limit protected health information to the minimum necessary to accomplish the research.

2.5 The Organization will use a compound authorization process for research where the HIPAA authorization is merged within the research ICF.

Note: PHI excludes education records covered by the Family Educational Rights and Privacy Act (FERPA) and employment records held by the Organization in its role as an employer.

3.0 Definitions
3.1 Protected Health Information (PHI):
A. PHI is individually identifiable health information, whether oral or recorded in any medium, that:
   1) Is created or received by the Organization; and
   2) Relates to the past, present, or future physical or mental health or condition of an individual; the provision of health care to an individual; or the past, present, or future payment for the provision of health care to an individual.

3.2 HIPAA Identifiers: PHI that includes the following direct identifiers of the individual or of relatives, employers, or household members of the individual:
   1) Names
   2) All geographic subdivisions smaller than a state, including street address, city county, precinct, zip code, and their equivalent geocodes, except for the initial three digits of a zip code, if, according to the current publically available data from the Bureau of the Census:
      a) The geographic unit formed by combing all zip codes with the same three initial digits contains more than 20,000 people, and
b) The initial three digits of a zip code for all such geographic units containing 20,000 or fewer people are changed to 000.

3) All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death; and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older;

4) Telephone numbers
5) Fax numbers
6) Electronic mail addresses
7) Social security numbers
8) Medical record numbers
9) Health plan beneficiary numbers
10) Account numbers
11) Certificate/license numbers
12) Vehicle identifiers and serial numbers, including license plate numbers
13) Device identifiers and serial numbers
14) Web Universal Resource Locators (URLs)
15) Internet Protocol (IP) address numbers
16) Biometric identifiers, including finger and voice prints
17) Full face photographic images and any comparable images
18) Any other unique identifying number, characteristic, or code
19) The Organization does not have actual knowledge that the information could be used alone or in combination with other information to identify an individual who is the subject of the information.

Note: Per 45 CFR 164.514(b)(2)(ii), this is not a “19th” individual identifier; rather it is in addition to removing the 18 individual identifiers indicated above.

3.3 Limited Data Set:
A. PHI that excludes the following direct identifiers of the individual or of relatives, employers, or household members of the individual:
   1) Names
   2) Postal address information, other than town or city, state, and zip code.
   3) Telephone numbers
   4) Fax numbers
   5) Electronic mail addresses
   6) Social security numbers
   7) Medical record numbers
   8) Health plan beneficiary numbers
   9) Account numbers
   10) Certificate/license numbers
   11) Vehicle identifiers and serial numbers, including license plate numbers
   12) Device identifiers and serial numbers
   13) Web Universal Resource Locators (URLs)
   14) Internet Protocol (IP) address numbers
   15) Biometric identifiers, including finger and voice prints
   16) Full face photographic images and any comparable images.

B. A covered entity may use or disclose a LDS for the purposes of research under HRPP policy #3.4. Workforce members can release a LDS for public health and healthcare operations in accordance with other hospital policies.
3.4 **Data Use Agreement:** A data use agreement specifies that a limited data set recipient will only use or disclose PHI for limited purposes.

3.5 **Data Transfer Agreement:** A data transfer agreement describes the requirements for disclosure of a data set that does not meet the definition of a limited data set as specified in Section 3.3 above.

3.6 **Research Preparation:** The PI requires access to records in order to determine: a) the feasibility of a research project, or b) prepare a research protocol.

3.7 **Research Involving the Use of PHI:** The PI has an IRB-approved research protocol which requires access to records containing PHI.

3.8 **Recruitment of Subjects:** The PI has an IRB-approved research protocol and requires access to records containing PHI in order to identify and recruit subjects.

3.9 **Data Registry:** The PI has an IRB-approved data registry which requires access to records containing PHI in order to add data to the registry.

3.10 **Health Information Without Associated PHI:** Health information that does not identify an individual and to which there is no reasonable basis to believe that the information can be used to identify an individual is not individually-identifiable health information. 

Note: The covered entity may make this determination only if:

1) A person with appropriate knowledge or an experience with generally accepted statistical and scientific principles and methods for rendering information not individually identifiable finds both of the following:
   a) Applying such principles and methods, determines that the risk is very small that the information could be used, alone or in combination with other reasonably available information, by an anticipated recipient to identify an individual who is a subject of the information, and
   b) Documents the methods and results of the analysis that justify such a determination.

2) The covered entity does not have actual knowledge that the information could be used alone or in combination with other information to identify an individual who is a subject of the information.

4.0 **Requirements for Permitting Access to Patient Records for the Purpose of Research:**

4.1 Any individual(s) requesting access to patient records containing PHI must be listed on an IRB-approved research protocol and meet one of the following criteria specified in A, B, or C below:

A. The individual(s) must have a professional or clinical relationship with the patients by virtue of either:
   1) Interacting with the patients in a clinical context. 
      Examples: 1) The patient’s attending physician, and 2) A physician or other healthcare professional accessing the patient’s PHI for the purposes of clinical care.

   2) Acting under the direct supervision of an individual qualifying under A.1 above who is listed on an IRB-approved protocol or registry.
B. The PI requesting access to PHI has received permission from the patient via an individual qualified under Section 4.1(A)(1) above to allow the PI, in accordance with an IRB-approved protocol or registry to: a) contact the patient directly for purposes of recruitment; b) access and use PHI for research purposes; or 3) inclusion of PHI in a registry.

Note: If permission is obtained for a person under this section, such permission extends to those employed by the person who has received permission.

1) The permission may be in writing, or if oral, permission is obtained and documented.

Note: This permission is not required to follow HRPP policy #5.1. However, written informed consent subsequent to permission is required, unless waived by the IRB.

2) Obtainment of patient permission includes the following elements of disclosure:
   a) The PHI will be used for research purposes under an IRB-approved protocol.
   b) Allowing access to the PHI is voluntary
   c) The subject may revoke that authorization at any time.
   d) Identify who will be accessing the patient’s records.
   e) Provide a description of the condition or characteristics which are being screened.
   f) Provide an expiration date or expiration event (e.g., “end of the research study”, “none.”)

Note: The templates for the ICFs are designed to provide a simple explanation of the subject’s rights under HIPAA as well as meet all of the regulatory requirements required under the HIPAA regulations.

C. PHI may not be used or disclosed without an IRB approved ICF signed by the individual to whom the PHI pertains, or a waiver of the requirements for consent and HIPAA authorization has been approved by the IRB under HRPP policy #5.2.

5.0 Data Use Agreements and Data Transfer Agreements

5.1 A PI may use PHI to create a limited data set or disclose PHI only if the Organization obtains satisfactory assurance in the form of:
   A. A Data Use Agreement (DUA) for disclosure of a limited data set.
   B. A Data Transfer Agreement (DTA) for disclosure of a data set that does not meet the definition of limited data set as specified in Section 3.3 above.

5.2 A DUA/DTA must:
   A. Establish the permitted uses and disclosures of the information by the data set recipient. The DUA may not authorize the data set recipient to use or further disclose the information in a manner that violates the agreement.
   B. Establish who is permitted use or receive the data set.
   C. Specify the recipient will:
      1) Not use or further disclose the information other than as permitted by the DUA/DTA or as otherwise required by law.
2) Use appropriate safeguards to prevent use or disclosure of the information other than as provided for by the DUA/DTA.

3) Report to the covered entity any use or disclosure of the information no provided for by its DUA/DTA of which it becomes aware.

4) Ensure that any agents, including a subcontractor, to whom it provides the limited data set agrees to the same restrictions and conditions that apply to the recipient with respect to such information.

5) Not attempt to identify or contact the individuals.

5.3 A DUA and/or DTA will be negotiated, as necessary, through Sponsored Programs Administration.

6.0 Procedures

6.1 Research Preparation

A. In accordance with the HIPAA Privacy Rule at 45 CFR 164.512(i) and applicable hospital policies, a PI/designee, qualified under Section 4.1(A-C) of this policy, may review patient records containing PHI providing the following requirements are met:

1) The use or disclosure is sought solely to review PHI as necessary to prepare a research protocol or for similar purposes preparatory to research.

2) The PI certifies that no PHI will be recorded from the original data set and then transferred to another data repository.

3) The PI certifies that access to records containing PHI is required in order to determine the feasibility of a research project or prepare a research protocol.

4) The PI certifies that no data with PHI will be used in research without IRB approval.

B. The individual requesting access to the medical records must complete a Research Preparation Request and submit it for approval to the official information systems administrator or custodian of the records or data set.

Note: The ORA or IRB does not review or approve this request.

6.2 Research Involving the Use of PHI

A. The PI must submit the IRB application that is appropriate for the proposed research in accordance with HRPP policy #2.1.

B. Applications which require review by the full IRB will be processed and reviewed in accordance with HRPP policy #2.2.

C. Applications that are eligible for review by the expedited method will be processed and reviewed in accordance with HRPP policy #2.3.

D. Applications which appear to be eligible for exemption under the categories specified at 45 CFR 46.101(b); 21 CFR 56.104(d) (if applicable) will be processed and reviewed in accordance with HRPP policy #2.6.
E. In order to ensure greater protection of patient confidentiality, individual(s) who have ethical access to patient records containing PHI for the purposes described in this policy should record the minimum amount of PHI. Whenever possible, data should be recorded without PHI.

F. Individuals who do not have ethical access to records containing PHI [as defined above in Section 4.1(A-C)] must obtain data from the official information systems administrator or custodian of the records data that has been de-identified where all 18 HIPAA subject identifiers have been removed with, or without, a one-way re-identification code [i.e., only the custodian of the records has the link and the code is not any part of the 18 HIPAA identifiers].

G. If the PHI will be sent to an external entity (e.g., single institution, consortium, commercial sponsor), a Data Use Agreement (as specified in Section 5.0 above) or sponsored agreement must be finalized by Sponsored Programs Administration prior to final IRB approval.

6.3 **Subject Recruitment**

A. The subject recruitment methods must be disclosed in the appropriate IRB applications.

B. Only individuals with permitted access as defined in Section 4.1 (A, B) above are permitted to contact prospective subjects directly for the purposes of recruitment providing the IRB has approved the contact method.

C. Only the person(s) who has permitted access may contact prospective subjects on behalf of the investigator providing the IRB has approved the contact method (e.g., personal conversation, telephone, and letter).

D. All subject recruitment methods must be in compliance with HRPP policy #3.6.

6.4 **Data Registries**

A. The Data Registry Application must be submitted in accordance with HRPP policy #2.1.

B. The IRB Administrator, in consultation as necessary with the IRB Executive Chair, will determine review requirements.
   1) Applications which require review by the full IRB will be processed and reviewed in accordance with HRPP policy #2.2.
   2) Applications that are eligible for review by the expedited method will be processed and reviewed in accordance with HRPP policy #2.3.
   3) Applications which appear to be eligible for exemption under the categories specified at 45 CFR 46.101(b); 21 CFR 56.104(d) (if applicable) will be processed and reviewed in accordance with HRPP policy #2.6.

C. In accordance with HHS regulations at 45 CFR 46.102(e), 46.102(b)(2), and 46.109(a), when a PI/designee qualified under Section 4.1 (A-C) of this policy, accesses and records PHI from records for the purpose of developing a data registry, the following requirements must be met:
POLICY #3.4
USE OF PROTECTED HEALTH INFORMATION IN RESEARCH & REGISTRIES

1) All criteria for IRB approval must be met in accordance with HRPP policy #2.5.

2) Informed consent must be obtained unless waived by the IRB under 45 CFR 46.116(d), 45 CFR 164.512(i)(2)(ii), and HRPP policy #5.2.

D. To approve the registry the IRB must be assured there are appropriate human subject protections and mechanisms in place to administer the registry (including the initial creation of the registry, process for adding data to the registry and process for the release of data for future individual research protocols.) All activities must be in compliance with all applicable federal regulations, state laws and Organizational policies.

E. If the registry is owned by this Organization, an IRB-approved protocol must be provided before data may be released from the registry. In addition, if the data will be sent to an external institution, a Data Use Agreement, as specified by Section 5.0 above, must be finalized by Sponsored Programs Administration before any data is provided to the external institution.

F. If the registry will be owned by an external entity (e.g., single institution, consortium, commercial sponsor, a Data Use Agreement (as specified in Section 5.0 above) or sponsored agreement must be finalized by Sponsored Programs Administration prior to IRB approval of the data registry.

6.5 Research Utilizing Decedent PHI
To utilize PHI from deceased individuals the PI must:

A. Certify that the use or disclosure sought is solely for research on the protected health information of decedents.

B. Provide documentation, at the request of the covered entity, of the death of the individuals.

C. Certify that the PHI is necessary for the purposes of the research.

ADMINISTRATIVE APPROVAL:
Ernest D. Prentice, PhD.  Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce Gordon, M.D.   IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for retention of research records by the PI.

2.0 Policy
It is the policy of the Organization that all research records must be maintained and stored securely, in accordance with Nebraska State Law, for at least seven (7) years beyond the termination of the study or longer as required by sponsors.

3.0 Required records
3.1 The research records maintained by the PI should include the initial version as well as all amendments of the:
   A. IRB application
   B. Detailed protocol
   C. Grant (if applicable)
   D. Investigator brochure (if applicable)
   E. ICF(s)/Information sheet(s)
   F. Case report forms
   G. Applications for continuing review
   H. DSMB reports (if applicable)
   I. IND/IDE correspondence and annual reports (if applicable)
   J. Requests for change
   K. Adverse event reports (internal, internal fatal and external) with corresponding documentation (e.g., safety reports) and applicable consent documents
   L. Reports of unanticipated problems involving risk to the subject or others
   M. Protocol deviations
   N. Issues of noncompliance.
   O. Quality improvement assessments
   P. IRB/PI correspondence
   Q. Sponsor correspondence, contracts, etc.
   R. If there is multi-site/off campus participation in the study: documentation of training in the protection of human subjects (CITI or other as approved by the IRB), external investigator agreements, and other contractual agreements as applicable.
   S. Any other protocol-related documentation not covered above
   T. Subject files including original signed consent documents, case report forms (CRFs), laboratory results and other applicable information.

4.0 Department Retention of Records
4.1 If the PI resigns or otherwise departs from the Organization before the end of the designated retention period, the department of record must maintain the research records unless otherwise specified.

4.2 The PI may request a copy of the research records in accordance with applicable organizational policies.

Administrative Approval:
Ernest D. Prentice, PhD.  Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD  IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for recruitment of subjects through advertisements.

2.0 Policy
2.1 It is the policy of the Organization that all subject recruitment strategies including printed newspaper advertisements, bulletins, fliers, multimedia, radio, and television must be reviewed and approved before they can be used to recruit potential subjects.

2.2 Once approved by the IRB, the PI cannot alter an advertisement without prior IRB approval. However, if minor editing is required by the editor or producer during the course of newspaper publication or a radio/television production, this is permitted providing the alteration does not in any way violate this policy.

3.0 Design of the Advertisements. Advertisements should be limited to information a potential subject may need to determine if they are interested and eligible to participate in a study.

3.1 Appropriate items to include in an advertisement are:
A. Name and address of the PI and associated institution.
B. A clear statement that activity is research.
C. Purpose of the research.
D. Eligibility criteria (in shortened form).
E. A brief list of potential benefits to the subject, if any.
F. Time or other commitments required from the subject.
G. Location of the research, contact person, and phone number for further information.
H. IRB number

3.2 The following are not permitted to be included in advertisements:
A. Statements implying a certainty of a favorable outcome or other benefits beyond what was described in the consent document and the protocol.
B. Claims, either explicitly or implicitly, that the research procedures (e.g. drug, biologic or device) are safe or effective for the purposes under investigation.
C. Claims, either explicitly or implicitly, that the research procedures are known to be equivalent or superior to other interventions off-study.
D. Terms such as “new treatment”, “new medication”, or “new drug”.
E. Promises of “free medical treatment” regardless of whether the treatment will be provided without charge.
F. A stated amount of compensation for participation, or indication of compensation is available in larger and/or bold font.

G. Compensation in the form of a coupon good for a discount on the purchase price of a product under study once it has been approved for marketing and/or the study has ended.

H. Any exculpatory language.

3.3 Printed advertisements (e.g., newspaper ads and bulletins) should use appropriate font size and bolding in order to ensure the prospective subject is not misled by having their attention inappropriately drawn to a particular section of the advertisement.

3.4 The layout of the advertisements must conform to the Organization’s requirements regarding the use of logos and brands.

3.5 In the case of newspaper ads, the investigator should ensure that the layout and font size approved by the IRB is reflected in the final published copy.

3.6 Advertisements via mass distribution emails are normally prohibited. Exceptions must be approved by the IRB with appropriate justification.

3.7 Any scripts utilized to determine basic eligibility for participation in a study must be reviewed to determine if the rights and welfare of the prospective subjects are adequately protected.

4.0 Submission of Advertisements
   All final versions of advertisements including: a) print media (e.g., bulletins, flyers), c) audio scripts (e.g., radio), d) video scripts (e.g., television) and e) any other media forms (e.g., internet) must be submitted to the ORA in accordance with HRPP policy #2.1 for review and approval.

5.0 IRB Review of Advertisements
   5.1 The final version of any advertisement may be reviewed by either the full IRB or by the expedited method if it qualifies in accordance with 45 CFR 46.110(b)(1) and (2) (HRPP policies #2.2 and 2.3).

   5.2 The IRB approval letter will cite the approved version of the advertisement.

6.0 IRB Record of Advertisements
   The IRB will maintain on file final copies of: a) all IRB-approved bulletin, b) published newspaper advertisements, c) audio-taped advertisements, d) video-taped advertisements or e) other media (e.g. link to website).

Administrative Approval:
Ernest D. Prentice, PhD.   Institutional Official and Associate Vice Chancellor for Academic Affairs
Bruce Gordon, M.D.     IRB Executive Chair
1.0 **Purpose**
The purpose of this policy and procedure is to describe the Organization’s requirements related to finder’s fees and recruitment bonuses.

2.0 **Policy**
HHS regulations at 45 CFR 46.116 and FDA regulations at 21 CFR 56.116 require minimization of the possibility of coercion or undue influence. Accordingly, it is the policy of the Organization that the utilization of finder’s fees and recruitment bonuses are not permitted due to the concern that potential subjects may be placed at risk of coercion, undue influence or inequitable subject selection.

3.0 **Finder’s Fees**
3.1 Finder’s fees which are paid for referring prospective research subjects (e.g. physicians, coordinators, nurses, office staff, companies or groups) are not permitted.

3.2 Reasonably justified cost-based reimbursement for time and effort to review patient records to identify eligible patients may be acceptable.

4.0 **Recruitment Bonuses**
4.1 Recruitment bonuses, of any type, which are tied to the enrollment of a set number of subjects or accelerated enrollment, are not permitted. These bonuses may potentially influence the judgment of the PI and/or research team as well as place into question the integrity of the research. However, the IRB accepts the propriety of cost-based per capita payments by sponsors to departments in order to fund clinical research where the cost is obviously related to the number of subjects enrolled in the protocol.

4.2 Examples of unacceptable recruitment bonuses include, but are not limited to:
A. Direct per capita payment(s) to PIs.

B. Accelerated recruitment incentives (e.g., the sponsor will provide additional funds if a specified number of subjects are enrolled by a specified date.)

C. Bonuses (including but not limited to stipends, educational grants, conference reimbursement, and gift cards) to coordinators and other enrollers based on increased and/or rapid enrollment of subjects.

**Administrative Approval:**
Ernest D. Prentice, PhD. Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s guidelines for compensation of research subjects.

2.0 Policy
In accordance with HHS regulations at 45 CFR 46.116 and FDA regulations at 21 CFR 50.20, compensation for research subjects may be acceptable if: 1) the possibility of coercion or undue influence is minimized, and 2) the compensation is considered a reasonable incentive either for participation in the research and/or reimbursement for study-related travel and other expenses. Compensation of any form is not considered a benefit in terms of the risk/benefit relationship of the research or the potential benefits section of the consent form.

3.0 General Principles
3.1 Compensation for participation in research is not a requirement.
3.2 The amount or type of compensation should not be coercive or serve as undue inducement in order to enroll subjects in a study.
3.3 The amount of compensation must never be tied to the degree of risk or discomfort associated with the study. However, compensation can be determined in consideration of the amount of time required of the subject.
3.4 The IRB will not consider compensation as a benefit to offset risks (either quantitative or qualitative) associated with the research.
3.5 Since the risks associated with “minimal risk” research do not exceed those of daily life or routine physical or psychological examination, compensation is not an inducement to offset risk. Therefore, there is no restriction on compensation for minimal risk research.
3.6 Participation in research should, if possible, not require any financial sacrifice on the part of the subject. Any additional costs to the subject that may result from participation in the research must be justified and disclosed in the consent form.

4.0 Specific Requirements
4.1 Compensation for research which involves greater than minimal risk should be based on a reasonable hourly wage for time spent in preparation for, participation in, and recovery from, research interventions. A reasonable hourly rate is $20.00 per hour.
4.2 The IRB has the authority to review the level of compensation and, in appropriate circumstances, limit the total value.
4.3 Interventions are understood to include such elements as procedures performed, visits to a clinic or research setting, phone interviews, or surveys completed. If appropriate, such hourly compensation should include all parties involved. For example, if a family member is required to be present to drive a research subject home after a procedure, his/her time may be compensated.
4.4 Compensation above these levels must be specifically justified by the investigator, and must comply with the general principles described Section 3.0 of this policy.
4.5 The terms of the compensation must be completely disclosed in the IRB application and in the informed consent process and ICF.

4.6 Payments to subjects must be prorated based upon the duration of participation of the subject in the research. Any credit for payment should accrue as the study progresses and not be contingent upon the subject completing the entire study. Prorated payment should be made regardless of whether withdrawal was voluntary (subject decided to withdraw from the study) or involuntary (based on withdrawal criteria of the research protocol). Prorated compensation should be provided, if possible, to subjects at defined intervals as opposed to at the end of a study. The amount of total compensation should not be emphasized during the process of consent or in the ICF.

4.7 The IRB does not allow bonuses paid for completion of a study as it may offer undue influence to a subject to initially participate in the study, or continue in a study when the subject may have chosen to withdraw.

4.8 Compensation for participation in research may not include free sample(s) or coupon(s) good for a discount on the purchase price of the test product (e.g. drug, vitamin, electrolyte replacement drink) upon conclusion of the study. The IRB views this form of compensation to be an inappropriate marketing tool when associated with research participation.

4.9 For studies where compensation is likely to total more than $600, the consent form must include a statement that an IRS form 1099 will be issued if the total compensation from participation in research reaches $600 in any given year.

4.10 Records should be maintained at the department or other level that tracks all forms of compensation and their distributions. The amount and type of compensation must be able to be tracked to a corresponding recipient for tracking purposes. If the accounting and/or payment office required the subject to provide their Social Security Number, this must be both justified and disclosed in the consent form.

4.11 Payments for involvement of young minors (<16 years) in research should not be made directly to the minor. It may be appropriate to offer children through their parents an age appropriate token for their participation, such as a small toy or gift certificate. With appropriate justification, 16-18 year olds may be directly compensated.

4.12 The IRB will evaluate the type and amount of compensation on a case-by-case basis, and make a determination of its acceptability in consideration of the general principles described Section 3.0 of this policy and any justification provided by the PI for an exception.

4.13 Due to the concerns relating to fairness and the potential subject’s overestimating the value of compensation the UNMC IRB will not allow the use of a lottery (or raffle) as a mechanism to provide compensation to subjects.

**Administrative Approval:**
Ernest D. Prentice, PhD. Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD IRB Executive Chair
**1.0 Purpose**
The purpose of this policy and procedure is to describe the contraception requirements for subjects participating in research.

**2.0 Policy**
It is the policy of the Organization that subjects must utilize appropriate contraception methods while participating in research with potential for reproductive toxicity.

2.1 Eligibility criteria concerning contraception requirements should be based on the FDA Use-In-Pregnancy Categories. If the FDA category is not available, the most appropriate template should be chosen by comparing the definitions of the categories with the reproductive toxicity data available for the protocol-specified medication of greatest concern. Phase III studies must provide animal data to support choice of template.

2.2 Female study volunteers who are not of reproductive potential (premenarchal, postmenopausal, or surgically or otherwise infertile) are eligible to participate in research without requiring the use of contraception.

2.3 Male study volunteers, who have undergone successful vasectomy with resulting azoospermia or have azoospermia for any other reason, are eligible to participate in research without requiring the use of contraception.

2.4 It is the responsibility of the investigator to discuss the risks and benefits of each form of contraception with potential study participants to ensure that subjects are making an informed choice.

**3.0 Definitions of the FDA Use-In-Pregnancy Categories**

3.1 **Category A: Controlled studies show no risk:** Adequate, well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus in any trimester of pregnancy.

3.2 **Category B: No evidence of risk in humans:** Adequate, well-controlled studies in pregnant women have not shown increased risk of fetal abnormalities despite adverse findings in animals nor, in the absence of adequate human studies, animal studies show no fetal risk. The chance of fetal harm is remote, but remains a possibility.

3.3 **Category C: Risk cannot be ruled out:** Adequate, well-controlled human studies are lacking, and animal studies have shown a risk to the fetus or are lacking as well. There is a chance of fetal harm if the drug is administered during pregnancy; but the potential benefits may outweigh the potential risk.

3.4 **Category D: Positive evidence of risk:** Studies in humans, or investigational or post-marketing data, have demonstrated fetal risk. Nevertheless, potential benefits from the use of the drug may outweigh the potential risk. For example, the drug may be acceptable if needed in a life-threatening situation or serious disease for which safer drugs cannot be used or are ineffective.
3.5 **Category X: Contraindicated in pregnancy:** Studies in animals or humans, or investigational or post-marketing reports, have demonstrated positive evidence of fetal abnormalities or risk that clearly outweighs any possible benefit to the patient.

4.0 **Procedure**

4.1 The ICFs must include the appropriate IRB-approved contraception language based upon the FDA Pregnancy-in-Use Category *(see Addendum 1 attached at the end of this policy)*.

A. **Studies Involving Category A Drugs:**
   1) The PI may not mandate use of contraception since adequate, well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus in any trimester of pregnancy.
   2) Exceptions to this policy (that is, to mandate women of childbearing potential use contraception) must be approved by the full IRB after adequate justification by the PI.
   3) The PI must utilize the contraceptive language found in the Biomedical ICF template.

B. **Studies Involving Category B Drugs:**
   1) The PI is not required to mandate use of contraception.
   2) Should the PI (or the sponsor) choose to mandate contraception, the mandate must be justified to the IRB.
   3) The PI must utilize the contraceptive language found in the Biomedical ICF template.

C. **Studies Involving Category C Drugs:**
   1) The PI should mandate use of contraception since there are no definitive studies which demonstrate the safety of these drugs for the fetus.
   2) Due to the unknown magnitude of the risk to the fetus, the PI, or the sponsor, may require that the subject and his/her partner should use one or two forms of contraception while on study and for a specified number of months afterwards.
   3) The PI must utilize the contraceptive language found in the Biomedical ICF template.

D. **Studies Involving Category D Drugs:**
   1) The PI should mandate use of contraception, since studies of the drug in humans, or investigational or post-marketing data, have demonstrated fetal risk. The PI should require that should require that the subject and his/her partner should use two forms of contraception. The PI should utilize the contraceptive language found in the Biomedical ICF template.
   2) In some situations, sponsors may mandate specific contraception language be included in the ICF. To utilize the sponsor’s language, the IRB must determine that the specified language is as protective (or more protective) than the requirements found in the IRB-approved template for Category D drugs.
E. Studies Involving Category X Drugs:

1) The PI must mandate use of contraception, since studies of the drug in humans, or investigational or post-marketing data, have demonstrated fetal risk. The PI must utilize the contraceptive language found in the Biomedical ICF template.

2) In most research involving Category X drugs, sponsors and/or the FDA are highly likely to mandate specific contraception language be included in the ICF. To utilize this language, the IRB must determine that the specified language is as protective (or more protective) than the requirements found in the IRB-approved template for Category X drugs.

4.2 If PI wishes to list specific forms of birth control in any of the above categories (rather than the generic “appropriate method(s) of birth control” found in the IRB-approved template), the list must include at least the following: 1) condoms (male or female) with or without a spermicidal agent; 2) diaphragm or cervical cap with spermicide, 3) IUD, and 4) hormonal contraceptives, unless the sponsor/PI presents justification that any of these are medically or scientifically inappropriate considering both the nature of the research and the subject population.

4.3 The IRB Executive Chair, on behalf of the IRB Executive Committee, is authorized to negotiate with sponsors and/or PIs to address requests for specific language modifications in the ICF provided the requested modifications are at least as protective as the requirements found in the IRB-approved template.

ADMINISTRATIVE APPROVAL:
Ernest D. Prentice, PhD. Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD IRB Executive Chair
ADDENDUM #1
ICF Pregnancy Risk Statements

Category A drugs:

PREGNANCY RISKS
It is possible that the medicines used in this study could injure a fetus [OR an unborn child] if you, or your partner, become pregnant while taking them. You have already been told what is known about this possibility, and you are encouraged to ask further questions.

Category B drugs when contraception is NOT required:

PREGNANCY RISKS
It is possible that the medicines used in this study could injure a fetus [OR an unborn child] if you, or your partner, become pregnant while taking them. You have already been told what is known about this possibility, and you are encouraged to ask further questions.

Category B drugs when contraception IS required:

PREGNANCY RISKS
It is possible that the medicines used in this study could injure a fetus [OR an unborn child] if you, or your partner, become pregnant while taking them. You have already been told what is known about this possibility, and you are encouraged to ask further questions.

You may want to discuss this with others before you agree to take part in this study. If you wish, we will arrange for a doctor, nurse, or counselor who is not part of this study to discuss the potential risks and benefits with you and anyone else you want to have present.

Because of the potential risks, you, or your partner, must not become pregnant while you are participating in this study. Women must have a negative pregnancy test before entering the study [and before each treatment – as appropriate].

If you are sexually active and can get pregnant, or can get your partner pregnant, you must use ONE appropriate method of birth control every time you have sex, or you must not have sex.

You can get additional information about methods to avoid pregnancy by calling the UNMC Research Subject Advocate’s Office at (402) 559-6941.

You will need to continue to avoid pregnancy for X months after finishing the research.

By signing this and being in the study, you are agreeing to not get pregnant while you are on the study and for X months after. Should you become pregnant while on this study, you should immediately notify the study personnel. The investigator will assist you in finding appropriate medical care. The investigator also may ask to be allowed to continue getting information about your pregnancy. You can refuse to provide this information.
**Category C drugs:**

**PREGNANCY RISKS**
It is possible that the medicines used in this study could injure a fetus [OR an unborn child] if you, or your partner, become pregnant while taking them. You have already been told what is known about this possibility, and you are encouraged to ask further questions.

You may want to discuss this with others before you agree to take part in this study. If you wish, we will arrange for a doctor, nurse, or counselor who is not part of this study to discuss the potential risks and benefits with you and anyone else you want to have present.

Because of the potential risks, you, or your partner, must not become pregnant while you are participating in this study. Women must have a negative pregnancy test before entering the study [and before each treatment – as appropriate].

If you are sexually active and can get pregnant, or can get your partner pregnant, you must use ONE [or TWO] appropriate method(s) of birth control every time you have sex, or you must not have sex.

Because of the nature of this research, methods of natural family planning are not, by themselves, sufficiently reliable to avoid pregnancy. [If required, the following statement may be included here:] Please note: The [name of institution] does not promote or condone the use of contraception.

You can get additional information about methods to avoid pregnancy by calling the UNMC Research Subject Advocate’s Office at (402) 559-6941.

You will need to continue to avoid pregnancy for X months after finishing the research.

By signing this and being in the study, you are agreeing to not get pregnant while you are on the study and for X months after. Should you become pregnant while on this study, you should immediately notify the study personnel. The investigator will assist you in finding appropriate medical care. The investigator also may ask to be allowed to continue getting information about your pregnancy. You can refuse to provide this information.
**Category D Drugs:**

**PREGNANCY RISKS**

It is possible that the medicines used in this study could injure a fetus [OR an unborn child] if you, or your partner, become pregnant while taking them. You have already been told what is known about this possibility, and you are encouraged to ask further questions.

You may want to discuss this with others before you agree to take part in this study. If you wish, we will arrange for a doctor, nurse, or counselor who is not part of this study to discuss the potential risks and benefits with you and anyone else you want to have present.

Because of the potential risks, you, or your partner, must not become pregnant while you are participating in this study. Women must have a negative pregnancy test before entering the study [and before each treatment – as appropriate].

If you are sexually active and can get pregnant, or can get your partner pregnant, you must use TWO appropriate methods of birth control every time you have sex, or you must not have sex.

Because of the nature of this research, methods of natural family planning are not, by themselves, sufficiently reliable to avoid pregnancy. *If required, the following statement may be included here:*  
Please note: The [name of institution] does not promote or condone the use of contraception.

You can get additional information about methods to avoid pregnancy by calling the UNMC Research Subject Advocate’s Office at (402) 559-6941.

You will need to continue to avoid pregnancy for X months after finishing the research.

By signing this and being in the study, you are agreeing to not get pregnant while you are on the study and for X months after. Should you become pregnant while on this study, you should immediately notify the study personnel. The investigator will assist you in finding appropriate medical care. The investigator also may ask to be allowed to continue getting information about your pregnancy. You can refuse to provide this information.

**Category X Drugs:**

_Since studies of the drug in humans, or investigational or post-marketing data, have demonstrated fetal risk, contraception is required and the language must be at least as protective as Category D language above. Often (as in the case of thalidomide and lenalidomide) the sponsor and/or FDA require inclusion of specific language relating to fetal risk, monitoring for pregnancy and prevention of pregnancy in the ICF. The IRB cannot change this language._

*If required, the following statement may be appended to the required FDA language:*  
The [name of institution] does not promote or condone the use of contraception.
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for determining how and when pregnancy testing should be performed on subjects who are females of childbearing potential enrolled in protocols that describe pregnancy as an exclusion criterion.

2.0 Policy
It is the policy of the Organization that when females of childbearing potential are enrolled in protocols which include a pregnancy exclusion criterion, the protocol must have procedures in place for either pregnancy testing or self-reporting depending on the teratogenic risk.

3.0 Definition
3.1 Female of childbearing potential (FOCBP): A female who has begun menstruating and not entered menopause (i.e., absence of menses for 12 months). Women who are sterile due to history of hysterectomy, bilateral oophorectomy, or radical pelvic irradiation are not considered females of childbearing potential.

4.0 Procedures
4.1 Protocols that describe pregnancy as an exclusion criterion must describe how pregnancy status will be determined.

4.2 For protocols that include an intervention considered potentially harmful to a fetus, pregnancy testing must be done prior to initiating the intervention(s).

4.3 If pregnancy testing is required (as indicated in Section 4.2 above), testing should be performed on urine unless blood is being drawn for another reason. In that case, serum qualitative pregnancy testing can be performed.

   A. Quantitative testing is not indicated for the purposes of this policy.

   B. Acceptable test results are those performed at Nebraska Medicine, CHMC, or a documented result from the subject’s provider.

   C. Home pregnancy test results are not acceptable.

4.4 Protocols that describe pregnancy as an exclusion criterion, but are not expected to cause fetal harm, may use subject self-report of pregnancy status.

4.5 A negative pregnancy test within 7 days prior to the intervention of interest should be considered current, consistent with Nebraska Medicine Pregnancy Testing Policy. For ongoing interventions or exposures, testing should be done at a frequency consistent with clinical practice (and not more often than monthly).

4.6 Subjects should be informed during the consent/assent process and in the ICF of:
   A. How often pregnancy testing will be done.

   B. How often they will be informed of results.

   C. Whether they will be removed from the study if they become pregnant.
4.7 Minor subjects should normally be informed during the consent/assent process and in the ICF that their parent/guardian will be informed of the test results.

4.8 Subjects should be informed of whether they will be charged for pregnancy testing:
   A. For protocols that require pregnancy testing, but are not expected to cause fetal harm, subjects may not be charged for pregnancy testing.
   B. The IRB strongly discourages pregnancy testing of females who are NOT of childbearing potential. However, if such subjects will be tested, they may not be charged for this test.

4.9 Subjects should be given pregnancy test results privately. Minors should be given pregnancy test results privately followed by disclosure by the research team to the subject’s parent or guardian.

4.10 Any subject with a positive pregnancy test should be referred to her primary care physician to review the positive test result. Subjects should be offered to have study information sent to their primary care physician if the subject received any intervention prior to the positive pregnancy test.

Administrative Approval:
Ernest D. Prentice, PhD. Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for training for all personnel involved in conducting human subject research.

2.0 Policy
2.1 It is the policy of the Organization that all personnel involved in the conduct of human subject research under the oversight of the UNMC IRB will be qualified through initial and continuing education in order to fulfill their responsibility to protect the rights and welfare of human subjects.

A. Training needs of research personnel are assessed on an ongoing basis. Any required training to meet those needs will be promptly initiated.

B. A list of all educational activities, including dates and hard copies, as appropriate, are maintained on file.

C. The IRB Administrator/Education Coordinator’s primary responsibility is to coordinate and conduct IRB education activities.

3.0 Procedures
The Organization utilizes the following education and training methods for research personnel:

3.1 Institutional Review Board (IRB) Working Together Brochure
The ORA distributes a brochure to research personnel, which describes the IRB submission requirements.

3.2 Collaborative Institutional Training Initiative (CITI)
A. Training in the protection of human subjects is primarily accomplished through completion of this web-based training program which is required for the following research personnel listed on IRB applications:
   1) PIs
   2) Secondary Investigators
   3) Participating Personnel
   4) Protocol Coordinators
   5) Other Coordinators
   6) Administrative and Data Management Personnel
   7) Faculty Advisors

B. CITI training course requirements
   1) The Biomedical course must be completed by:
      a) Faculty, staff, students or other representatives of the Organization conducting biomedical research (non-exempt and exempt) within the Organization or at external sites where the UNMC IRB serves as the IRB of record.
         Note: This requirement applies to UNO research personnel conducting exercise science studies.
      b) External research personnel conducting biomedical research (non-exempt and exempt) at external sites where the UNMC IRB is the IRB of record.
2) The Behavioral and Social Science course must be completed by:
   a) Faculty, staff, students or other representatives of UNO conducting behavioral and social science research (non-exempt and exempt) within the Organization or at external sites where the UNMC IRB serves as the IRB of record.
   b) External research personnel conducting behavioral and social science research (non-exempt and exempt) at external sites where the UNMC IRB is the IRB of record.

C. **Subcontract recipients.** The IRB will accept certificates of training from other institutions when research personnel who have been trained elsewhere and are under the legal jurisdiction of that institution with respect to compliance with federal regulations. A copy of any certification must be provided to the ORA.

D. **New research personnel added to IRB-approved research via a Request for Change or Application for Continuing Review.** All new research personnel must complete CITI training prior to addition to any research study. The IRB will accept certificates of training from prior institutions only if the other institution utilized the CITI training courses specified in Section 3.2 above.

E. **IRB approval of research.** All research personnel must be CITI certified prior to IRB approval of initial research applications.
   *Note:* Current project personnel whose prior certification may have lapsed must renew certification prior to IRB approval of any new application.

F. **Access to the CITI training program.** The CITI Training Program is accessible via [http://www.citiprogram.org](http://www.citiprogram.org). A link to the CITI Training Program is also available through the UNMC IRB website ([http://www.unmc.edu/irb](http://www.unmc.edu/irb)). Following registration, the individuals will be able to immediately access the system.

G. **Test data confidentiality.** Individual test scores are confidential. The webmaster and staff supporting the distance learning software at the University of Miami where the data are processed and stored have access to individually identifiable quiz scores. Additionally, the ORA staff has access to the individual test scores. Aggregate, anonymous quiz data is used by CITI course faculty to help improve course content and quick questions. There will be no further disclosure of individually identifiable quiz results or aggregate institutionally identifiable results beyond that mentioned above.

H. **Minimum passing score required for certification.** The Organization requires a passing score of 75% to receive CITI certification, which is consistent with the VA requirement.

I. **CITI certification renewal.** CITI certification is valid for 3 years from the original date of completion. Certification must be renewed at that time in order for the individual to be listed on new IRB applications or added to existing IRB-approved applications as an authorized research personnel. Certification renewal is available through the CITI Refresher Course. In order for certification to be renewed, the individuals identified in Section 3.1B above must complete either the Refresher course or the specified Basic course.
3.3 UNMC IRB Website
A. Research personnel can access the IRB website at http://www.unmc.edu/irb.

B. HRPP policies and procedures are posted on the IRB website.

C. The IRB website contains the links to OHRP, FDA, Office of Civil Rights and other websites where research personnel can access the federal regulations, guidance documents and other information pertinent to human subject research.

D. Presentations and other educational materials are available on the IRB website.

3.4 IRB Education Series
The IRB Education Series is scheduled on a monthly basis and consists of didactic presentations by the IO, IRB Executive Chair, Chief Compliance Officer and IRB Administrators. The Series is advertised in advance and the lectures are on topics germane to human subject protection. The primary target audience is research personnel within the Organization.

3.5 “HRPP: Working Together” Bulletins
The bulletins are issued electronically six to eight times per year and contain practical information from HRPP policies, often in a question and answer format.

3.6 UNMC IRB Workshops
Workshops are scheduled on various topics, such as the IRB online submission system, informed consent and how to work more effectively with the IRB.

3.7 Student Education
Didactic classroom presentations are frequently given to UNMC and UNO students on topics pertaining to human subject protection by request.

3.8 Webinars
The UNMC IRB schedules webinars for research personnel on germane topics.

3.9 Individual Training Upon Hire
Upon hiring a new employee, the new hire’s supervisor can select an IRB Introduction and Overview as mandatory training. This training is generally provided by the IRB Administrator/ Education Coordinator.

3.10 Individual Training upon Request
The IRB Administrators provide individualize training to any research personnel on request. This training may be conducted in the ORA or at any requested location.

3.11 Conflict of Interest Training
Conflict of Interest Training is required in accordance with UNMC Conflict of Interest policy #8010 and HRPP policy #3.12

4.0 Procedures for Assessing Training Needs
4.1 Training needs of research personnel are assessed on an ongoing basis by the following methods:
A. Review of the current literature and evolving federal guidance regarding various aspects of research ethics and human subject protection.
B. Attendance by the IO, IRB Executive Chair, IRB Vice-Chairs, and IRB Administrators at national meetings (e.g. PRIM&R).

C. Feedback from research personnel regarding their training needs.

D. Assessment of the quality and completeness of IRB submissions by IRB members and the IRB Administrators

E. Implementation of new IRB requirements, which require training.

5.0 Procedures for Maintaining Training Records
   The IRB Administrator/Education Coordinator maintains on file all training records for the activities specified in Sections 3.2 and 3.4-3.10 above.

ADMINISTRATIVE APPROVAL:
Ernest D. Prentice, PhD. Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD  IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s procedures for identification, management, and minimization or elimination of financial conflict (COI) of responsible personnel, senior administrators, and the Organization itself that could influence the conduct of research or the integrity of the HRPP.

2.0 Policy
2.1 It is the policy of the Organization that all potential financial COIs of responsible personnel engaged in non-exempt research under oversight of the Organization’s IRBs and Organizational officials must be identified and minimized through appropriate management in accordance with a) PHS regulations at 42 CFR 50, Subpart F; b) National Science Foundation (NSF) regulations; c) FDA regulations at 21 CFR 54; and d) the University of Nebraska Board of Regents Policies #3.2.8.10 and #4.4.2, e) the UNMC policy #8010, f) UNO Academic and Research Financial Conflict of Interest Policy, g) Children’s Hospital & Medical Center policy #ADM100, and h) Children’s Hospital & Medical Center Board of Directors Conflict of Interest Policy.

2.2 The IRB will interact with the COI Officers, COICs, and senior administrators of the applicable components of the Organization in accordance with the above specified regulations and policies to ensure that appropriate COI management plans are in place to protect the rights and welfare of human subjects when investigators, senior administrators, or the Organization itself has a COI.

2.3 Any changes in financial interest must be promptly disclosed in accordance with Section 2.1 above.

2.4 The IRB will ensure that responsible personnel are appropriately trained concerning the identification, disclosure, and management of COI. This includes initial education, immediate re-education when there are policy changes and appropriate re-education when there is noncompliance with the COI policy.

3.0 Definitions
3.1 Responsible Personnel: Responsible Personnel are defined as those study personnel listed in Section I of the IRB application who are responsible for the design, conduct, or reporting of research, or the development of proposals to conduct research. This includes: PI, Secondary Investigator(s), Participating Personnel, and Protocol Coordinator(s). Data and Administrative Personnel are not considered Responsible Personnel for the purposes of this policy.

3.2 Covered Persons: Responsible Personnel, as defined above, are considered Covered Persons for the purposes of this policy. In addition, any financial interest related to the research accruing to the immediate family, including the following: spouse, child, brother, sister, grandchild, or grandparent, by blood, marriage, or adoption of the Covered Person are bound by this policy.

3.3 Conflict of Interest (COI): A COI refers to situations when the Covered Persons’ direct or indirect personal financial interests or fiduciary duties owed to third parties may compromise, or have the appearance of compromising, a Covered Person’s professional judgment or behavior in carrying out his or her research obligations.
including the individual’s obligation to protect the rights and welfare of research subjects. This includes indirect personal financial interests of a Covered Person that may be obtained through third parties such as a Covered Person’s immediate family, business relationships, fiduciary relationships, or investments.

3.4 **Significant Financial Interest:** A significant financial interest means a financial interest of the Covered Person that reasonably appears to be related to the Responsible Person’s institutional responsibilities during the course of the research. A significant financial interest is defined as anything of monetary value that exceeds $5,000 which the Covered Person has received in the past 12 months preceding the disclosure, or any equity in a non-publicly traded company.

3.5 **Non-Significant Financial Interest:** The Covered Person has a non-significant financial interest defined as any financial interest that does not qualify as a significant financial interest as defined in Section 3.4 of this policy.

3.6 **Financial Interests not Considered:** The following are financial interests that are not covered by this policy:
   A. Salary or other remuneration from the Organization
   B. Income from seminars, lectures, or teaching engagements sponsored by governmental entities
   C. Income from service on advisory committees or review panels for governmental entities

3.7 **Organizational COI:** Organizational financial COI includes: a) licensing, technology transfer, patents; b) investments of the Organization; c) gifts to the Organization when the donor has an interest in the research; d) financial interests of senior administrators; e) other financial interests.

3.8 **COI Committees (COICs):** The UNMC COIC, UNO COIC, and the CHMC COI Office are responsible for reviewing potential conflicts of interest which have been determined to be significant, developing the management plan, and providing the information to the IRB.

3.9 **IRB COI Administrator:** The IRB COI Administrator is the individual assigned responsibility for facilitating IRB review of COI management plans.

4.0 **Procedures for Disclosure of Potential COI**

4.1 Any Responsible Personnel listed on the IRB application who has a COI must disclose that financial interest in accordance with the applicable policy specified in Section 2.1 above.

4.2 Responsible Personnel conducting FDA regulated research must disclose their financial interests in accordance with 21 CFR 54.4 by also submitting Form FDA 3455 to the sponsor. The IRB does not require a copy of this form.
5.0 COI Management Plan

5.1 The COI management plan will include an appropriate disclosure of the financial interest(s) of the Responsible Person(s) in the consent form as well as in any presentations, publications, or news articles (e.g., UNMC Today).

5.2 The COI management plan may also include any of the following in consideration of the nature and magnitude of the financial interest of the Covered Person:

A. More frequent monitoring of the research

B. Independent monitoring of the research

C. Modification of the research protocol to manage potential bias through means such as blinding; modifying the scope of the project; and setting timetables for delivery of the product.

D. Designation of a peer or supervising co-investigator with no COI in the project to assume the lead investigative role.

E. Monitoring of the consent process.

F. Divesting or appropriately reducing the financial interest giving rise to the COI with restrictions on re-investment for an appropriate period to provide for publication and critique of the completed research.

G. Severing relationships existing between the Covered Person and the company or other entity that is the source of the COI.

H. Removing contract terms which create the COI. For example, under no circumstances shall UNMC engage in projects where payment is defined by the outcome of the research.

I. Disqualification from participation in all or a portion of the research (e.g., may not enroll human subjects, obtain informed consent or analyze data).

J. Any additional management strategies as determined by the appropriate COIC and/or the IRB.

5.3 The following are strictly prohibited:

A. Any arrangement where the value of ownership interests will be affected by the outcome of the research.

B. Any arrangement where the amount of compensation will be affected by the outcome of the research.

6.0 Full IRB Review of Significant Risk COI Management Plans

6.1 The COI Officer will provide the full IRB with the committee’s approved COI Management Plan.
6.2 The COI Officer or the IRB Executive Chair/designee will verbally describe the nature of the financial interest, and the specifics of the COIC management plan. 

  *Note: Members of the full IRB are not provided written copies which detail the specifics of the financial interest, but are given ranges of the financial interest (e.g., $5,000 to $9,999; $10,000 to $19,999…). It is the position of the Organization that the financial interests of its employees should remain as confidential as possible.*

6.3 The full IRB must approve the COI Management Plan before the protocol is approved and released.

6.4 The IRB may require a more stringent COI management plan, but may not adopt a less stringent plan approved by the COIC.

6.5 Organizational officials cannot overrule the IRB’s determination.

7.0 Management of COI in Research Conducted by Subgrantees, Contractors, and Collaborators

7.1 If the research is conducted at an external site and involves subgrantees, external contractors or collaborators with any financial interest related to the research, the PI must provide verification to the ORA that the individual(s) are in compliance with the external institution’s COI policy which meets the requirements of 42 CFR 50.604.

7.2 If the external site does not have a COI policy which meets the requirements of 42 CFR 50.604 the requirements of the applicable policy under Section 2.1 above must be met.

8.0 Documentation of COI Management

8.1 The COI Management Plan approved by the IRB will be maintained in the protocol file in the ORA for no less than seven (7) years following cessation of the outside activity to which they relate.

9.0 Management of Organizational Financial COI

9.1 Organizational financial COI may occur when the Organization, itself, has a financial interest in the design, conduct, or outcome of human subject research.

9.2 In accordance with Board of Regents Policies 3.2.8.10 and 4.4.2 the University of Nebraska may accept royalties, equity, or other forms of compensation when technology is licensed, or new companies are formed to commercialize University technology.

9.3 Every potential Organizational COI must be reported to the appropriate COI Officer as soon as it is identified.

  **A.** Organizational COI may be identified through the required disclosure of financial interest of the Responsible Personnel at the time the IRB application is submitted.
B. Organizational COI may be identified through the required annual disclosure of financial interest of senior administrators when it relates to human subject research.

C. Organization COI may be identified by technology transfer officials or other officials at UNMC, UNO, and CHMC.

9.4 When Organizational COI is identified communication will be carried out with appropriate officials in order to ascertain the specifics of the Organizational COI.

9.5 The COI Officer of Component shall convene a group of senior Organizational officials and unaffiliated individual(s) who will be appointed by the appropriate Chancellor, CEO or designee to review the potential Organizational COI and propose any required management plans for approval.

9.6 The COI Officer will provide the approved management plan to the ORA.

9.7 The IRB will review the management plan and if any concerns are identified, these will be conveyed to the COI officer for further consideration and action.

9.8 The IRB must be assured that any Organizational COI is appropriately managed in the interest of the safety and welfare of human subjects.

9.9 Organizational COI management plans approved by the IRB will be maintained in the ORA for no less than seven (7) years following cessation of the activity.

**Administrative Approval:**
Ernest D. Prentice, PhD.  Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD  IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for the qualifications and responsibilities of the PI during the conduct of research within the Organization and at external sites under the PI’s protocol.

2.0 Policy
It is the policy of the Organization that the PI and all other personnel involved in the conduct of research must possess the required experience, skill, and appropriate medical licensure to safely conduct the research in full compliance with all applicable regulatory and Organizational requirements specified in HRPP policy #1.1.

3.0 Definitions
3.1 Principal Investigator (PI): The individual under whose direction the research is conducted and who assumes overall responsibility for the safe and proper conduct of the research (single or multi-site) in full compliance with all applicable regulations and UNMC HRPP policies.

   Note: HHS and FDA definitions of “investigator” can be found in HRPP policy #1.7.

3.2 Secondary Investigator (SI): The individual(s) who share responsibility with the PI for the safe and proper conduct of the research in full compliance with all applicable regulations and UNMC HRPP policies.

3.3 External Investigator (XI): The individual(s) who is conducting research under a UNMC IRB-approved research protocol at an external site and who is not employed by or otherwise representing the Organization.

3.4 Investigational New Drug: A new drug or biologic that is used in a clinical investigation.

3.5 Investigation New Drug Application (IND): An application submitted to FDA to conduct a clinical investigation with an investigational new drug.

3.6 Investigational Device: A device, including a transitional device that is the object of the investigation.

3.7 Investigational Device Exemption (IDE): An application submitted to FDA to conduct a clinical investigation with an investigational device that is classified as a significant risk device (SRD).

3.8 Sponsor-Investigator: The individual, who initiates the research, assumes overall responsibility for the research as indicated in #3.1 above and also fulfills the FDA-required responsibilities of a sponsor.

3.9 External Investigator’s Assurance (XIA): An assurance of compliance which must be completed by all XIs when the UNMC IRB is the IRB of record.

4.0 Qualification Requirements for the PI
4.1 The PI must be an employee, faculty, or student associated with the Organization.
4.2 The PI must be qualified by education, training, experience and medical licensure (as applicable) to assume overall responsibility for the safe and proper conduct of the research in full compliance with all applicable regulations and UNMC HRPP policies.

5.0 Responsibilities of the PI During the Conduct of Research

5.1 The PI will conduct protocols with sound research design consistent with current methods and ethical standards. The PI will seek independent review and consultation by other experts prior to submission to the IRB when appropriate.  
*Note: Research designed and conducted by students and trainees must be thoroughly reviewed by the faculty advisor and exhibit sound research design.*

5.2 The PI is responsible for obtaining IRB approval (or exempt determination) prior to initiating the research. Documentation of this approval must be written and dated.

5.3 The PI is responsible for conducting research in compliance with the IRB application, detailed protocol and any other documents approved by the IRB.

5.4 The PI will ensure compliance with applicable regulatory and HRPP requirements specified in *HRPP policy #1.1*.

5.5 The PI must oversee and be responsible for ensuring all research personnel comply with all applicable requirements, including, but not limited to, implementing the research in accordance with the IRB-approved protocol and completing all educational requirements as specified in *HRPP policy #3.11*.

5.6 The PI is responsible for ensuring that research is conducted in accordance with the terms of any grant, contract, and/or signed agreement.

5.7 The PI will ensure all secondary investigators (sub-investigators) and other study personnel conducting the research are qualified by education, training, experience, and medical licensure (as applicable) to safely conduct the research in full compliance with the applicable federal regulations, HRPP policies and the protocol.

5.8 The PI will provide all secondary investigator(s) conducting the research and other study personnel (as appropriate) with a copy of the: a) UNMC IRB-approved application and ICF(s)/information sheet(s), b) detailed protocol, c) Investigator’s Brochure, and d) other necessary documents.

5.9 The PI will ensure that all secondary investigator(s) and other study personnel fully understand the study and their obligations consistent with assigned responsibilities.

5.10 The PI will ensure risks to subjects and others have been minimized to the greatest extent possible.  
*Note: See *HRPP policy #3.2* for more information related to the requirements for minimization of risk.*

5.11 The PI will ensure the protocol contains a plan for just, fair, and equitable recruitment and selection of subjects.

5.12 The PI will ensure the protocol contains adequate provisions for monitoring the data collected to ensure the safety of subjects.

5.13 The PI will ensure there are adequate provisions to protect the privacy of subjects.
5.14 The PI will ensure there are adequate provisions to maintain the confidentiality of data. This includes an information security plan that includes consideration of the collection, storage, maintenance, analysis and transmission of data and other identifiable information.

5.15 The PI will ensure there are adequate resources to carry out the research safely. This includes, but is not limited to, sufficient investigator time, appropriately qualified research team members, equipment and space.

5.16 The PI may not make any changes in the research without IRB approval, except in accordance with 45 CFR 46.103(b)(4) and 21 CFR 56.108(b) where necessary to eliminate apparent immediate hazards to human subjects or provide the subject/LAR with critical information that is vital to the subject’s continued participation in the research in accordance with HRPP policy #2.4. Note: This includes changes in study personnel, changes in local accrual, and administrative changes in the full protocol.

5.17 Any change to the research, which is made to eliminate immediate hazards to subjects without prior IRB approval, shall be reported promptly to the IRB in accordance with HRPP policy #2.4. The report shall include a description of the change and the reason(s) for immediate implementation. As appropriate, a proposed amendment to the research should be submitted to the IRB for review and approval, as well as the funding agency.

5.18 The PI will ensure that when some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects in accordance with HRPP policy #4.1.

5.19 The PI is ultimately responsible for ensuring that legally effective informed consent is developed, obtained and documented in accordance with, and to the extent required by 45 CFR 46.116, 45 CFR 46.117, 21 CFR 50 (as applicable) and HRPP policy #5.1.

5.20 When consent is obtained by other authorized study personnel, the PI will ensure the individual is appropriately trained to obtain valid informed consent. In addition, the PI will exert ongoing supervision of all authorized study personnel. Note: Within this Organization, HIPAA authorizations have been combined with the research ICF as indicated in HRPP policy #3.4.

5.21 The PI will ensure that all secondary investigator(s) and other study personnel promptly report to the PI the following as applicable:
A. Internal adverse events which are unexpected and related, or possibly related to the study interventions (HRPP policy #8.2)
B. Unanticipated adverse device effects (HRPP policy #8.2)
C. Unanticipated problems involving risk to the subject or others (HRPP policy #8.4)
D. Noncompliance (HRPP policy #8.5)
E. Protocol deviations (HRPP policy #8.1)
F. Complaints (HRPP policy #8.3)

5.22 The PI will ensure that all of the incidents listed under Section 5.21 above are reported to the IRB in accordance with the applicable HRPP policies.
5.23 The PI will permit and facilitate monitoring and auditing of research, at reasonable times, by the IRB, funding agencies, and other authorized federal and state regulatory agencies.

5.24 The PI, or a qualified person(s) designated by the PI, shall conduct periodic audits of research records.

5.25 The PI is responsible for the accuracy, completeness, legibility, and timeliness of the data recorded and reported in presentations and publications about the research.

5.26 The PI will maintain records after the study ends for at least seven years or longer as required by applicable FDA, HIPAA, state, or sponsor requirements and should take measures to prevent accidental or premature destruction of these documents.

5.27 The PI is responsible for submitting continuing review reports to the IRB in accordance with the approval period specified by the IRB. The PI should fulfill the requirements for continuing review in time for the IRB to carry out the review prior to the expiration date of the current IRB approval.

5.28 If the PI closes the study early, the PI will provide the IRB with the Study Completion Report, and promptly inform the funding agency (if applicable).

5.29 Upon completion of the research, the PI will provide the IRB with the Study Completion Report and will also provide the funding and regulatory agencies with any required reports.

5.30 Once a study has been completed or closed, the PI must continue to honor any confidentiality protections of the data as well as other commitments agreed to as part of the approved research.

5.31 If a study is reclassified as completed or closed, the PI has a period of two (2) months from the date of completion to reactivate the study by providing appropriate justification. In order to reactivate after the two (2) month grace period, a new application must be submitted for IRB review and approval. Exceptions will only be made under extenuating circumstances.

6.0 Responsibilities of the PI for the Conduct of PI-Initiated Multicenter Research

6.1 The PI will fulfill all the applicable responsibilities described in Section 5.0 above.

6.2 The PI assumes overall responsibility for the safe and proper conduct of the research at all sites (within the Organization and external sites) in full compliance with all applicable regulations and UNMC HRPP policies.

6.3 The PI must have a process in place to coordinate and communicate issues related to the protection of human subjects to all performance sites including:
A. IRB initial review
B. IRB continuing review
C. IRB review of amendments
D. Consent requirements
E. HIPAA requirements
F. Information security including the confidential collection and transmission of data
G. Reporting requirements for:
   1) Unanticipated problems involving risks to the subject or others
   2) Adverse events
   3) Protocol deviations
   4) Noncompliance
   5) Complaints

H. Confidentiality of data including transmission of data

6.4 The PI will ensure that all external investigators promptly report to the PI the following:
   A. Adverse events which are unexpected, related or possibly related to the research.
   B. Adverse device effects which are unanticipated
   C. Unanticipated problems involving risk to the subject or others
   D. Noncompliance
   E. Protocol deviation
   F. Complaints
   G. Audits by sponsors, CRO’s, FDA, OHRP, or other federal authorities,
   H. Study reports as required by the protocol,
   I. Continuing review reports
   J. Interim results
   K. DSMB results (if appropriate)

6.5 The PI, or a qualified person(s) designated by the PI, shall conduct periodic audits of research records maintained by external investigator(s) at all sites.

6.6 If the PI determines the research presents an unreasonable risk to subjects, the PI will discontinue the study immediately and notifications shall be sent immediately to all investigators, the IRBs of record for all sites, the sponsor and FDA (as required).

6.7 When the external performance site(s) utilize(s) their own local IRB for oversight of the research, the PI must assure:
   A. The IRB application identifies the external sites.
   B. A copy of all of the following documents from the external sites are maintained in the research records:
      1) A copy of the external IRB approval letter(s) and approved ICF(s)/information sheet(s).
      2) The external site’s FWA number (required for HHS funded research)
      3) The external site’s IRB Registration number (required for FDA registered research)
      4) The external site’s HRPP accreditation status

6.8 When the external performance site(s) utilize(s) the UNMC IRB for oversight of research. The PI must assure:
   A. Compliance with HRPP policies #1.3 and 1.4 which addresses the requirements for research conducted under a Reliance Agreement.
   B. The IRB application identifies the external site(s).
   C. A ICF is developed for each site deferring to UNMC IRB review.
   D. The research records contains:
      1) Signed copies of each signed External Investigator Assurance (XIA).
2) A copy of each external investigator’s Curriculum Vitae (CV).

3) Copies of all signed ICFs obtained from subjects enrolled in the research by the external investigator(s) when the UNMC IRB is the IRB of record.

7.0 Additional Responsibilities of the PI during the Conduct of Research under the Oversight of an External IRB

7.1 The PI will fulfill all applicable external IRB requirements, as well as applicable requirements specified in HRPP policy #1.3.

7.2 The PI will comply with HRPP policies #1.3 and 1.4 which addresses the requirements for research conducted under a Reliance Agreement.

8.0 Additional Responsibilities of the PI During Conduct of FDA Regulated Research

8.1 The PI is responsible for ensuring every member of the study personnel:
   A. Reads and understands the information in the Investigator’s Brochure, including the potential risks and side effects of the drug or device.
   B. Ensures that a clinical investigation is conducted according to the signed investigator statement for clinical investigations of drugs, including biological products, or agreement for clinical investigations of medical devices, the investigational plan and other applicable FDA regulations and any conditions of approval imposed by the IRB or FDA.
   C. Controls drugs, biological products, and devices according to FDA regulations.

8.2 The PI must maintain a list of the appropriately qualified persons to whom significant trial-related duties have been delegated. This list should also describe the delegated tasks, identify the training that individuals have received that qualifies them to perform delegated tasks (e.g., CV, certifications), and identify the dates of involvement in the study. The PI should maintain separate lists for each study conducted by the investigator.

Note: PIs who conduct clinical investigations of drugs and devices under the FDA regulations commit themselves to personally conduct or supervise the investigation. When certain study-related tasks are delegated by a PI, the PI is responsible for providing adequate supervision of those to whom the tasks are delegated.

8.3 The PI is accountable for regulatory violations resulting from failure to adequately supervise the conduct of the clinical study (see HRPP policy #8.5).

8.4 The PI is responsible for protecting the rights, safety, and welfare of subjects under their care (or care of other study personnel) during the clinical trial (in compliance with 21 CFR 312.60 and 21 CFR 812.100). This responsibility includes:
   A. Providing reasonable medical care for subjects who experience a medical problem arising during participation in the trial that is, or could be, related to the study intervention.
   B. Adhering to the protocol so that subjects are not exposed to unreasonable risks.
8.5 The PI is responsible for maintaining adequate records in accordance with FDA regulations and to make those records available for inspection by the FDA (in compliance with 312.62):

A. **Disposition of drug.** The PI is required to maintain adequate records of the disposition of the drug, including dates, quantity, and use by subjects. If the investigation is terminated, suspended, discontinued, or completed, the investigator shall return the unused supplies of the drug to the sponsor, or otherwise provide for disposition of the unused supplies of the drug under 21 CFR 312.59.

B. **Case histories.** The PI is required to prepare and maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual administered the investigational drug or employed as a control in the investigation. Case histories include the case report forms and supporting data (e.g., signed and dated ICFs, and medical records). The case history for each individual shall document that informed consent was obtained prior to participation in the study.

C. **Record retention.** A PI shall retain records required to be maintained for a period of 2 years following the date a marketing application is approved for the drug for the indication for which it is being investigated and shall also retain records for seven years as required by Nebraska State Law.

8.6 The PI is responsible for timely submission of the following reports (in compliance with 21 CFR 312.64):

A. **Progress reports.** The PI shall furnish all reports to the sponsor of the drug who is responsible for collecting and evaluating the results obtained.

B. **Safety reports.** A PI must immediately report to the sponsor any serious adverse event, whether or not considered drug related, including those listed in the protocol or investigator brochure and must include an assessment of whether there is a reasonable possibility that the drug caused the event. Study endpoints that are serious adverse events must be reported in accordance with the protocol unless there is evidence suggesting a causal relationship between the drug and the event (e.g., death from anaphylaxis). In that case the investigator must immediately report the event to the sponsor. The investigator must record non-serious adverse events and report them to the sponsor according to the timetable for reporting specified in the protocol.

C. **Final report.** A PI shall provide the sponsor with an adequate report shortly after completion of the PI’s participation in the investigation.

D. **Financial disclosure reports.** The PI shall provide the sponsor with sufficient accrual financial information to submit complete and accurate certification or disclosure statements as required by the FDA. The PI shall promptly update this information if any relevant changes occur during the course of the investigation and for 1 year following the completion of the study.

*Note: Conflict of interest disclosures must also be submitted to the Organization for review as specified in HRPP policy #3.12.*

8.7 The PI shall, upon request from any properly authorized officer or employee of FDA, at reasonable times, permit such officer or employee to have access to and copy and
verify any records or reports made by the investigator. The PI is not required to divulge subject names unless the records of particular individuals require a more detailed study of the cases, or unless there is reason to believe that the records do not represent actual case studies, or do not represent actual results obtained (in compliance with 21 CFR 312.68).

8.8 If the investigational drug is subject to the Controlled Substances Act, the PI shall take adequate precautions, including storage of the investigational drug in a securely locked, substantially constructed cabinet or other securely locked, substantially constructed enclosure, access to which is limited to prevent theft or diversion of the substances into illegal channels of distribution (in compliance with 21 CFR 312.69).

Note: Within the Organization, all investigational drugs are dispensed per the respective hospital policy and HRPP policy #6.1.

9.0 Additional Responsibilities of a Sponsor-Investigator under an Investigator-Initiated IND

9.1 The PI is responsible for submitting to the IRB Addendum O: Principal Investigator Responsibilities-Investigator Initiated Drug Trials.

9.2 The PI is responsible for submitting to the FDA an IND in accordance with the requirements of 21 CFR 312.23, which includes all of the following which must also be maintained on file by the PI:
   A. FDA Form 1571: Investigational New Drug Application (IND)
   B. FDA Form 1572: Statement of Investigator
   D. FDA Form 3454: Certification: Financial Interests and Arrangements of Clinical Investigators (PI completes)
   E. FDA Form 3455: Disclosure: Financial Interest and Arrangements of Clinical Investigators (PI and sub-investigators complete)

9.3 The PI shall ensure there is on-going review and evaluation of evidence relating to the safety and effectiveness of the drug and report to: a) FDA in accordance with 21 CFR 312.33, and b) the UNMC IRB when there is a safety concern.

9.4 If the PI determines the investigational drug presents an unreasonable risk to subjects, the PI will discontinue the study immediately and notifications shall be sent immediately to all external investigators, the IRBs of record for all sites and FDA.

9.5 The PI will ensure that the disposition of all stocks of the investigational drug are in accordance with 21 CFR 312.59 (as described in 8.5(A) above) and will notify the FDA of any deviations to this policy.

9.6 The PI will maintain all records required by 21 CFR 312.57 (as described in 8.5(C) above) and HRPP policy #3.14.

10.0 Additional Responsibilities of a Sponsor-Investigator under an Investigator-Initiated IDE

10.1 The PI is responsible for submitting to the IRB Addendum P: Principal Investigator Responsibilities-Investigator Initiated Device Trials.
10.2 The PI is responsible for submitting to the FDA an IDE in accordance with the requirements of 21 CFR 812.20, which includes all of the following which must also be maintained on file by the PI:
   B. *FDA Form 3454:* Certification: Financial Interests and Arrangements of Clinical Investigators (PI completes)
   C. *FDA Form 3455:* Disclosure: Financial Interest and Arrangements of Clinical Investigators (PI and sub-investigators complete)

10.3 The PI must submit to FDA a certification of any IRB approval of an investigation or a part of an investigation not included in the IDE application in accordance with the requirements of 21 CFR 812.35(b).

10.4 If the PI or sponsor classifies a device as NSR, but the IRB determines the device to be SR, the PI is responsible for notifying the sponsor of the IRB’s determination.

10.5 The PI will provide the reports in a timely manner to the FDA, the IRBs of record, and all investigators participating in the research, in accordance with 21 CFR 812.150:
   A. Unanticipated adverse device effects
   B. Withdrawal of IRB approval
   C. Withdrawal of FDA approval
   D. Current list of investigators
   E. Progress reports
   F. Recalls and device disposition
   G. Final report
   H. Informed consent
   I. Significant risk device determination
   J. Other reports as necessary

10.6 The PI will assure that the investigational device or its immediate package bears a label in accordance with 21 CFR 812.5.

10.7 If the PI is storing the devices, he/she must maintain a log indicating the identification/serious number of the device, name of the subject, date dispensed, by whom it was dispensed, and the amount remaining.

10.8 The PI shall select monitors qualified by training and experience to monitor the investigational study.
   A. Monitors may be employees of the PI or an organization contracted by the PI to perform the duties of the study monitor.
   B. The PI must provide the FDA with the identity (the name and address) of the monitor and written monitoring procedures in compliance with 21 CFR 812.25(e).
   C. The monitor is responsible for assuring compliance with the requirements of 21 CFR 812.46 and: a) the signed agreement, b) investigational plan, c) IDE requirements, d) and other applicable FDA regulations or any other conditions of approval imposed by the IRB or FDA.

10.9 The PI shall ensure there is on-going review and evaluation of evidence relating to the safety and effectiveness of the device.
10.10 If the PI determines the investigational device presents an unreasonable risk to subjects, the PI will discontinue the study immediately and notifications shall be sent immediately to all investigators participating in the research, the IRBs of record and FDA. The PI must immediately conduct an evaluation of the event. In accordance with 21 CFR 812.45, study discontinuation must occur no later than 5 working days after the PI makes this determination and no later than 15 working days after the PI first receives notice of the event.

10.11 The PI will ensure that the disposition of all stocks of the investigational device are in accordance with 21 CFR 812.140 and will notify the FDA of any deviations to this policy.

10.12 The PI will maintain all records required by 21 CFR 812.140 and 812.2(b) and HRPP policy #3.5.

**Administrative Approval:**
Ernest D. Prentice, PhD  Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce Gordon, M.D  IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for initiating an External Investigator Assurance (XIA).

2.0 Policy
It is the policy of the Organization that an XIA is required when the UNMC IRB is the IRB of record for non-exempt research conducted at an external site involving an external investigator(s) (XI) who are not employed by or otherwise representing the Organization.

3.0 Requirements for Filing An XIA

3.1 An XIA is required when:
   A. An XI is involved in conducting research under a UNMC IRB approved research protocol at an external site.

   B. A subject participating in a UNMC IRB approved research protocol returns home and their private clinician will administer a test article (investigational drug under an IND or an investigational device under an IDE) or a non-standard treatment and provide specific data to the PI for use in research. The private clinician is considered an XI.

   C. A subject participating in a UNMC IRB approved research protocol returns home and their private clinician will perform follow-up intervention(s) (e.g., bone marrow biopsy, CAT scans) solely for research purposes. The private clinician is considered an XI.

3.2 An XIA is not required when:
   A. A subject participating in a UNMC IRB approved research protocol returns home and their private clinician will continue to provide standard of care treatment according to the protocol and standard treatment-related data will be sent to the PI for both clinical and research purposes. The private clinician is not considered an XI.

   B. A subject participating in a UNMC IRB approved research protocol returns home and their private clinician will perform routine clinical follow-up tests which would be performed outside of the research context anyway and the data will be provided to the PI for both clinical and research purposes. The private clinician is not considered an XI.

   C. A subject participating in a UNMC IRB approved protocol returns home under the care of their private clinician and continues to self-administer an investigational drug, with the private clinician responsible only for incidental care and for providing the PI with routine clinical follow-up data. Even though the data will also be used by the PI for research purposes, the private clinician is not considered an XI.

4.0 Initiating the Research at an External Site
Before UNMC IRB approved research can be initiated at the external site:

4.1 An XIA must be in effect for each XI at that site and a copy maintained on file with the PI.
4.2 An XIA is effective for all studies that the XI conducts under the oversight of the UNMC IRB; therefore only one XIA is required

4.3 The PI must comply with *HRPP policies #1.3, 1.4, and 3.13.*

**Administrative Approval:**
Ernest D. Prentice, PhD. Institutional Official Associate and Vice Chancellor for Academic Affairs
Bruce Gordon, M.D. IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for additional protections for vulnerable populations.

2.0 Policy
2.1 It is the policy of the Organization that the vulnerability of a potential subject population will be evaluated to ensure: a) there is sufficient justification for inclusion of the vulnerable subject population, and b) appropriate protections are in place for any subject who may be vulnerable in accordance with HHS regulations at 45 CFR 46.111(a)(3) and FDA regulations at 21 CFR 56.111(a)(3).

2.2 For federally funded research, the Organization will apply the requirements for special protections specified under HHS regulations at 45 CFR 46 Subpart B (pregnant women, human fetuses and neonates of uncertain viability or non-viable), Subpart C (prisoners), and Subpart D (children).

2.3 For non-federally funded research, the Organization will apply equivalent protections. These protections will be based upon the ethical principles in the Belmont Report. In addition, the requirements in 45 CFR 46, Subpart B, C, and D will be applied to the greatest extent possible in consideration of the nature of the research. When an exception is made, it must not reflect a lower standard of human subject protection.

2.4 For FDA regulated research, the Organization will apply the additional safeguards for children in clinical investigations under FDA regulations at 21 CFR 50 Subpart D.

2.5 It is the policy of the Organization to apply additional protections for other vulnerable populations such as decisionally-impaired persons, terminally ill, economically or educationally disadvantaged persons, or other vulnerable populations. In these situations, the IRB, in consultation with the PI, will determine the appropriate methods to protect the rights and welfare of the individuals in consideration of the Belmont Report, the nature of the research, and other factors determining vulnerability.

3.0 Definition
3.1 Vulnerable population is defined as an individual or group of individuals with limited autonomy (i.e., lacks independence in decision making for a variety of reasons) or is otherwise at increased risk compared to non-vulnerable individuals. Within any population of vulnerable subjects, individuals may have different levels of vulnerability based on the level of capacity, circumstance, or condition affecting independent decision-making.

4.0 Categories of Vulnerable Populations
Vulnerable populations may be categorized according to the following groups:

4.1 Pregnant women (Subpart B) (see HRPP policy # 4.2)
4.2 Fetuses and neonates (Subpart B) (see HRPP policy # 4.2)
4.3 Prisoners (Subpart C) (see HRPP policy # 4.3)
4.4 Children (Subpart D) (see HRPP policy # 4.4)
4.5 Decisionally impaired (see HRPP policy # 4.6)
4.6 Comatose
4.7 Terminally ill
4.8 Blind persons
4.9 Deaf persons
4.10 Economically disadvantaged
4.11 Educationally disadvantaged
4.12 Socially disadvantaged
4.13 Employees and students (see HRPP policy # 4.7)
4.14 Non-English speaking persons
4.15 Others as determined by the IRB and investigator

5.0 Factors Determining Vulnerability
5.1 The nature of the research.
5.2 The risks of the research.
5.3 The overall probability of risk occurrence in the subject population.
5.4 Degree of autonomy, or limited autonomy, present in the subject population.
5.5 The clinical status or impairment of the subject population.
5.6 The educational status of the subject population.
5.7 The economic status of the subject population.
5.8 The presence of a support system (i.e., family and friends) for the subject population.
5.9 Cultural or social factors associated with the subject population.
5.10 Others as determined by the IRB and investigator

6.0 Additional Protections for Vulnerable Populations
6.1 Upon determining the vulnerability of an individual or population, the IRB and investigator will provide special protections against risk. These additional protections will include those specified by HRPP policies for research involving pregnant women, fetuses, neonates (uncertain viability or non-viable), prisoners, children, or decisionally impaired subjects.

6.2 Other additional protections, as deemed necessary by the IRB, may also be included:
A. The use of an extended consent process.
B. The use of a consent monitor.
C. Appointment of a subject advocate.
D. Involvement of the subject’s family and/or friends.
E. The requirement for re-consenting of subjects/LARs.
F. Limits placed on risk.
G. Exclusion from participating in the research.
H. Increased safeguards to protect privacy and confidentiality.
I. Increased monitoring of the research through use of a Data Safety Monitoring Board (DSMB), the IRB or other mechanisms.
J. More stringent withdrawal criteria.
K. Longer study follow-up.

7.0 IRB Review of Research Involving Vulnerable Populations
7.1 The IRB will require the PI to address additional protections for vulnerable subjects in the IRB Application. In addition, depending upon the subject population the investigator is required to submit the appropriate addendum (i.e., B, C, D, E, F, and H).

7.2 Applications which require review by the full IRB will be processed and reviewed in accordance with HRPP policy #2.2. Applications that are eligible for review by the expedited method will be processed and reviewed in accordance with HRPP policy #2.3. In most cases, research involving vulnerable subjects will be reviewed by the full IRB.
7.3 If the IRB reviews and approves a protocol which does not involve vulnerable subjects but a subject, after enrollment, becomes vulnerable (e.g., incarceration, pregnant, or economically disadvantaged), the PI must notify the IRB and complete any required addendum. The IRB will review the submission in order to determine that the vulnerable subject(s) has appropriate additional protections. Subjects participating in federally funded research who fall under the requirements of Subparts B, C, or D must be withdrawn from the study unless their participation is in compliance with the Subpart.

7.4 The IRB determinations regarding inclusion of pregnant women, prisoners, and children will be documented in accordance with HRPP policies #2.2, 2.3, 4.2, 4.3, and 4.4.

7.5 The IRB determinations regarding inclusion of other vulnerable populations will documented in accordance with HRPP policies #2.2 and 2.3.
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for IRB review and approval of research involving pregnant women, fetuses, and neonates (nonviable or of uncertain viability).

2.0 Policy
2.1 Federally funded research involving pregnant women, fetuses, and neonates (nonviable or of uncertain viability) involved in research will be reviewed and approved in accordance with the requirements of 45 CFR 46 Subpart B. The IRB will classify the research in accordance with Subpart B and document how and why the proposal meets the requirements.

2.2 For non-federally funded research, the Organization will apply equivalent protections. These protections will be based upon the ethical principles in the Belmont Report. In addition, the requirements in 45 CFR 46, Subpart B will be applied to the greatest extent possible in consideration of the nature of the research. When an exception is made, it must not reflect a lower standard of human subject protection.

2.3 Females who are pregnant should not be routinely excluded from participating in research unless there are sound medical and/or scientific reasons not to include them. However, if pregnant women are justifiably excluded, it is important to ensure that the protocol contains a valid way to screen for pregnancy in accordance with HRPP policy #3.10.

3.0 Definitions
3.1 Pregnancy: Period from confirmation of implantation of a fertilized egg within the uterus until the fetus has been delivered. Implantation is confirmed through a presumptive sign of pregnancy (e.g., missed periods or a positive pregnancy test). While confirmation may be in error, investigators must presume that a living fetus was present until evidence is presented to the contrary.

3.2 Fetus: The product of conception from implantation until delivery.

3.3 Viable neonate: A neonate, after delivery, that can survive to the point of independently maintaining heartbeat and respiration. (A viable neonate is covered by HHS regulations at 45 CFR 46, Subparts A and D.)

3.4 Nonviable neonate: A neonate after delivery that, although living, is not viable.

4.0 IRB Review
In addition to review of research under HHS regulations at 45 CFR 46 (Subpart A), the IRB must assure additional protections are in place for pregnant women, fetuses and/or neonates involved in research in accordance with the following:

4.1 Research involving pregnant women or fetuses
Pregnant women may be involved in research if all of the following conditions are met:

A. Where scientifically appropriate, preclinical studies, including studies on pregnant animals and appropriate clinical studies involving non-pregnant women, have been
conducted and provide data for assessing potential risks for the enrollment of pregnant women and fetuses.

B. Any risk to the fetus is caused solely by interventions that offer direct benefit for the woman or fetus, or if there is no prospect of direct benefit, the risk to the fetus must not be greater than minimal, and

1) The purpose of the research is the development of important biomedical knowledge (interpreted in a broad context) that cannot be obtained by any other means OR

2) If the research is behavioral or social science in nature and is not federally funded, the purpose of the research must be to develop knowledge which has sufficient value which justifies the enrollment of pregnant women.

C. Any risk to the pregnant woman or the fetus is the least possible to achieve the research objectives.

D. Consent of the pregnant woman alone is required for research which:
   1) Offers direct benefit to the pregnant woman only, OR

   2) Offers direct benefit to the woman and fetus, OR

   3) Will not directly benefit the woman or fetus but: 1) there is no more than minimal risk to the fetus, and 2) the purpose of the research is to develop important biomedical knowledge and the data cannot be obtained by any other means.

E. Consent of the pregnant woman and father is required if the research offers direct benefit to only the fetus. However, the fathers' consent is not required if he is unavailable, decisionally impaired, temporarily incapacitated, or if the pregnancy resulted from rape or incest.

F. The consent must fully disclose the reasonable foreseeable impact of the research on the fetus or neonate (e.g., risk).

G. Parental permission for a pregnant child’s participation in research must also be obtained in accordance with HHS regulations 45 CFR 46, Subpart D (see HRPP policy # 4.4).

H. No inducements, monetary or otherwise, will be offered to terminate a pregnancy.

I. Individuals engaged in research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy.

J. Individuals engaged in research will have no part in determining the viability of a neonate.

4.2 Research Involving Neonates

A. Neonates of uncertain viability and nonviable neonates may be involved in research if:
1) Scientifically appropriate preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.

2) Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate.

3) Individuals involved in the research will have no part in determining the viability of the neonate.

4) The requirements listed below for uncertain and nonviable neonates have been met.

B. Neonates of Uncertain Viability: In addition to the conditions listed above in Section 4.2A, the following requirements must be met:

1) The research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability and any risk is the least possible for achieving that objective, or the purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research.

2) The legally effective informed consent of either parent of the neonate or, if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent’s legally authorized representative is obtained, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.

3) The consent fully discloses the reasonable foreseeable impact of the research on the neonate.

C. Nonviable Neonates: In addition to the conditions listed above in Section 4.2A, the following requirements must be met:

1) The vital functions of the neonate will not be artificially maintained.

2) The research will not terminate the heartbeat or respiration of the neonate.

3) There is no additional risk to the neonate resulting from the research.

4) The purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means.

5) The legally effective informed consent of both parents of the neonate is required, except that the waiver and alteration provisions do not apply. However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable neonate will suffice.

6) The consent of the father is not required where the pregnancy resulted from rape or incest.
7) The consent of a legally authorized representative of either or both of the parents of a nonviable neonate is not permitted.

4.3 Research involving placenta, dead fetus(s) or fetal material
Research involving the placenta, dead fetus, or fetal material after delivery may occur if all federal, state, or local laws and regulations are met. If any information associated with the material used in the research can be linked in any way to a living person, HHS regulations view the living person as a research subject and the research is subject to the regulations discussed in this policy.

Note: The State of Nebraska has no applicable local or state laws or regulations.

4.4 Research not otherwise approvable
The HHS Secretary may conduct or fund research that the IRB does not feel meets the above policy if the following conditions are met:

A. The IRB finds that the research, which will be funded by HHS, presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates, and the Secretary has determined through consultation with a panel of experts, that the research either does, in fact, meet the requirements of 45 CFR 46.204 or 45 CFR 46.205, OR

B. The Secretary determined that the research 1) presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health and welfare of pregnant women, fetuses or neonates, 2) will be conducted in accord with sound ethical principles and 3) informed consent will be obtained.

Note: For non-HHS funded research, involving pregnant women, fetuses, or neonates, the UNMC IRB will convene an equivalent panel of experts to advise the IRB.

5.0 Non-pregnant subjects who become pregnant during research
If a subject becomes pregnant while actively participating in a research protocol, the investigator must:

5.1 Determine if it is in the best interest of the pregnant subject to continue participating in the study or terminate participation in the study because there is increased risk in accordance with HRPP policy #8.4.

5.2 If it is in the best interest of the pregnant subject to remain in the study, adequate justification must be provided to receive IRB Chair approval for the subject to continue participation. If it is not in the best interest of the subject to continue, the subject’s participation must be terminated.

5.3 The study must be re-reviewed by the full IRB, as soon possible, in consideration of this policy.

6.0 Documentation of IRB Findings under Subpart B
The IRB will fully document compliance with Subpart B in the minutes of the IRB meeting.
7.0 Special Circumstances

7.1 When a previously enrolled subject becomes a pregnant

A. When a previously enrolled subject becomes pregnant and the research was not reviewed and approved by the IRB in accordance with this policy, the PI must report the situation to the IRB immediately.

B. Upon notification that a previously enrolled subject has become a pregnant and the PI wishes to have the subject continue to participate in the research, the IRB will promptly re-review the protocol in accordance with the requirements of this policy.

C. All research activities and interventions for the pregnant subject must stop until the protocol is reviewed under the requirements of this policy, except where the PI can justify that it is in the best medical interests of the subject to remain in the study. In this case, the IRB Chair may grant temporary approval for the subject to remain in the study until the IRB has met and determined that all of the applicable requirements of this policy have been met.

D. If the PI determines that the pregnant subject should be withdrawn from the study, the PI must make provisions for the continuation of any necessary treatment of the subject. The IRB should be promptly notified of this subject’s withdrawal and plans for continuity of treatment.

ADMINISTRATIVE APPROVAL:
Ernest D. Prentice, PhD.  Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD  IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for IRB review and approval of research involving prisoners.

2.0 Policy
2.1 Federally funded research involving prisoners will be reviewed and approved in accordance with the requirements of 45 CFR 46 Subpart C.

2.2 For non-federally funded research involving prisoners, the Organization will apply equivalent protections. These protections will be based upon the ethical principles in the Belmont Report. In addition, the requirements in 45 CFR 46, Subpart C will be applied to the greatest extent possible in consideration of the nature of the research. When an exception is made, it must not reflect a lower standard of human subject protection.

3.0 Definitions
3.1 Prisoner is defined by HHS regulations at 45 CFR 46.303(c) as “any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures that provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.”

Note: In accordance with OHRP guidance, application of the regulatory definition of prisoner includes the following: 1) Individuals detained in a residential facility for court-ordered substance abuse treatment; or 2) Individuals with psychiatric illnesses that have been committed involuntarily to an institution as an alternative to criminal prosecution or incarceration.

Note: Individuals who are on probation or parole regardless of whether they are required to wear a monitoring device are generally not considered prisoners. Individuals who have been voluntarily admitted to an institution for treatment of a psychiatric illness are also not considered prisoners. However, the aforementioned subject populations are vulnerable and, therefore, must be afforded additional appropriate protections as required by 45 CFR 46.111(b).

3.2 Minimal risk in prisoner research is defined by HHS regulations at 45 CFR 46.303(d) as “the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons.”

Note: The IRB interprets the term “healthy persons” to mean the average healthy person in the general population who is not incarcerated or otherwise qualifies as a prisoner in accordance with the definition in Section 3.1 of this policy.

4.0 IRB Membership Requirements
The UNMC IRB will satisfy the following additional requirements when the research involves prisoners:

4.1 The majority of the members of the IRB will not have an association with the prison(s) involved in the study (excluding the prisoner members).

4.2 At least one member of the IRB will be a prisoner or a prisoner representative.
4.3 The prisoner or prisoner representative must have a close working knowledge, understanding, and appreciation of prison conditions from the perspective of the prisoner.

4.4 A prisoner or prisoner representative must be involved in: a) initial review of the protocol, b) continuing review, c) protocol/consent amendments, d) review of reports of unanticipated problems involving risks to subjects, and e) all other IRB matters pertaining to protocols involving prisoners. When research involving prisoners is reviewed by the convened IRB the prisoner representative must be present as part of the quorum.

4.5 The prisoner or prisoner representative will present his/her review either orally, or in writing, at the convened meeting of the IRB when the research involving prisoners is reviewed.

5.0 Permitted Research Involving Prisoners

In accordance with HHS regulations at 45 CFR 46.306(a)(2), research may involve prisoners as subjects only if the research falls under one or more of the categories listed below:

5.1 Study of the possible causes, effects, and processes of incarceration and of criminal behavior, provided that the study presents no more than minimal risk, and no more than inconvenience to the subjects.

5.2 Study of prisons as institutional structures, or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk, and no more than inconvenience to the subjects.

5.3 Research on conditions particularly affecting prisoners as a class (for example, vaccine trials and other research on hepatitis, which is much more prevalent in prisons than elsewhere; and research on social and psychological problems, such as alcoholism, drug addiction and sexual assault).

5.4 Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subject.

Note: If HHS-funded research fits either category 5.3 or category 5.4 where prisoners are assigned to control groups which may not benefit from the research, final approval rests with the Secretary of HHS with OHRP acting on behalf of the Secretary. Following IRB approval, the entire research proposal (including the IRB-approved protocol, any relevant HHS grant application or proposal, consent documents, any IRB application forms, and any other information requested or required by the IRB for initial review) will be submitted to OHRP. OHRP will consult with appropriate experts, including experts in penology medicine and ethics, and publish notice, in the Federal Register, of intent to approve such research. HHS, through OHRP, will issue its approval in writing to the IRB.

Note: For research which is not funded by HHS, neither certification to OHRP nor expert review for Categories 5.3 and 5.4 is required. The IRB may however, at its discretion convene an equivalent expert review body to review studies classified as 5.3 or 5.4.

6.0 Procedures for IRB Review of Research Involving Prisoners

6.1 If a research protocol will involve prisoners that meet the definition of “prisoner” under Section 3.1 of this policy, the IRB application must also include completion of
Addendum C: Research Involving Prisoners as Subjects

which contains a requirement for provision of information necessary in order for the Board to determine that the proposed research meets all of the requirements of 45 CFR 46, Subpart C.

6.2 Expedited review of research involving prisoners

The UNMC IRB will normally not use expedited review for protocols, changes, or continuing review of research involving prisoners.

6.3 Research involving prisoners and exemption from IRB review

The UNMC IRB does not allow exemption from IRB review of research involving prisoners.

7.0 IRB Findings

The IRB will make the following additional findings for research involving prisoners:

7.1 The research represents one of the categories permissible under Section 5.0 of this policy.

7.2 Any possible benefits to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited-choice environment of the prison is impaired.

7.3 The risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers.

7.4 Procedures for the selection of subjects within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the PI provides to the IRB justification in writing for following some other procedures, control subjects will be selected randomly from the group of available prisoners who meet the characteristics needed for that particular research project.

7.5 The information is presented in language which is understandable to the subject population.

7.6 Adequate assurance exists that parole boards will not take into account a prisoner’s participation in research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole.

7.7 If the IRB finds there may be a need for follow-up examination or care of participants after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoners’ sentences and for informing participants of this fact.

7.8 The IRB may grant a waiver or alteration of informed consent in accordance with HRPP policies #5.2 or 5.3. However, exception circumstances and strong justification would be required in order for the IRB to grant the waiver.

7.9 The IRB may grant a waiver of signed consent in accordance with HRPP policy #5.5.
8.0 Documentation of IRB Findings
The IRB will prepare and maintain documentation of the specific findings required under this policy in order to approve research involving prisoners.

9.0 HHS Funded Research - Certification To OHRP
9.1 The IRB is responsible for providing certification to OHRP that the IRB has made the seven findings applicable to HHS-funded research involving prisoners. The IRB will send OHRP a certification letter to this effect, which includes:

A. The name and address of the institution.

B. Identification of the research protocol and relevant HHS grant application or protocol.

C. A copy of all paperwork necessary for IRB initial review (detailed protocol, relevant HHS grant application or proposal, IRB application, ICF(s), etc.).

D. Verification of the presence of a prisoner representative during consideration of the study.

E. Verification of the seven required findings (listed above).

F. Determination that the research meets one of the above categories of research permissible by federal regulations.

10.0 Special Circumstances
10.1 When a previously enrolled subject becomes a prisoner
A. When a previously enrolled subject becomes a prisoner and the research was not reviewed and approved by the IRB in accordance with this policy, the PI must report the situation to the IRB immediately.

B. Upon notification that a previously enrolled subject has become a prisoner and the PI wishes to have the prisoner continue to participate in the research, the IRB will promptly re-review the protocol in accordance with the requirements of this policy.

C. All research activities and interventions for the now incarcerated prisoner-subject must stop until the protocol is reviewed under the requirements of this policy, except where the PI can justify that it is in the best medical interests of the subject to remain in the study while incarcerated. In this case, the IRB Executive Chair may grant temporary approval for the subject to continue in the study until the IRB has met and determined that all of the applicable requirements of this policy have been met.

D. If the PI determines that the prisoner should be withdrawn from the study, the PI must make provisions for the continuation of any necessary treatment of the subject. In general, this would entail consultation with prison authorities and transfer of medical records. The IRB should be promptly notified of this subject’s withdrawal and plans for continuity of treatment.

10.2 When a potential subject is an adolescent detained in a juvenile detention facility
If a potential subject is an adolescent detained in a juvenile detention facility, the individual is both a child and a prisoner. In such a case additional protections for
prisoners and children who are research subjects must be provided in accordance with HRPP policies #4.3 and #4.4.

10.3 When the PI indicates that the proposed subject population may have a high risk of incarceration during the course of the study (but currently does not include prisoners)

Any proposed subject population that has a high risk of incarceration during the course of the study is generally considered to be a vulnerable population. Therefore, the IRB will provide for appropriate additional protections in accordance with 45 CFR 46.111(b).

11.0 Waiver of Requirements for Epidemiologic Studies

Epidemiological studies involving prisoners as subjects need not meet the requirements of Section 5.0 of this policy providing the research satisfies the following criteria:

11.1 The sole purpose of the research is (i) to describe the prevalence or incidence of a disease by identifying all cases, or (ii) to study potential risk factor associations for a disease.

11.2 The research presents no more than minimal risk and no more than inconvenience to the prisoner-subjects, and

11.3 Prisoners are not a particular focus of the research.

Note: On June 20, 2003, HHS approved a waiver of the applicability of 45 CFR 46.305(a)(1) and 46.306(a)(2) for specified epidemiologic research conducted or supported by HHS. This means that the research under this waiver provision need not fall within the categories specified in Section 5.0 of this policy. For such studies, the IRB will certify to OHRP that the IRB approved the research and fulfilled its duties under 45 CFR 46.305(a)(2)-(7). Non-HHS funded studies do not require this certification.

Note: The range of studies to which the proposed waiver would apply includes epidemiological research related to chronic diseases, injuries, and environmental health. This type of research uses epidemiologic methods (such as interviews and collection of biologic specimens) that generally entail no more than minimal risk to the subjects.

Administrative Approval:
Ernest D. Prentice, PhD. Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for research involving children.

2.0 Policy
2.1 Federally funded research involving children will be reviewed and approved in accordance with the requirements of HHS regulations at 45 CFR 46 Subpart D; FDA regulations at 21 CFR 50 Subpart D (as applicable), and applicable state law. The IRB will classify the research in accordance with Subpart D and document how and why the proposal meets the requirements.

2.2 For non-federally funded research and non-FDA regulated research, the Organization will apply equivalent protections. These protections will be based upon the ethical principles in the Belmont Report. In addition, the requirements in 45 CFR 46, Subpart D will be applied to the greatest extent possible in consideration of the nature of the research. When an exception is made, it must not reflect a lower standard of human subject protection.

3.0 Definitions
3.1 Children are defined as persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.

In the state of Nebraska, the age of majority is defined, according to Nebraska State Statute 43-2101 as “all persons under nineteen years of age are declared to be minors, but in case any person marries under age of nineteen years, his or her minority ends.”

If the subject is Native American living on federal tribal lands, regardless of the state law, federal law has set the age of majority at age 18.

If the research is conducted in another state under the oversight of the UNMC IRB, the age of majority is set by that state.

3.2 Assent is defined as a child’s affirmative agreement to participate in research. Federal regulations and sound ethical practice require that assent be obtained when, in the judgment of the IRB, the children are capable of providing assent. Mere failure to object, absent affirmative agreement, is not construed as assent.

3.3 Commensurate is defined as the requirement that children and/or their parents/guardians are familiar with procedures that are reasonably similar in nature and risk proportional to those the child has experienced, or is expected to experience, and not restricted to specific situations the child has experienced.

3.4 Disorder or condition is defined as a specific (or set of specific) physical, psychological, neurodevelopmental, or social characteristic(s) that an established body of scientific evidence or clinical knowledge has shown to negatively affect children’s health and well-being or to increase their risk of developing a health problem in the future.

3.5 Dissent is defined as a child’s affirmative decision to decline participation in research.
3.6 **Minimal risk** means "The probability (of occurrence) and magnitude (seriousness) of harm or discomfort (e.g., psychological, social, legal, economic) associated with the research are not greater than those ordinarily encountered in daily life (of the average child in the general population) or during the performance of routine physical or psychological examinations or tests." Minimal risk, therefore, is used to define a threshold of anticipated harm or discomfort associated with the research that is low.

The determination of minimal risk should take into account that a) children face differing risks at different ages, b) risks associated with repetitive tests may increase, and c) special/unique characteristics may make a certain population more vulnerable than average children (e.g., hemophilia). The risks associated with routine examinations or tests are equivalent to a routine well-child examination.

3.7 **Minor increase over minimal risk** is defined as a slight increase over minimal risk. In determining whether the research procedures or interventions present a minor increase over minimal risk, the IRB will consider the following criteria: 1) magnitude, probability, and duration of the potential harm in consideration of the characteristics of the subject population and 2) irreversibility of the harm to the child.

3.8 **Vital importance:** There must be clear and significant scientific evidence that the interventions or procedures in the research are likely to yield generalizable knowledge that will contribute to understanding the etiology, prevention, diagnosis, pathophysiology, amelioration, or treatment of the subject’s disorder or condition.

3.9 **Parent** is defined as a child’s biological or adoptive parent.

3.10 **Guardian** is defined as an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care. In Nebraska the governing statute is Neb Rev Stat 30-2627.

3.11 **Permission** is defined as the agreement (consent) of parent(s) or guardian(s) to the participation of the child or ward in research.

4.0 **Categories of Research**

HHS and FDA regulations specify that research involving children must be approvable under one or more of the following four (4) categories and meet the specified criteria:

4.1 **Research not involving greater than minimal risk (45 CFR 46.404; 21 CFR 50.51)**
A. The IRB will determine and document (including protocol-specific information justifying each IRB finding) that no greater than minimal risk to children is presented.

B. Adequate provisions must be made for soliciting assent of the children and permission of their parents or guardians, as set forth in 45 CFR 46.408, 21 CFR 50.55, and Sections 5.0 and 6.0 of this policy.

4.2 **Research involving greater than minimal risk, but presenting the prospect of direct benefit to the individual subjects (45 CFR 46.405; 21 CFR 50.52)**
A. The IRB finds and documents (including protocol-specific information justifying each IRB finding) that more than minimal risk to children is presented by an intervention to procedure that holds out the prospect of direct benefit for the individual subject,
or by a monitoring procedure that is likely to the contribute to the subject’s well being.

B. The IRB finds that:
   1) The risk is justified by the anticipated benefit to the subjects.
   2) The relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches.
   3) Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians, as set forth in 45 CFR 46.408, 21 CFR 50.55, and Sections 5.0 and 6.0 of this policy.

4.3 Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject’s disorder or condition (45 CFR 46.406; 21 CFR 50.53)
   A. The IRB finds and documents (including protocol-specific information justifying each IRB finding) that more than minimal risk to children is presented by an intervention or procedure that does not hold out the prospect of direct benefit for the individual subject, or by a monitoring procedure which is not likely to contribute to the well-being of the subject.
   B. The IRB finds that:
      1) The risk represents a minor increase over minimal risk.
      2) The intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations.
      3) The intervention or procedure is likely to yield generalizable knowledge about the subjects’ disorder or condition, which is of vital importance for the understanding or amelioration of the subjects’ disorder, or condition.
      4) Adequate provisions are made for soliciting assent of the children and permission of their parents or guardians, as set forth in 45 CFR 46.408, 21 CFR 50.55, and Sections 5.0 and 6.0 of this policy.

4.4 Research, not otherwise approvable, which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children (45 CFR 46.407; 21 CFR 50.54)
   A. The IRB will submit this category of research to HHS and/or FDA for approval, if the research is funded by HHS or is FDA-regulated. If the research is not HHS-funded or subject to FDA requirements, the IRB will, at the Board’s discretion, convene an equivalent expert review panel.
   B. In order to determine whether the research should be submitted for review at the Federal level, the IRB must find and document the following:
      1) The research does not qualify under 45 CFR 46.404, 405, 406; 21 CFR 50.51, 52, 53.
      2) The research presents a reasonable opportunity to further the understanding, prevention or alleviation of a serious problem affecting the health or welfare of children.
3) The research meets applicable requirements of 45 CFR 46; 46.408; 46.409; 21 CFR 50, 56, (as applicable).

4) Research will be conducted in accordance with sound ethical principles.

5) Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians.

4.5 Research Involving Wards

A. HHS regulations at 45 CFR 46.409 and FDA regulations 21 CFR 50.56 have set specific requirements for children who have been declared wards of the state, other agency, institution or entity.

B. Wards may participate in research classified as 45 CFR 404 or 405 and 21 CFR 50.51 or 50.52 providing all of the requirements under Subpart D are met.

C. Wards may participate in research classified as 45 CFR 406 or 407 and 21 CFR 50.53 or 50.54 only if all of the following additional conditions are met:

   1) The research is related to their status as wards or will be conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.

   2) An advocate will be appointed for each child who is a ward. The advocate must be approved by the IRB and fulfill the following requirements:

      a) The advocate will serve in addition to any other individual acting on behalf of the child as guardian or in loco parentis.

      Note: One individual may serve as an advocate for more than one child.

      b) The advocate must have appropriate education and training in order to take into consideration the nature of the research, the expectation of the advocacy role and the ability to act in the best interest of the child for the duration of the child’s participation in the research.

      Note: The advocate must have a) the ability to make a determination regarding each ward’s participation in research that is independent and free of all conflicts of interest, b) ability to become familiar with the child’s health, behavior, social and physical environment, and c) a willingness to serve an intermediary role between the child, investigator, guardians, and the IRB. This may include, as appropriate, meeting with wards, biological parents, foster parents, and investigators as necessary.

      c) The advocate must not be associated in any way with the research, the investigator(s) or the guardian organization, except in the role as advocate or a member of the IRB.

      d) The advocate must promptly notify the investigator and the IRB of any concerns about the child’s participation in research.

D. The enrollment of wards in the research is justified and permitted by Nebraska State Law. Children, who are wards of the state or any other agency, institution, or entity, can be included in research only if there is sufficient justification for including this
vulnerable population. In the state of Nebraska Department wards are not permitted to participate in research unless the Department allows an exception.

5.0 Requirements for Parental Permission

5.1 Permission (hereafter referred to as “consent”) of the parent(s)/guardian(s) is required for research involving children unless a waiver is granted by the IRB under the provisions of 45 CFR 46.408(c) or 45 CFR 46.116(d).

A. In addition to the provisions for waiver, if the IRB determines that a research protocol is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children), it may waive the consent requirements, provide an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted, ad provide further that the waiver is not inconsistent with federal, state, or local law.

B. The choice of an appropriate mechanism would depend upon the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research subjects, and their age maturity, status, and condition.

*Note: Waiver of parental consent is not applicable for FDA regulated research.*

5.2 Permission by parents/guardian must be documented in accordance with and to the extent required.

5.3 The IRB shall determine, in accordance with and to the extent that consent is required, that adequate provisions are made for soliciting the permission of each child’s parents/guardians.

5.4 Consent of one parent/guardian is sufficient for research conducted under 45 CFR 46.404; 21 CFR 50.51, unless the IRB specifically finds that consent of two parents is necessary

5.5 Consent of one parent/guardian is required for research conducted under 45 CFR 46.405; 21 CFR 50.52, unless the IRB specifically finds that consent of two parents is necessary.

5.6 Consent of both parents/guardians is required for research conducted under 45 CFR 46.406; 21 CFR 50.53 unless one parent/guardian is deceased, unknown, incompetent, and not reasonably available or when only one parent/guardian has legal responsibility for the care and custody of the child.

5.7 Consent of both parents/guardians is required for research conducted under 45 CFR 46.407; 21 CFR 50.54 unless one parent/guardian is deceased, unknown, incompetent, not reasonably available, or when only one parent/guardian has legal responsibility for the care and custody of the child.

5.8 The IRB requires utilization of a Parental/Guardian ICF written in accordance with the IRB template.

6.0 Requirements for Child Assent

6.1 The IRB will determine that adequate provisions are made for soliciting the assent of the children, when in the judgment of the IRB the children are capable of providing assent.
6.2 The IRB believes that given age, maturity, intellect, decision-making capacity and psychological state, children younger than 7 years of age, as a group, cannot reasonably be involved in a formal process of assent. However, dependent upon the cognitive ability of an individual child the investigator should engage that child in an appropriate discussion about participation in the research to the extent possible [45 CFR 46.408(a); 21 CFR 50.55(b)].

6.3 Assent is required from children 7 to 18 years of age unless, the investigator justifies a waiver of assent in Addendum L in accordance with the following:

A. The IRB is able to determine that the capacity of some, or all, of the children is so limited that they cannot be reasonably consulted. In making this determination the IRB shall take into account the ages, maturity, intellect, decision-making capacity, and psychological state of the children involved. This judgment may be made for all children involved in the research, a subset of children, or for each child as the IRB deems appropriate [45 CFR 46.408(a); 21 CFR 50.55(b)]. OR

B. The IRB is able to determine that the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research [45 CFR 46.408(c) and 21 CFR 50.55(c)]. OR

C. The IRB is able to determine that the research meets the requirements for a waiver of assent under 45 CFR 46.116(d); 21 CFR 50.55(d).

D. Unless assent has been waived as above, children who do not provide assent, or who actively dissent may not be enrolled in the research.

E. Even where the IRB determines that the subjects are capable of assenting the IRB may still waive the assent requirement under circumstances in which consent may be waived.

7.0 Procedures for Child Assent

7.1 If a child is between the ages of 7 and 12 the following procedure for assent must be followed:

A. The child should be given a copy of the Child Study Information Sheet which includes a description of the research written at the appropriate language level. It should include (at least) the following: purpose, methods, risks, and the voluntary nature of participation.

B. The investigator should engage the child in an appropriate discussion about participation in the research to the extent possible in consideration of the child's age and cognitive ability. The child's parent(s) should be included in this discussion.

C. If the child agrees to participate, the investigator should document the child's assent in the research record.

7.2 If a child is between the ages of 13 and 18 the following procedure for assent must be followed:

A. The child should be given a copy of the Youth Study Information Sheet which includes a description of the research written at the appropriate language level. It should include (at least) the elements of assent specified in Section 7.1(A) above.
B. The investigator should engage the child in an appropriate discussion about participation in the research. For younger children, it may be appropriate to include the child’s parent(s) in this discussion.

C. If the child agrees to participate, assent should be documented by having the child sign the assent signature blank on the parental ICF.

8.0 Consent of Subjects Reaching the Age of Majority

8.1 Children who reach the age of majority while actively participating in an IRB-approved study must give their consent to continue participation in the research, at the first visit after reaching the legal age of majority in the manner described in IRB application. Subjects must then sign the IRB-approved adult informed consent document.

8.2 If the study only involves data analysis (that is, all research interventions have been completed) children who reach the age of majority do not need to provide consent. However, it may be respectful to remind them of their participation in the research protocol.

8.3 If, upon reaching the age of majority, the now adult subject is unable to execute legally effective informed consent, the parental/legal guardian consent remains in effect. This must be documented in the study records or patient medical record and the IRB must be notified.

The now adult subject has the right to refuse to continue participation in the study. This is to be respected and undue pressure or coercion to continue may not be applied. While new data may not be collected on subjects refusing participation, existing prior data collected under the parent/guardian consent process can be used.

9.0 Waiver or Alteration of Parental Consent and/or Child Assent

9.1 If the IRB application includes a request for waiver/alteration of parent consent or child assent, the following addenda must be completed (as applicable) [45 CFR 46.408(c); the HIPAA Privacy Rule; 45 CFR 46.116(d)]:

A. Addendum J: Waiver or Alteration of Informed Consent and HIPAA Authorization in Biomedical, Medical Records, HBM Research, Biorepositories, and Data Banking

B. Addendum K: Waiver or Alteration of Informed Consent and HIPAA Authorization in Social Science and Behavioral Research

C. Addendum L: Waiver or Alteration of Child Assent

9.2 A waiver of parental/guardian consent is not permitted in FDA regulated research.

10.0 Waiver for the Requirement for Documentation of Parental Consent

10.1 If the IRB application includes a request for waiver of the requirement to obtain a signed consent, Addendum M: Waiver of Requirement to Obtain Signed Consent must be included [45 CFR 46.117(c); 21 CFR 56.109(c)].

11.0 Procedures for IRB Review

11.1 IRB Assignment:

A. The IRB-04 will review research involving only children (less than 19 years of age) conducted within the Organization in accordance with the authorization specified in HRPP policy #1.2.
B. The responsible IRB for research which includes both children and adults will be determined on a case-by-case basis by the IRB Executive Chair/designee. In general, protocols will be reviewed by the IRB-04 if the PI is: 1) a faculty member of the Department of Pediatrics or a pediatric subspecialty department or section (for example, Pediatric Anesthesia or Pediatric Surgery), or 2) a pediatrician or pediatric subspecialist with admitting privileges at CH&MC. The IRB Executive Chair/designee, or the full IRB, may request appropriate consultation to assist in review of protocols involving adults.

C. In general, where the majority of subjects are adults but also include older children (i.e., adolescents), the research will be reviewed by IRB-01 or IRB-02.

11.2 IRB Application Submission Requirements:

A. For research involving only children, the investigator must submit the IRB application for Pediatric Biomedical Research or Pediatric Social Science and Behavioral Research.

B. For research including both children and adults which will be reviewed by the PedsIRB (per Section 11.1 above), the investigator must submit the 1) Pediatric Biomedical Research or Pediatric Social Science and Behavioral Research, and 2) Addendum Y: Research Involving Adults

C. For research where the majority of subjects are adults but also include adolescents or young adults under review by IRB-01 or IRB-02 (per Section 11.1 above), the investigator must submit: 1) the IRB Application for Biomedical Research or Social Science and Behavioral Research, and 2) Addendum D: Research Involving Children.

D. If the research includes children who are wards of the state or any other agency, institution, or entity, the IRB application must also include Addendum H: Research Involving Children Who Are Wards. If the investigator may reasonably anticipate that some subjects may become wards during the course of research which provides a vitally important therapeutic option, the above addendum should be submitted.

E. If a child becomes a ward while participating in the research, the IRB must be promptly notified and Addendum H should be submitted.

11.3 IRB Review Process:

A. Applications which require review by the full IRB will be processed and reviewed in accordance with HRPP policy # 2.2.

B. Applications that are eligible for review by the expedited method will be processed and reviewed in accordance with HRPP policy #2.3.

C. The assigned IRB reviewer(s) for both expedited and full board reviews will utilize the Subpart D Addendum Checklist. Completion of the form is not required.

12.0 Documentation of Compliance with Subpart D

12.1 IRB review and approval of research involving children must include all necessary documentation that the research meets the additional requirements of 45 CFR 46, Subpart D; 21 CFR 50, Subpart D (as applicable); and applicable HRPP policies.
12.2 Research qualifying for a waiver or alteration of parental/guardian consent/child assent must be documented in accordance with applicable requirements of 45 CFR 46.116(d), HIPAA Privacy Rule, or 45 CFR 46.408(c). FDA-regulated research does not qualify for a waiver of parental/guardian consent. Documentation will include a copy of the IRB-approved Addendum L.

12.3 Research qualifying for a waiver of the requirement for the investigator to obtain a signed ICF must be documented in accordance with applicable requirements of 45 CFR 46.117(c); 21 CFR 56.109(c), (d). Documentation will include a copy of the IRB-approved Addendum M.

**Administrative Approval:**
Ernest D. Prentice, PhD.  Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD  IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for convening a local 407 Panel to consider pediatric research which is not federally funded or FDA regulated.

2.0 Policy
It is the policy of the Organization that the IRB Executive Chair may convene a local 407 Panel if all of the following conditions are met:

2.1 The IRB determines, by two-thirds majority vote, that:

   A. A research protocol presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children, and

   B. The IRB does not believe the research meets the requirements of HHS regulations at 45 CFR 46.404, 46.405, or 46.406.

2.2 The research is not funded by DHHS, or one of the Common Rule agencies, or involves an investigational drug, device, or biologic regulated by the FDA.

3.0 Membership
3.1 The local 407 Panel will include at least 4 voting members and 1 non-voting member:

   A. Two or more experts in a discipline relevant to the research being reviewed. At least one must be unaffiliated with the institution.

   B. One expert with general pediatrics experience

   C. One non-scientist

   D. The IRB Executive Chair (non-voting) will serve as the Chair of the local 407 panel.

3.2 If a member with the expertise in a discipline relevant to the research being reviewed is not available locally, then the IRB Executive Chair will enlist the services of a non-local consultant. The consultant will receive the materials described below and will provide a written response to the general and specific questions noted below for consideration by the Panel.

3.3 The role of the IRB Executive Chair will be to:

   A. Chair the meeting and focus relevant discussion.

   B. Provide relevant regulatory information and guidance to the 407 Panel to assist their analysis.

   C. Present a summary of the research.

   D. Present the analysis of the IRB with respect to classification under 45 CFR 46.404, 405, and 406.
E. Answer questions from the panel relevant to the deliberations of the IRB.

4.0 407 Panel Review

4.1 At least one week prior to the meeting, the IRB administrator will circulate the following to 407 Panel members:

A. A copy of the IRB application, full protocol, ICF(s)/information sheet(s), and all other relevant protocol related documents.

B. A copy of 45 CFR 46, Subparts A and D.

C. Questions for consideration.

4.2 At the scheduled local 407 Panel meeting, the Chair will present a summary of the research, followed by the analysis of the IRB with respect to the classification under 45 CFR 46.404, 405, and 406.

Note: The analysis will include a discussion of the regulatory definitions of all relevant terms (e.g., minimum risk and minor increase over minimal risk) as well as current guidance (from the HHS Office of Human Research Protections (OHRP), the HHS Secretary’s Advisory Committee on Human Research Protections (SACHRP), and/or other advisory committees) regarding interpretation of regulatory language.

4.3 The local 407 Panel will determine the following:

A. The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; and

B. The research will be conducted in accordance with sound ethical principles, or

C. The research meets the requirements of 46.404, 405 or 406.

4.4 The written 407 local Panel Report will be transmitted to the IRB within one week of the Panel meeting.

5.0 Full IRB Review

5.1 Based on the Panel Report, the IRB, at its subsequent convened meeting, will make one of the following determinations:

A. The research, in fact, satisfies the regulatory criteria for approval under HHS regulations at 45 CFR 46.404, 405, or 406.

B. The research satisfies the criteria for approval under 45 CFR 46.407:

   1) Presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; and

   2) Has made adequate provisions for soliciting the assent of children and the permission of their parents or guardians, as set forth in 46.408.

C. The research is not approved.
5.2 A two-thirds majority vote will be required to approve the research under Section 4.7 (A) or (B) above. If a two-thirds majority vote is not obtained for either 4.7 (A) or (B), then the research is not approved.

5.3 The investigator will be informed, in writing, of the decision of the IRB within one week of the meeting of the convened IRB.

5.4 If the research is not approved, the PI has the right to appeal in writing to the IRB and address the IRB at a convened meeting.

**Administrative Approval:**
Ernest D. Prentice, PhD.  Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD  IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for IRB review of research involving subjects who have impaired decision-making capacity rendering them unable to provide legally effective informed consent and vulnerable to undue influence and coercion.

2.0 Policy
It is the policy of the Organization that research involving subjects who have impaired decision-making capacity and therefore cannot provide legally effective informed consent must include appropriate additional protections in accordance with the requirements of HHS regulations at 45 CFR 46.111(b) and FDA regulations at 21 CFR 56.111(b) as applicable.

3.0 Definitions
3.1 Decisionally impaired subject is defined as a person that lacks the ability to reason, exhibit sound judgment and provide legally effective consent to participate in research. The impairment may fluctuate (e.g., mental disorders such as schizophrenia), decline with time (e.g., Alzheimer’s), or result from health conditions (e.g., coma or other infirmity).

3.2 Legally Authorized Representative (LAR) is defined as follows:
A. The parent or parents having legal custody of the decisionally impaired person.
C. The individual authorized to consent on behalf of a decisionally impaired person pursuant to a legally effective Health Care Power of Attorney (POA-HC).
D. An Institutionally Authorized Surrogate per Section 3.3 below.

3.3 Institutionally Authorized Surrogate (IAS) is defined in the priority order listed below in accordance with Nebraska Medicine policy MS14:
A. The nominee of an attorney-in-fact who is given authority by the decisionally-impaired person’s power of attorney or durable power of attorney for health care to name a surrogate.
B. A spouse.
C. An adult child.
D. A parent, or the written nominee of a deceased parent.
E. Any relative the incapacitated person with whom he or she has resided for more than six months.
F. An adult sibling.
G. An adult person in the next degree of kindred in the order named by the succession laws in the state of Nebraska.
H. Significant others who have a current sustained relationship with the decisionally impaired person and can present the person’s preferences.  

*Note: An individual who has a sustained relationship with a decisionally impaired person has known that person for a reasonable period of time and has either lived with the person or has interacted on a regular basis and is, therefore, knowledgeable about the family (social) history and life experiences of the decisionally impaired person.*

3.4 **Adult assent** is defined as the affirmative agreement of a decisionally impaired person to participate in research.

4.0 **Assessment of Capacity to Consent**

4.1 The determination that a prospective subject is decisionally-impaired and, therefore, lacks the capacity to provide legally effective informed consent may have been: 1) adjudicated by the Court, or b) determined by an investigator, who, by their professional training, licensure, or experience, is qualified to determine competency, or an independent assessor.

4.2 When assessing capacity to consent one of the following should be used: a) a standard assessment instrument (e.g., mini-mental status exam), or b) the *Assessment of Capacity to Consent to Participate in Research* instrument available on the IRB website at [http://unmc.edu/irb](http://unmc.edu/irb).

4.3 It is generally recommended that the PI use an independent, experienced assessor or a consent monitor who can observe the process of informed consent.

4.4 If an individual lacks the capacity to consent they can only be enrolled in research if an LAR provides consent on their behalf.

5.0 **Appointment and Authority of the LAR**

5.1 If a prospective subject does not have an LAR as defined in Section 3.2 A, B, or C above, an IAS should be appointed.

5.2 The prospective subject’s capacity to choose an IAS should be assessed and, when possible, the subject’s choice should be honored.

5.3 Availability, willingness and capacity to serve as a responsible surrogate decision-maker should be considered in the appointment of an IAS.

5.4 If multiple IASs are available, and the prospective subject is incapable of choosing, appointment of the IAS should be in the prior listed in Section 3.3.

5.5 The LAR should normally use “substituted judgment” where possible as opposed to “best interests”. It is important for the LAR to consider what would be the subject’s position given a choice whether or not to participate in the research when they were not cognitively impaired.

5.6 An IAS is only permitted to provide proxy consent for a decisionally impaired person’s participation in research when, a) the research offers the prospect of direct medical benefit to that person, and b) it is not possible to appoint a legal guardian or a POA-HC.
An IAS is not permitted to act as an LAR for research which does not offer the prospect of direct medical benefit to the subject.

6.0 Assent and Dissent

6.1 Investigators have an obligation to ensure that a decisionally-impaired person with sufficient cognitive ability is provided an opportunity to give their assent to participate in research.

6.2 If a decisionally impaired person actively dissents to *initially participate in research*, that dissent *must* be honored as long as the research does *not* hold out the prospect of direct subject benefit that is only available in the context of the research.

If the research holds the prospect of direct subject benefit, approval to override the decisionally impaired person’s dissent and enroll the individual in the research must be obtained from the IRB Executive Chair. However, any dissent override requires very strong justification. The full IRB will be notified of the IRB Executive Chair’s decision. The Board has the option to accept the IRB Executive Chair’s decision, require additional actions, or require withdrawal of the subject.

6.3 If a decisionally impaired person actively dissents *while participating in research*, that dissent *must* be honored as long as the research does *not* hold out the prospect of direct subject benefit that is only available in the context of the research.

If the research holds the prospect of direct subject benefit, approval to override the decisionally impaired person’s dissent and continue the subject’s participation in the research must be obtained from the IRB Executive Chair. The full IRB must subsequently review the IRB Executive Chair’s decision. The Board has the option to accept the IRB Executive Chair’s decision, require additional actions, or require withdrawal of the subject.

7.0 Acceptable Research Involving Decisionally Impaired Subjects

7.1 *Minimal risk:* A decisionally impaired subject may participate in research involving *minimal risk* with no direct subject benefit if an LAR (as defined in Section 3.2 A, B, and C above) provides consent. However, an IAS is not authorized to consent for participation in minimal risk research without the prospect of direct subject benefit.

7.2 *Minor increase over minimal risk:* A decisionally impaired subject may participate in research involving a *minor increase over minimal risk* without direct subject benefit if an LAR (as defined in Sections 3.2A, B, C above) provides consent. A minor increase over minimal risk is defined as a slight increase in risk based upon the characteristics of the subject population and the risk(s) of the intervention(s). The IRB will determine if the study present no more than a minor increase over minimal risk. An IAS is not authorized to consent for participation in research involving a minor increase over minimal risk without the prospect of direct subject benefit.

7.3 *Greater than minimal risk:* A decisionally impaired subject may participate in research involving *greater than minimal risk only* if the research potentially offers an acceptable level of direct medical benefit to that subject and an LAR (as defined in Section 3.2 A, B, C, and D above) provides consent.

7.4 *Significant risk:* A decisionally impaired subject may participate in research involving significant risk *only* if the research potentially offers an acceptable level of direct
medical benefit to the subject which is available only in the context of the research and an LAR or IAS (as defined in Sections 3.2 A, B, C, and D above) provides consent.

Note: Individuals who are under a court mandated therapy for a psychiatric disorder are not eligible to participate in research.

8.0 Additional Protections
In consideration of the characteristics of the subject population, the nature of the research and the risk level, the IRB will determine what additional protections are necessary. Additional protections for vulnerable subject populations which include individuals who are decisionally impaired are described in HRPP policy #4.1.

9.0 IRB Review
9.1 In addition to the submission of the appropriate IRB application, the PI will also complete Addendum E: Research Involving Decisionally-Impaired Persons.

9.2 Applications which require review by the full IRB will be processed and reviewed in accordance with HRPP policy #2.2.

9.3 Applications that are eligible for review by the expedited method will be processed and reviewed in accordance with HRPP policy #2.3.

9.4 In most cases, research involving decisionally impaired subjects will be reviewed by the full IRB. In consideration of the nature of the protocol, one or more IRB members who are knowledgeable about and experienced in working with decisionally impaired persons will be involved in the review. In some circumstances, a consultant will be appointed to assist the IRB in their review.

9.5 The IRB will consider the characteristics of the subject population in terms of their ability to provide assent and ensure that the IRB application provides for an appropriate assent process when warranted.

9.6 The IRB will consider the characteristics of the subject population in terms of possible fluctuating capacity (e.g., intermittent capacity, drug related capacity), regaining capacity, or progressively diminishing capacity. In this case the IRB will advise the investigator on the necessity of reassessment of capacity to provide informed consent and the need to obtain informed consent from the subject (refer to Section 10.0 below).

9.7 The IRB will document the required additional protections which must be in place in accordance with 45 CFR 46.111(b); 21 CFR 56.111(b).

10.0 Consent Forms/Adult Information Sheet
10.1 LAR ICF: The LAR ICF must include all required elements of the informed consent and be written in the proxy consent style that indicates that the LAR/IAS is providing permission to allow the decisionally impaired subject to participate in the study (see LAR ICFTemplate).

10.2 Adult information sheet: The adult information sheet should be written in simple language aimed at the appropriate cognitive level of the decisionally impaired subjects to be enrolled in the study. The adult information sheet should contain the elements of assent that are found in the Adult Information Sheet Template.
11.0 Disclosure and Consent for Continuing Participation
If a subject regains competency while the research is ongoing, the subject must be fully informed about the study, the circumstances of the subject’s enrollment, and re-consented using an adult ICF.

12.0 Disclosure After the Research has Been Completed
If a subject regains competency after the research has been completed (i.e., all data has been collected) the subject must be fully informed about the research and the circumstances of the subject’s enrollment.

ADMINISTRATIVE APPROVAL:
Ernest D. Prentice, PhD.  Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD  IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for IRB review and approval of research involving faculty, staff, and/or students.

2.0 Policy
A subject population consisting of faculty, staff, or students operating under the direction/supervision of the PI or other study personnel is considered potentially vulnerable because of the potential for coercion or undue pressure.

2.1 It is the policy of the Organization that recruitment of faculty, staff, or students working in the laboratory or in other capacities under the supervision of the PI or under other study personnel (e.g., Secondary Investigator) is generally discouraged.

2.2 It is the policy of the Organization that recruitment of students taking classes from the PI or other study personnel is generally discouraged.

3.0 Requirements
If a PI or other study personnel wish to recruit subjects from within their laboratory, office, or class, the IRB application must clearly address:

3.1 The nature of the professional relationship.

3.2 Justification of the need to recruit the subject population. This justification must be particularly strong for any study which involves greater than minimal risk procedures.

3.3 Description of the method of subject recruitment and how situational coercion will be minimized to the greatest extent possible.

Note: The PI should consider: 1) use of a general bulletin board posting and not engage in one-on-one solicitation; and 2) use of an individual to obtain consent that does NOT have any supervisory or instructional role relative to the prospective subject.

4.0 IRB Review
The IRB will carefully examine the proposed inclusion of the subject population and must ensure that special protections for this population are in place to minimize the potential for coercion or undue influence.

Administrative Approval:
Ernest D. Prentice, PhD. Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for the process and documentation of informed consent.

2.0 Policy
2.1 It is the policy of the Organization that the process of informed consent obtained from subjects or their Legally Authorized Representatives (LARs) will be conducted in accordance with, and to the extent required by HHS regulations at 45 CFR 46.116, FDA regulations at 21 CFR 50.20 (as applicable) and UNMC HRPP policies.

2.2 It is the policy of the Organization that informed consent will be appropriately documented in accordance with, and to the extent required by 45 CFR 46.117, 21 CFR 50.27 (as applicable) and UNMC HRPP policies.

3.0 General Requirements
3.1 No human being may be enrolled as a subject in research unless the PI or authorized study personnel (e.g., secondary investigator, participating personnel or research coordinator) has prospectively obtained the legally effective (valid) informed consent of the subject (or LAR) unless a waiver or alteration of informed consent has been approved by the IRB in accordance with HRPP policy #5.2 or 5.3.

3.2 The PI, in accordance with HRPP policy #3.13, is ultimately responsible for the development, obtainment, and documentation of valid informed consent from the subject or subject’s legally authorized representative (or LAR) prior to participation in the research, unless these requirements have been waived by the IRB.

3.3 Except as provided in HRPP policy #5.5, informed consent must be documented by the use of a written informed consent form (ICF) approved by the IRB. The PI (or authorized designee) shall seek such consent only under circumstances that provide the prospective subject (or LAR) sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence.

3.4 The information contained in the ICF and conveyed to the subject (or LAR) during the process of consent shall be in language understandable to the subject (or LAR). To the extent possible, the language should be understandable by a person who is educated to the 8th grade level and, where appropriate, layman’s terms shall be used in the description of the research.

3.5 No ICF or process may include any exculpatory language through which the subject (or LAR) is made to waive or appear to waive any of the subject’s legal rights, or releases or appears to release the PI or other study personnel, the sponsor, the institution, or its agents from liability for negligence.

3.6 The obtaining of consent for the participation of pregnant women, fetuses and neonates (nonviable or uncertain viability) in research must be conducted in accordance with this policy and HRPP policy #4.2.

3.7 The obtaining of consent for the participation of prisoners in research must be conducted in accordance with this policy and HRPP policy #4.3.
3.8 The obtainment of parental permission (consent) for participation of children in research must be conducted in accordance with this policy and HRPP policy #4.4 which also describes the requirement for assent.

3.9 The obtainment of consent for the participation of decisionally impaired individuals in research must be conducted in accordance with this policy and HRPP policy #4.6.

4.0 Elements of Informed Consent

4.1 Basic Elements of Informed Consent [45 CFR 46.116(a) and 21 CFR 50.25(a)]

A. To be valid the consent process must provide the following basic elements of information to prospective subjects (or LARs).

   Note: This requirement is satisfied by utilizing the appropriate ICF/information sheet template(s) listed in sections 5.0, 6.0 and/or 7.0 below.

   1) A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental; a description of any reasonably foreseeable risks or discomforts to the subject.

   2) A description of any benefits to the subject or to others which may reasonably be expected from the research.

   3) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.

   4) A statement describing the extent, if any, to which confidentiality of records identifying the subject must be maintained.

   5) For research involving more than minimal risk, an explanation as to the availability of medical treatment in the case of research-related injury, including who will pay for the treatment and whether other financial compensation is available.

   6) An explanation of whom to contact on the research team for answers to pertinent questions about the research or to voice concerns or complaints about the research, and whom to contact in the event of a research-related injury to the subject.

   7) IRB contact instructions to allow the subject to obtain answers to questions about:
   a) The research
   b) To voice concerns or complaints about the research
   c) To obtain answers to questions about their rights as a research subject
   d) What to do in the event the research staff could not be reached
   e) Who to contact in the event the subject wishes to talk to someone other than the research staff.

   8) A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.
9) A statement which indicates that the IRB, institutional officials designated by the IRB, OHRP, FDA, NIH, sponsors/CROs, other AMCs/universities, third party payers, and the SRC will, as necessary, have access to research records containing PHI.

10) A statement that FDA-regulated clinical trials and federally funded interventional (as well as observational trials) must be listed on http://ClinicalTrials.gov. In addition, the International Committee of Medical Journal Editors (ICMJE) requires listing as a condition for publication.

4.2 Additional Elements of Informed Consent [45 CFR 46.116(b), 21 CFR 50.25(b)]

A. When appropriate, one or more of the following additional elements of information must also be provided to prospective subjects (or LARs). Utilizing the appropriate template(s) listed in Sections 5.0, 6.0 and/or 7.0 below satisfy this requirement.

1) A statement that the particular treatment or procedure may involve risks to the subject, which are currently unforeseeable (e.g., when the research involves investigational test articles or other procedures in which the risks to the subject are not well known).

2) A statement that if the subject is or becomes pregnant, the particular treatment or procedure may involve risks to the embryo or fetus, which are currently unforeseeable (e.g., when the research involves pregnant women or women of childbearing potential and the risks to the fetus or embryo associated with the drugs, devices, or other procedures involved in the research are not well known). Where appropriate, a statement regarding unforeseeable teratogenic risk transferred to females from male subjects should be included.

3) Anticipated circumstances under which the subject’s participation may be terminated by the investigator without regard to the subject’s/LAR’s consent (e.g., when there are medical circumstances or compliance requirements that would necessitate involuntary withdrawal of the subject from the research).

4) Any additional costs to the subject/LAR that may result from participation in the research (e.g., additional bone marrow biopsies, MRIs or other interventions performed for research purposes which are not covered by the sponsor).

5) The consequence(s) of a subject/LAR decision to withdraw from the research (e.g., when withdrawal from the research is associated with adverse medical consequences, such as an interruption of treatment).

6) An explanation whether already collected data about the subject will be retained and analyzed even if the subject chooses to withdraw from the research. The ICF cannot give the subject the option of having the existing data removed from future analysis.

7) Procedures for orderly termination of the subject’s research participation (e.g., voluntary notification of the PI, follow up and treatment substitution).

8) If a subject withdraws consent to participate in a study, the subject must provide additional written consent for continued routine follow-up of clinical outcomes which will be used for research purposes. This must be clearly disclosed in the ICF.
Note: While an investigator may review study data related to the subject collected prior to the subject’s withdrawal from the study, the investigator may not access the subject’s medical record or any other confidential record for purposes related to the study which would require the subject’s consent for such access.

9) A statement that significant new findings developed during the course of the research which may relate to the subject’s willingness to continue participation will be provided to the subject. LARs will be provided the same information. If the subjects are capable of assenting, this information will also be provided to them.

10) The approximate number of subjects involved in the study. It may be appropriate to inform subjects when there is a small number of participants (e.g., pilot studies), a large number of subjects (e.g., multi-center studies) or research involving a highly experimental intervention (e.g., investigational left ventricular assist device).

5.0 ICF Templates
5.1 All investigators are required to utilize one or more of the following ICF templates as applicable:
A. Adult biomedical research ICF template
B. Adult social and behavioral research ICF template
C. Adult tissue banking ICF template
D. Adult registry ICF template
E. Parental biomedical research ICF template
F. Parental social and behavioral research ICF template
G. Parental tissue banking ICF template
H. Parental registry ICF template
I. Legally authorized representative biomedical research ICF template
J. Legally authorized representative Social and behavioral research ICF template
K. Legally authorized representative tissue banking ICF template
L. Legally authorized representative registry ICF template
M. Humanitarian use device ICF template
N. Emergency treatment ICF template

6.0 Study Information Sheet Templates
6.1 All investigators are required to utilize one or more of the following information sheet templates as applicable:
A. Youth information sheet
B. Child information sheet
C. Adult information sheet (for the decisionally impaired)

7.0 Other Consent Templates
7.1 All investigators are required to utilize one or more of the following other consent templates as applicable:
A. Cover letter consent template
B. Narrative ICF template
C. National Cancer Institute Central IRB ICF template
8.0 Process of Informed Consent

8.1 Informed consent may only be obtained from subjects who have the legal and mental capacity to give consent. For subjects without that capacity, consent must be obtained from an LAR. 

*Note: Per HRPP policy #4.6, the Legally Authorized Representative (LAR) is defined as:

1) The parent, or parents, having legal custody of a prospective subject.
2) The court-appointed legal guardian of a prospective subject in accordance with Neb Rev Stat 30-2627.
3) An Institutionally Authorized Surrogate (IAS) in accordance with the specified hospital’s policy.
4) The individual authorized to consent on behalf of a prospective subject pursuant to a legally effective Health Care Power of Attorney.*

8.2 Prospective subjects (or LARs) should be approached sufficiently far in advance of their involvement in research to enable them to have time to make an informed decision to participate in the study. This helps minimize the possibility of coercion or undue influence.

8.3 The environment where informed consent will be obtained should be a private and quiet location, conducive to discussion and thoughtful consideration by the prospective subject with consideration given to the need to minimize the possibility of coercion or undue influence.

8.4 The process of informed consent can be described as the transmission of relevant information to the prospective subject (or LAR). The exchange of information between the PI/authorized study personnel and the prospective subject (or LAR) should occur via an appropriate mode of communication such as face-to-face contact, mail, telephone, and fax. In most cases, informed consent should be obtained in a face-to-face contact. However, depending upon the nature and risks of the study or other factors, the IRB may permit an alternate consent procedure.

8.5 The PI/authorized study personnel must fully explain all required elements of informed consent to the prospective subject (or LAR).

8.6 The PI/authorized study personnel involved in the process of consent should take all necessary steps to minimize the possibility of coercion or undue influence. In addition, no exculpatory language should be used which suggests or implies in any way the subject is waiving any of their legal rights or appears to release the investigator, sponsor, or the institution from liability for negligence.

8.7 Subjects such as those who are educationally or economically disadvantaged or disabled may be vulnerable to coercion or undue influence to participate in research. Additional protections during the process of consent may include but are not limited to appointment of a subject advocate, involvement of the subject’s family or friends, use of a short form (verbal) consent, reading the consent to the subject, and use of teaching aids.

8.8 The PI/authorized study personnel must fully explain the rights of research subjects and provide the prospective subject (or LAR) with a written copy of the *Rights of Research Subjects* or *los Derechos de los Participantes de Investigaciones* (Spanish version). Copies are available on the IRB website (http://www.unmc.edu/irb).
8.9 The PI/authorized study personnel must provide a written copy of *What Do I Need to Know before being in a Research Study?* to use as a guide for questions to be answered before agreeing to participate in the study.

8.10 The prospective subject (or LAR) must be given sufficient time and opportunity to read the ICF, ask questions, which must be fully answered. In some cases, the consent process should be extended over several days and involve other individuals such as the prospective subject’s family members, clergy, nurses, and other ancillary personnel. In all cases, if at any time the prospective subject (or LAR) is uncomfortable making a decision, he/she should be encouraged to consult with family members or other individuals of their choosing.

8.11 The PI/authorized study personnel have a legal and an ethical obligation to ensure that the prospective subject (or LAR) has sufficient knowledge and comprehension of all of the elements of informed consent to enable him/her to make an informed and enlightened decision whether or not to participate in research.

*Note: The fact that an individual is prepared to sign the ICF and has no unanswered questions does not necessarily represent sufficient evidence of an adequate level of comprehension. A prospective subjects’ comprehension may be assessed by: a) questioning the individual concerning his/her understanding of all the elements of informed consent, or b) asking the individual to describe the research in sufficient detail whereby the subject demonstrates an acceptable level of comprehension of all of the elements of consent.*

8.12 In certain studies, it may be appropriate to seek active re-consent from subjects (or LARs). A subject's preferences and interests may change over time, even in the absence of material changes in the research protocol. Therefore, investigators should consider obtaining re-consent, or at least reaffirmation of the willingness to continue participation, on a routine basis. In most cases, such re-consent need only be a verbal agreement on the part of the subject after questioning by the investigator or research team member. In some cases, more formal re-consent (for example, quarterly or at the time of each research intervention) may be appropriate. Re-consent whether verbal or written should be documented in the research record.

8.13 Each subject (or LAR) must be given a copy of the signed and dated ICF upon completion of the consent process. If the IRB has approved a waiver of signed informed consent, each subject (or LAR) must be given a copy of the unsigned ICF upon completion of the consent process.

8.14 The IRB is authorized to randomly audit any on-going process of informed consent (see HRPP policies #1.18 and 8.5).

9.0 Documentation of Informed Consent

9.1 Unless a waiver of the requirement to obtain signed consent in accordance with *HRPP policy #5.5*, informed consent must be documented by the use of a written ICF approved by the IRB.

9.2 Study personnel who are permitted to document informed consent must be:
   A. Authorized by the PI.
   B. Listed by name in the documentation of consent section of the IRB Application.
   C. Approved by the IRB.
9.3 Individuals authorized to document consent must have the:
A. Necessary expertise
B. Sufficient knowledge of the protocol, as well as UNMC HRPP policies.
C. Any required medical/dental licensure.
D. Authorization per hospital policy to perform the procedures in a non-research clinical care/diagnostic context.
E. The subject (or LAR), PI (or authorized designee), and the witness (if required per 9.5 below) must sign and date the ICF in the physical presence of each other. The PI (or authorized designee) must be present at this time to certify that the subject (or LAR) provided valid informed consent.

9.4 Once it is determined the prospective subject (or LAR) has fully understood all of the elements of the consent, has no further questions, and has voluntarily (without coercion or undue influence) agreed to participate in the study, the subject (or LAR) should sign and date the current IRB-approved and stamped ICF at the time of consent.

9.5 The signature of a witness is required for all research studies involving populations where the IRB has determined that a witness provides an additional safeguard. Depending upon the nature of the study and the vulnerability of the subject population, the witness should be someone who is not listed on the IRB Application and ICF as study personnel.
Note: A witness may be a clinic nurse from an unrelated area, a protocol coordinator involved in other studies, or a relative of the subject.

9.6 For clinical studies involving significant risk, the only individuals who are authorized to obtain and document consent are investigators (or authorized designees) approved by the IRB who are licensed physicians or dentists.

9.7 A short form written consent document must be used in accordance with HRPP policy #5.6.

10.0 Documentation in the Research and Medical Records
10.1 The research record must contain the original signed ICF.

10.2 For clinical research or any research where any research procedure or interventions may result in a billable charge from the hospital or clinic, the subject’s medical record must contain a copy of the signed ICF (per specified hospital policy).
Note: Consent/addendum forms for genetic research will not be placed in the subject’s medical record when the IRB has concerns over: 1) third party accessibility and subject confidentiality, 2) the subject’s health insurance status or employability may be jeopardized, and 3) the subject’s medical safety will not be compromised by excluding the ICF from the medical record (e.g., biochemical/molecular studies which have predictive implications; family history studies). The IRB reserves the right to require that ICF not be maintained in the research record for other studies where breach of confidentiality constitutes a risk.

10.3 The process of consent must be documented in the medical or study record. This should include:
A. The names of the individuals involved in the explanation of the study to the subject (or LAR).
B. The period of time over which the study was discussed.
C. Any other relevant information that is important [e.g. questions or concerns expressed by the subject (or LAR)].
11.0 Special Consent Circumstances

11.1 Non-English Speaking Subjects

A. **Expected enrollment of non-English speaking subjects**

1) In some protocols, the PI may expect non-English speaking subjects to enroll because, for example, the protocol is studying a disease or condition that is likely to attract them or the PI is actively recruiting them. When the study subject population will include non-English speaking persons, the IRB requires a translated ICF to be used. Unless a certified translator is used, translated ICF must be back-translated. Exceptions for back-translation may be granted by the IRB on a case-by-case basis (e.g., translated ICF provided by the study sponsor).

2) An Official Interpreter who is fluent in both English and the language of the subject/LAR must be identified and can be any of the following in order of priority listing:

   a) A UNMC, Nebraska Medicine, CH&MC, UNO or study site staff or contracted person who is a specifically trained interpreter/translator. This individual must be fluent in both languages and have a basic understanding of the research.

   b) A commercial interpretation/translation service (such as CyraCom).

3) If a prospective subject/LAR/parent wishes to designate their own interpreter, then:

   a) This must be documented in the medical/research record.

   b) The Official Interpreter that qualifies under 11.1A(2)(a-b) above must be present to ensure the quality and accuracy of the interpretation and this must also be documented.

   *Note:* Minors cannot be used as an interpreter.

B. **Procedures for Using an Interpreter**

1) Interpreters should be provided with a copy of the IRB-approved ICF. Whenever possible, the ICF(s) should be provided at least 24 to 48 hours in advance of initiating the consent process with the subject/LAR.

2) Upon conclusion of the consent process the subject/LAR and the Interpreter must sign and date the non-English version of the ICF.

3) The person obtaining consent must sign and date the English version of the ICF.

4) A copy of the signed and dated non-English and English version of the ICFs must be given to the subject/LAR.

5) The process of consent must be fully documented and maintained on file which includes the following:

   a) The time over which the process of consent was conducted.

   b) The name and contact information of the interpreter.
C. **Unexpected enrollment of a non-English speaking subject**

If a non-English speaking prospective subject is unexpectedly eligible to enroll in research and there is no IRB-approved translated ICF, the following requirements apply:

1) If the research offers no prospect of direct therapeutic benefit, the person can only be enrolled a) after the IRB has reviewed and approved a translated ICF, and b) an interpreter who is fluent in both languages is used during the process of consent. The PI or other study personnel may serve as the interpreter.

2) If the research offers the prospect of direct therapeutic benefit, the person can be enrolled using the IRB-approved short form, providing the requirements of **HRPP policy #5.6** are satisfied.

### 11.2 Braille consent

For a blind subject (or LAR) who reads Braille, the IRB may require an ICF prepared in Braille. In order to ensure that a Braille ICF is accurate, the IRB may require a transcription into print text or review of the document by a qualified person who reads Braille. If possible, the subject (or LAR) will sign the Braille ICF; otherwise verbal consent will be obtained, witnessed and documented in accordance with Section 9.5 of this policy.

### 11.3 Consenting in American Sign Language (ASL)

For a deaf subject (or LAR) who is fluent in ASL, the IRB may require a consent process using ASL and the IRB-approved ICF. When this process is approved, the individual authorized to consent the prospective subject (or LAR) must use a qualified interpreter fluent in ASL to conduct the consent process and the documentation of the consent process must conform to the requirements set forth previously in this policy.

### 11.4 Oral Consent

A. When a subject (or LAR) is unable to read an ICF (such as blind or illiterate subjects), the IRB may approve an oral consent process, provided the subject (or LAR):

1) Retains the ability to understand the concepts of the study and evaluate the risk and benefit of being in the study when it is explained verbally, and

2) Is able to indicate approval or disapproval to study entry.

B. The ICF must be read to the subject (or LAR) and the subject (or LAR) must be given an opportunity to ask questions. If capable of doing so, the subject (or LAR) signs, or marks an X to signify consent. If that is not possible, the subject (or LAR) will provide verbal consent.

C. A witness must be given a copy of the ICF in advance for their review and be present throughout the entire process of informed consent.

D. The person obtaining consent and the witness will sign the written ICF with a statement that documents that an oral process was used and, if necessary, that the subject (or LAR) gave verbal consent. Whenever possible, the verbal presentation and explanation of ICF(s) should be provided to the subject (or LAR) on audio or video tape.
E. The consent process must also be documented in accordance with 10.3 above. Signed copies of the ICF are given to the subject (or LAR).

F. For research that is no more than minimal risk, documentation of consent may be waived in accordance with HRPP policy # 5.5.

G. In an ongoing study when a subject (or LAR) is encountered who cannot read a written ICF, a protocol deviation form must be submitted to the ORA before enrollment takes place (HRPP policy #8.1).

12.0 Requirements for Re-Consent of Subjects

12.1 A formal re-consent procedure is not required for minor changes (e.g., changes in personnel, administrative changes in the ICF, and other changes that do not alter the risk-benefit relationship of the research). This new information may be presented, as necessary, through a verbal exchange between the subject/LAR and PI/authorized designee).

12.2 Significant, new information (e.g., new efficacy data; unanticipated adverse events; additional clinical tests; changes in the duration of the study; major changes in the methods of the trial) requires formal re-consent of the subject (or LAR) through the use of an IRB-approved revised ICF or an addendum to the ICF. This process of re-consent must follow the requirements for the process of initial consent discussed above, as well as include full documentation in the medical and research record.

12.3 When new information could potentially have a significant impact on the health and welfare of subjects (e.g., information concerning a serious adverse event), subjects/LARs should be notified immediately by telephone with the transmission of information documented and witnessed. If contact cannot be achieved by telephone, certified mail with required signature must be used. The ORA must be notified as soon as possible, but no later than two (2) business days from the time the change was initiated.

12.4 The PI is required to notify the ORA when all subjects/LARs have been contacted. This notification should include identification of subjects by number and the date they were contacted. Notification must be followed up as soon as possible by re-consent using the IRB-approved revised ICF or addendum. This process of re-consent must follow the requirements for the process of initial consent discussed above, as well as include full documentation in the medical and research record.

12.5 Re-consent of currently enrolled subjects (or LARs) is not required following issuance of IRB-approved ICF(s)/study information sheet(s) associated with continuing review unless the IRB identified new information during the process of continuing review which requires re-consent of the subject (or LAR).

12.6 Since consent must be an on-going process throughout the duration of the study, investigators (or authorized designees) should verbally reaffirm the subject’s (or LAR’s) willingness to continue participation in the study as well as solicit and answer questions from the subject (or LAR).

13.0 Telephone Consent

Refer to HRPP policy # 5.4.
14.0 Short Form
Refer to *HRPP policy # 5.6.*

15.0 Waiver or Alteration of Informed Consent
Refer to *HRPP policies # 5.2 and 5.3.*

16.0 Waiver of the Requirement to Obtain a Signed ICF
Refer to *HRPP policy # 5.5.*

**Administrative Approval:**
Ernest D. Prentice, PhD.  Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD    IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for granting an IRB waiver or alteration of informed consent and HIPAA authorization requirements in research involving the use of protected health information (PHI). Research involving the use of PHI may include: biomedical, medical records, human biological materials research, biorepositories, and data banking.

2.0 Policy
2.1 It is the policy of the Organization that the IRB will also serve as the Privacy Board for human subject research. HIPAA requirements are applied to all research involving protected health information (PHI).

2.2 A waiver or alteration of informed consent and HIPAA authorization requirements may be approved provided that the IRB finds and documents the criteria specified in HHS regulations at 45 CFR 46.116(d), equivalent sections of the Common Rule as adopted by other Federal Departments or Agencies, and 45 CFR 164.514(b)(2)(i) [HIPAA] have been satisfied.

2.3 In addition to granting a waiver under sections of the regulations cited in 2.2 above, the IRB may also grant a waiver of parental permission under 45 CFR 46.408(c).

2.4 Research involving FDA-regulated investigational drugs, biologics and devices (test articles) is not eligible for waiver or alteration of informed consent except in accordance with 2.5 below.

2.5 Exceptions to the FDA’s general requirements for informed consent for emergency use of a test article may be granted in accordance with 21 CFR 50.23(a)(b)(c) and HRPP policy #6.4.

2.6 Exceptions to FDA’s informed consent requirement for emergency research may be granted in accordance with 21 CFR 50.24 and HRPP policy #5.7.

2.7 If the research involves subjects who are prisoners, the IRB will use the criteria at 45 CFR 46.116(d) and HIPAA, with the following exceptions: a) a complete waiver of informed consent will not be granted, and b) prisoners must be clearly informed in advance that their participation in research will have no effect on their parole, if such notification is relevant [45 CFR 46.305(a)(6)].

2.8 In general, the ORA will apply the waiver criteria specified at 45 CFR 46.116(d) to exempt research where a determination is made that written informed consent should be obtained unless a waiver is ethically justified.

3.0 Criteria for IRB approval of a waiver of adult, parental/guardian/LAR consent under HHS regulations at 46.116(d) and HIPAA regulations at 45 CFR 164.514(l)(2)(ii)
The following are the IRB requirements that must be met in order to approve a waiver or alteration of informed consent/authorization under HHS regulations at 46.116(d) and HIPAA regulations at 45 CFR 164.514(l)(2)(ii):

3.1 The research involves no more than minimal tangible or intangible risk to the subject. Note: Minimal risk means "The probability (of occurrence) and magnitude (seriousness)
of harm or discomfort (e.g., psychological, social, legal, economic) associated with the research are not greater than those ordinarily encountered in daily life (of the average person in the general population) or during the performance of routine physical or psychological examinations or tests."

Minimal risk is used to define a threshold of anticipated harm or discomfort associated with the research that is low. The evaluation of whether or not research involves minimal risk must take into consideration not only the risk associated with interventions (e.g., a blood draw), but also the risk of violating the privacy of subjects in the case of unauthorized use or disclosure of PHI. In this case, the determination of whether the research involves more than minimal risk is also based upon a) the adequacy of the plan to protect subject identifiers from improper use and disclosure and b) the adequacy of the plan to destroy the identifiers at the earliest opportunity. **A waiver of consent/authorization is not permitted if the research is more than minimal risk.**

### 3.2

The waiver or alteration of informed consent/authorization will not adversely affect the rights and welfare of the subjects.

*Note: This justification should be based on the “reasonable person” standard; that is, whether or not a reasonable person in the subject’s position would consider the waiver as adversely affecting his/her rights and welfare. For example, a “reasonable person” would probably not object to innocuous identifiable medical information, such as height or weight being entered into a database without their knowledge or informed consent. The same reasonable person might, however, object if the identifiable information was sensitive (e.g., previous psychiatric treatment, HIV status, age at first pregnancy). It should also be recognized that in some cultures any waiving of informed consent may well be interpreted by the community as adversely affecting the rights and welfare of members of that community. **A waiver of informed consent/authorization is not permitted if the waiver will adversely affect the rights and welfare of the subjects.**

### 3.3

The research could not practicably be carried out without the waiver or alteration of informed consent or waiver of HIPAA authorization.

*Note: In some research projects it would not be practicable to perform the research (as it has been defined in the application by its specific aims and objectives) if informed consent was required. For example:

1) **The sample size required is so large (epidemiological studies) that including only those samples/records/data for which informed consent could be obtained would prohibit conclusions to be drawn or bias the sample such that conclusions would be skewed.**

2) **The subjects for whom records would be reviewed may be lost to follow-up. Individuals likely to have relocated or died may be a significant percentage of the proposed subject population, thus decreasing the statistical power of the study if informed consent was required.**

3) **Disclosure of the study purpose would bias the research subjects so that study results are not meaningful.**

4) **There is a risk of creating additional threats to privacy by having to link otherwise de-identified data with nominal identifiers in order to contact individuals to seek informed consent.**

5) **There is a risk of inflicting psychological, social, or other harm by contacting individuals or families with particular conditions.**
6) Because of the nature of the research and/or circumstances of the prospective subject, there is not sufficient time to obtain informed consent. For example, a study involves interviewing emergency room patients. The interview consists of sensitive questions. There is not enough time to obtain written informed consent in this case. Verbal informed consent may be acceptable.

Finally, it should be noted that, in general, investigator inconvenience or cost does not determine "impracticality" and there should be a clear rationale why the research could not be conducted with a population from whom informed consent could be obtained. A waiver of informed consent/authorization is not permitted if the research could practicably be conducted without a waiver.

3.4 The research could not be practicably carried out without access to and use of the protected health information (PHI).
Note: Research involving the collection and use of PHI is subject to HIPAA requirements. In order for a waiver to be granted, it must be clear that the research could not be practicably conducted without access to PHI. A waiver of HIPAA authorization is not permitted if the research could be practicably conducted without access to the PHI.

3.5 There is a plan to protect subject identifiers from improper use and disclosure.
Note: In order for a waiver to be granted, there must be an adequate plan to protect confidentiality of research data which contains PHI. It is important that the data contain as few of the 18 HIPAA-specified subject identifiers as possible. This section may be answered by referencing the information in the Privacy and Confidentiality section of the IRB application. A waiver of HIPAA authorization requires an adequate plan to protect data which contains subject identifiers from improper use and disclosure as a result of a breach of confidentiality.

3.6 There is written assurance that the PHI collected and used in this research will not be reused or disclosed to any other person or entity, except as required by law or for authorized oversight of the research.
Note: This PI should include a brief assurance attesting to compliance with the above-specified HIPAA requirement for a waiver. A waiver of HIPAA authorization cannot be granted without this assurance.

3.7 Whenever appropriate, the subjects will be provided with additional pertinent information after participation.
Note: In general, this criterion is designed to address de-briefing after research is conducted. In these situations, it may be ethically required or determined to be respectful to provide the subject with pertinent information pertaining to their participation in research under the waiver of informed consent/authorization granted by the IRB. When this is the case, the subject must be presented with an ICF (ICF) for continued participation in the research. The ICF must include a provision for the subject to withdraw their data and/or samples from use in research should they choose not to continue participation. Use of the reasonable person standard can help assess when and how this criteria should be satisfied. For example, research involving a deception strategy would generally require disclosure of pertinent information. A waiver of informed consent/authorization can be granted only if the subject is provided with additional pertinent information whenever appropriate.
4.0 Criteria for a Waiver of Parental/Guardian Permission (Consent) Under HHS Regulations at 45 CFR 46.408(c)

The following are the IRB requirements that must be met in order to approve a waiver of parental/guardian permission under HHS regulations at 45 CFR 46.408(c):

4.1 The research must be designed for conditions or for a subject population for which parental/guardian permission is not a reasonable requirement to protect the subjects.

Note: The following are considerations which may justify a waiver:

1) Informing parents or guardians may result in harm to the child. For example, the study involves STD testing of 15-18 year old females which is permitted by state law without parental/guardian permission.

2) The research is important to the health and well-being of adolescents and the subjects are capable of understanding informed consent at an adult level. For example, the research involves asking 15-18 year old females about their sexual practices, prescribing contraception in accordance with described sexual practices and an annual follow up for three years. The questions are reasonably commensurate with questions asked during gynecologic services which the adolescents are permitted by law to receive without parental permission and the prescribed contraceptive methods are also permitted by state law without parental/guardian permission.

4.2 There is an appropriate mechanism in place for protecting the children who will participate as subjects in the research.

Note: The choice of an appropriate mechanism depends upon the nature and purpose of the research activities, the risks and anticipated benefit to the subjects, and their age, maturity, status, and condition. For example, the appointment of an advocate, provisions for referral to counseling or other safeguards may be necessary.

5.0 Process of Review

5.1 To request a waiver or alteration of informed consent under HHS regulation and HIPAA, the investigator must complete and submit with the appropriate IRB application, one of the following addendums to the IRB application:

A. Addendum J: Waiver or Alteration of Informed Consent & HIPAA Authorization in Biomedical, Medical Records & HBM Research, Biorepositories & Data Banking and/or Waiver or Alteration of Parental Permission (Consent) (because the research is designed for conditions or for a subject population for which parental/guardian permission is not a reasonable requirement to protect the subjects)

B. Addendum L: Waiver of Alteration of Child Assent

Note: The above referenced addenda contain the criteria that must be met along with accompanying notes which provide guidance on interpretation of the criteria.

5.2 The IRB will review the proposed waiver or alteration of informed consent at convened IRB meetings in accordance with HRPP policy #2.2, unless the IRB Executive Chair/designee determines study qualifies for expedited review in accordance with HRPP policy #2.3.

5.3 The IRB may review the request for waiver of HIPAA authorization using the expedited review procedure if the research involves no more than minimal risk to the privacy of the individuals who are the subject of the PHI for which use or disclosure is being sought.
5.4 ORA will review all requests for waiver or alteration of informed consent and HIPAA authorization for all research classified as exempt in accordance with HRPP policy #2.7.

5.5 The Checklist for Waiver or Alteration of Informed Consent and HIPAA Authorization in Research will be used to determine whether or not a waiver can be granted in accordance with the federal regulations.

5.6 Documentation of IRB approval of waiver or alteration of informed consent and HIPAA authorization will appear in the IRB review letter.

ADMINISTRATIVE APPROVAL:
Ernest D. Prentice, PhD.  Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD  IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organizations requirements for granting an IRB waiver or alteration of informed consent and HIPAA authorization requirements in Social Science and Behavioral Research.

2.0 Policy
2.1 It is the policy of the Organization that a waiver or alteration of informed consent and HIPAA authorization requirements may be approved provided that the IRB finds and documents criteria specified in HHS regulations at 45 CFR 46.116(d) or 46.116(c), equivalent sections of the Common Rule as adopted by other Federal Departments or Agencies, and 45 CFR 164.514(b)(2)(i) [HIPAA] have been satisfied.

2.2 The Organization applies HIPAA requirements to all social science and behavioral research involving protected health information (PHI).

2.3 In addition to granting a waiver under sections of the regulations cited in Section 2.1 above, the IRB may also grant a waiver of parental permission under 45 CFR 46.408(c).

2.4 If the research involves subjects who are prisoners, the IRB will apply the waiver criteria at 45 CFR 46.116(d) and HIPAA with the exception of the requirement in Subpart C that prisoners be clearly informed in advance that their participation in research will have no effect on their parole, if such notification is relevant [45 CFR 46.305(a)(6)].

2.5 In general, the ORA will apply the waiver criteria specified at 45 CFR 46.116(d) to exempt research where a determination is made that written informed consent should be obtained unless a waiver is ethically justified.

3.0 Criteria for IRB Approval of a Waiver of Adult or Parental/Guardian Consent under HHS Regulations at 46.116(d) and HIPAA Regulations as 45 CFR 164.514(b)(2)(i)

The following are the IRB requirements that must be met in order to approve a waiver or alteration of informed consent/authorization under HHS regulations at 46.116(d) and HIPAA regulations as 45 CFR 164.514(b)(2)(i):

3.1 The research involves no more than minimal tangible or intangible risk to the subject.

*Note: Minimal risk means "The probability (of occurrence) and magnitude (seriousness) of harm or discomfort (e.g., psychological, social, legal, economic) associated with the research are not greater than those ordinarily encountered in daily life (of the average person in the general population) or during the performance of routine physical or psychological examinations or tests."*

Minimal risk is used to define a threshold of anticipated harm or discomfort associated with the research that is low. The evaluation of whether or not research involves minimal risk must take into consideration not only the risk associated with evaluations, but also the risk of violating the privacy of subjects in the case of unauthorized use or disclosure of PHI. In this case, the determination of whether the research involves more than minimal risk is also based upon a) the adequacy of the plan to protect subject identifiers from improper use and disclosure and b) the adequacy of the plan to destroy the identifiers at the earliest opportunity. A waiver of informed consent/authorization
is not permitted if the research is more than minimal risk.

3.2 The waiver or alteration of informed consent/authorization will not adversely affect the rights and welfare of the subjects.  
**Note:** This judgment should be based on the “reasonable person” standard; that is, whether or not a reasonable person in the subject’s position would consider the waiver as adversely affecting his/her rights and welfare. For example, a “reasonable person” would probably not object to innocuous identifiable information (e.g., number of children, automobile preference) being entered into a database without their knowledge or informed consent. The same reasonable person might, however, object if the identifiable information was sensitive (e.g., number of divorces, age at first pregnancy).

It should also be noted that the Family Education Rights and Privacy Act (FERPA; 20 U.S.C. §1232g; 34 CFR Part 99) is a federal law that protects the privacy of personally identifiable information contained within a student’s educational record. FERPA applies to all schools (K-12 and postsecondary institutions) that receive funds under various programs from the U.S. Department of Education. Generally, schools must have written permission from the student (or parent if the student is a minor) in order to release any information from a student’s education record unless it meets some of the specified criteria for which release is allowed. (For example studies conducted by organizations for or on behalf of the school). Other than this exception, if an investigator from a local university’s college of education requests a waiver of informed consent to review the educational records (grades and GPA) of students at the university for the past 20 years and maintain identifiers for a research project, the rights granted to students under the federal legislation of FERPA would be violated and this condition could not be met. **A waiver of informed consent/authorization is not permitted if the waiver will adversely affect the rights and welfare of the subjects.**

3.3 The research could not practicably be carried out without the waiver or alteration of informed consent or waiver of HIPAA authorization.  
**Note:** In some research projects it would not be practicable to perform the research (as it has been defined in the application by its specific aims and objectives) if informed consent was required. For example:

1) The sample size required is so large (studies involving public records) that including only those samples/records/data for which informed consent could be obtained would prohibit conclusions to be drawn or bias the sample such that conclusions would be skewed.

2) The subjects for whom records would be reviewed maybe lost to follow-up. Individuals likely to have relocated or died may be a significant percentage of the proposed subject population, thus decreasing the statistical power of the study if informed consent was required.

3) Disclosure of the study purpose would bias the research subjects so that study results are not meaningful.

4) There is a risk of creating additional threats to privacy by having to link otherwise de-identified data with nominal identifiers in order to contact individuals to seek informed consent.
5) There is a risk of inflicting psychological, social, or other harm by contacting individuals or families with particular conditions.

6) Because of the nature of the research and/or circumstances of the prospective subject, there is not sufficient time to obtain informed consent. For example, a study involves interviewing emergency room patients. The interview consists of sensitive questions. There is not enough time to obtain written informed consent in this case. Verbal informed consent may be acceptable.

Finally, it should be noted that, in general, investigator inconvenience or cost does not determine "impracticality" and there should be a clear rationale why the research could not be conducted with a population from whom informed consent could be obtained. A waiver of informed consent/authorization is not permitted if the research could practicably be conducted without a waiver.

3.4 The research could not be practicably carried out without access to and use of the protected health information (PHI).

Note: Social Science and Behavioral Research involving the collection and use of PHI is subject to HIPAA requirements. In order for a waiver to be granted, it must be clear that the research could not be practicably conducted without access to PHI. A waiver of HIPAA authorization is not permitted if the research could be practicably conducted without access to the PHI.

3.5 There is a plan to protect subject identifiers from improper use and disclosure.

Note: In order for a waiver to be granted, there must be an adequate plan to protect confidentiality of research data which contains PHI. It is important that the data contain as few of the 18 HIPAA-specified subject identifiers as possible. This section may be answered by referencing the information in the Privacy and Confidentiality section of the IRB Application. A waiver of HIPAA authorization requires an adequate plan to protect data which contains subject identifiers from improper use and disclosure as a result of a breach of confidentiality.

3.6 There is written assurance that the PHI collected and used in this research will not be reused or disclosed to any other person or entity, except as required by law or for authorized oversight of the research.

Note: This section should include a brief assurance attesting to compliance with the above-specified HIPAA requirement for a waiver. A waiver of HIPAA authorization cannot be granted without this assurance.

3.7 Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

Note: In general, this criterion is designed to address de-briefing after research is conducted. In these situations, it may be ethically required or determined to be respectful to provide the subject with pertinent information pertaining to their participation in research under the waiver of informed consent/authorization granted by the IRB. When this is the case, the subject must be presented with an ICF (ICF) for continued participation in the research. The ICF must include a provision for the subject to withdraw their data and/or samples from use in research should they choose not to participate. Use of the reasonable person standard can help assess when and how this criteria should be satisfied. For example, research involving a deception strategy would generally require disclosure of pertinent information. A waiver of informed consent/authorization can be granted only if the subject is provided
with additional pertinent information whenever appropriate.

4.0 Criteria for IRB Approval of a Waiver under 45 CFR 46.116(c)
The following are the IRB requirements that must be met in order to approve a waiver or alteration of informed consent under HHS regulations at 45 CFR 46.116(c):

4.1 The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine at least one of the following:

Note: Examples of public benefit programs include those under the social security act, low income housing programs, and family medical leave. The IRB must ensure that subjects will not be denied benefits or services to which they are otherwise legally entitled.

A. Public benefit of service programs.
B. Procedures for obtaining benefits or services under those programs.
C. Possible changes in or alternatives to those programs or procedures; or
D. Possible changes in methods or levels of payment for benefits or services under those programs.

4.2 The research could not practicably be carried out without the waiver or alteration. Note: See the note under Section 3.3.

5.0 Criteria for a Waiver of Parental/Guardian (Consent) Permission Under 45 CFR 46.408(c)
The following are the IRB requirements that must be met in order to approve a waiver or alteration of parental/guardian permission:

5.1 The research must be designed for conditions or for a subject population for which parental guardian permission is not a reasonable requirement to protect the subjects. Note: The following are considerations which may justify a waiver:

1) Informing parents or guardians may result in harm to the child. For example, the study seeks to identify patterns of psychological risk and resilience in high school students who consider themselves gay or lesbian, but have not made this identity known to their parents or guardians.

2) There is a conflict in the parental/guardian role as it relates to the research. For example, the study seeks to examine coping behaviors of adolescents who have joined an Al-Anon group. If there were only one parent and that parent was an alcoholic, there might be a conflict that would render the parent unable to make a decision in the child’s best interest.

3) The research is important to the health and well-being of adolescents and the subjects are capable of understanding informed consent at an adult level. For example, the research involves asking female subjects about their sexual practices and use of birth control. Such questions are reasonably commensurate with questions asked during gynecologic services which the adolescents are permitted by law to receive without parental permission.
5.2 There is an appropriate mechanism in place for protecting the children who will participate as subjects in the research. 

Note: The choice of an appropriate mechanism depends upon the nature and purpose of the research activities, the risks and anticipated benefit to the subjects, and their age, maturity, status, and condition. For example, the appointment of an advocate, provisions for referral to counseling or other safeguards may be necessary.

6.0 Process of Review

6.1 The investigator must complete and submit the a) Addendum K: Waiver or Alteration of Informed Consent and HIPAA Authorization in Social Science and Behavioral Research Involving Adult Subjects or Parent(s)/Guardian(s) of Child Subjects, and/or b) the Addendum L: Waiver of Alteration of Child Assent together with the appropriate IRB application.

Note: The above references addenda contain the criteria that must be met along with accompanying notes which provide guidance on the interpretation of the criteria.

6.2 The process of IRB review will be conducted in accordance with the classification of the study: 1) Exempt research (HRPP policy #2.6); 2) Expedited review of research (HRPP policy #2.3); or 3) Full Board review (HRPP policy #2.2). The Checklist for Waiver or Alteration of Informed Consent and HIPAA Authorization in Research will be used to determine whether or not a waiver can be granted.

6.3 Documentation of IRB approval of waiver or alteration of informed consent and HIPAA authorization will appear in the IRB review letter.

Administrative Approval:
Ernest D. Prentice, PhD. Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for use of a telephone consent process in clinical and non-clinical research.

2.0 Policy
2.1 It is the policy of the Organization that use of a telephone consent process may be used in both clinical and non-clinical research when it is required for:

A. The convenience of the subject (e.g., weather-related travel or distance impediments).

B. Provision of new information (e.g., unanticipated risk) germane to the subject/legally authorized representative’s (LAR) decision to continue participating in research.

C. The safety or therapeutic benefit of the subject.

2.2 Telephone consent may be approved by the following mechanisms:
A. Full IRB review (HRPP policy #2.2).

B. Expedited review (HRPP policy #2.3)

C. Expedited review of a single subject protocol deviation (HRPP policy #8.1).

3.0 Procedures for Use of Telephone Consent in Clinical Research
3.1 Consent to determine subject eligibility

A. The telephone consent process can be used for the purpose of conducting screening procedures at external sites (e.g., private physician’s office or clinic) which are necessary to determine subject eligibility to participate in the clinical research.  

*Note: The subject/LAR must be re-consented in person before performance of any clinical research intervention or additional screening procedures within the Organization.*

B. The screening procedures are no greater than minimal risk.

C. Appropriate justification for use of the telephone screening process is provided.

D. The ICF (either a screening ICF or the main study ICF) and copies of *Rights of Research Subjects* and *What do I need to know?* must be provided to the subject/LAR for review prior to the telephone consent process. The ICF can be provided to the subject/LAR by mail, fax or email.

E. A telephone call is scheduled for after the subject has received the ICF and has time to review it.

F. The minimum required participants in the informed consent process are: 1) the subject/LAR and 2) the investigator or IRB authorized designee.
G. Each element of informed consent must be explained to the subject/LAR, and the subject/LAR’s comprehension must be assessed. The investigator/designee must also explain the subject’s rights as a research subject. The subject/LAR must be given the opportunity to have all of his/her questions answered.

H. If the subject/LAR has no further questions and agrees to participate in the screening portion of the research, the subject/LAR is instructed to sign and date the ICF and return the signed document to the investigator/designee by mail, fax or a scanned copy via email.

I. No screening procedures to determine subject eligibility can be conducted until a signed copy of the ICF has been received by the investigator/designee by email, fax or mail.

J. The ICF must be signed and dated by the investigator/designee upon receipt of the document with a note added on the form which explains the lapse in time between signatures (for example, “received in the mail 10/30/08”, “telephone consent obtained 10/27/08”).

K. A copy of the signed ICF must be provided to the subject/LAR.

L. In addition to the requirements for documentation of the process of informed consent described in HRPP policy #5.1, the telephone consent documentation must also include:
   1) The rationale for use of telephone consent,
   2) The date and time of telephone consent.
   3) Identification of all personnel involved in obtaining and documenting informed consent.

M. Prior to the performance of any clinical research interventions beyond the eligibility screening procedures, informed consent of the subject/LAR must be obtained in person using the main study ICF.

3.2 Re-consent to disclose protocol changes

A. The telephone consent process may be used for the purpose of disclosing protocol changes (e.g. additional follow up tests).

B. Appropriate justification for use of the telephone screening process is provided.

C. The ICF (revised ICF or addendum) must be provided to the subject/LAR for review prior to the telephone consent process. The ICF can be provided to the subject/LAR by mail, fax or email.

D. A telephone call is scheduled for after the subject has received the ICF and has time to review it.

E. The minimum required participants in the informed consent process are: 1) the subject/LAR and 2) the investigator/designee.

F. Each element of informed consent must be explained to the subject/LAR, and the subject/LAR’s comprehension must be assessed. The subject/LAR must be given
the opportunity to have all of his/her questions answered. It may be necessary to extend the process over several days and include other individuals such as the subject/LAR’s family members.

G. If the subject/LAR has no further questions and agrees to continue participation in the research, the subject/LAR is instructed to sign and date the ICF and return the signed document to the investigator/designee by mail, fax or a scanned copy via email.

H. No research interventions can be conducted until a signed copy (fax, scanned or original) of the ICF has been received by the investigator/designee.

I. The ICF must be signed by the investigator/designee upon receipt of the original document with a note added on the form which explains the lapse in time between signatures (for example, “received in mail 10/30/08”, “telephone consent obtained 10/27/08”).

J. A copy of the signed ICF must be provided to the subject/LAR.

K. The process of telephone consent should be documented in the research and/or medical record by indicating the reason for the alternative method used, date, time, and all personnel involved in obtaining and documenting informed consent.

3.3 **Provision of new information to subjects/LARs**

A. The telephone consent process may be used for the purpose of disclosing new information which may relate to the subject’s willingness to continue participation in the research (e.g., new risk information).

B. Appropriate justification for use of the telephone screening process is provided.

C. When new information (e.g., serious adverse event) requires immediate verbal transmission to the subject/LAR, the following procedure should be utilized:
   1) Subjects/LARs should be notified immediately by telephone with verbal transmission of information documented and witnessed.

   2) The minimum required participants in the informed consent process are: 1) the subject/LAR, 2) the investigator/designee and 3) a witness from the Institution. *Note: The witness should be someone who is not listed on the IRB Application and ICF as study personnel. A witness may be a clinic nurse from an unrelated area, a protocol coordinator involved in other studies, or a relative of the subject.*

   3) If contact cannot be achieved immediately by telephone, certified mail with required signature should be used.

   4) The PI is required to notify the IRB when all subjects/LARs have been contacted. This notification should include identification of subjects by number and the date they were contacted.

   5) Transmission of information via telephone must be followed by written re-consent utilizing a revised ICF/addendum or written notification (e.g., certified mail).
D. When new information does not require immediate verbal transmission to the subject/LAR, the following procedure should be utilized:

1) The ICF (revised ICF or addendum) must be provided to the subject/LAR for review prior to the telephone consent process. The ICF can be provided to the subject/LAR by mail, fax or email.

2) A telephone call is scheduled for after the subject has received the ICF and has time to review it.

3) The minimum required participants in the consent process are: 1) the subject/LAR and 2) the investigator/designee.

E. Each element of informed consent must be explained to the subject/LAR, and the subject/LAR’s comprehension must be assessed. The subject/LAR must be given the opportunity to have all of his/her questions answered. It may be necessary to extend the process over several days and include other individuals such as the subject/LAR’s family members.

F. If the subject/LAR has no further questions and agrees to continue participation in the research, the subject/LAR is instructed to sign and date the ICF and return the signed document to the investigator/designee by mail, fax or a scanned copy via email.

G. No research interventions can be conducted until a signed copy (fax, scanned or original) of the ICF has been received by the investigator/designee.

H. The ICF must be signed by the investigator/designee upon receipt of the original document with a note added on the form which explains the lapse in time between signatures (for example, “received in mail 10/30/08”, “telephone consent obtained 10/27/08”).

I. A copy of the signed ICF must be provided to the subject/LAR.

J. The process of telephone consent should be documented in the research and/or medical record by indicating the reason for the alternative method used, date, time, and all personnel involved in obtaining and documenting ICF.

### 3.4 Informed consent to enroll a subject whose LAR is unavailable in person

A. Under compelling clinical circumstances, the IRB or the IRB Executive Chair/designee may approve the use of a telephone consent procedure, for the purpose of enrolling a subject whose LAR is unavailable in person.

B. Compelling justification for use of the telephone screening process must be provided.

C. The ICF and copies of Rights of Research Subjects and What do I need to know? must be provided to the LAR for review prior to the telephone consent process. The ICF can be provided to the LAR by mail, fax or email.

D. A telephone call is scheduled for after the subject has received the ICF and has time to review it.
E. The minimum required participants in the informed consent process are: 1) the LAR; 2) the investigator/designee; and 3) a witness from the Institution.  
   
   Note: Depending upon the nature of the study and the vulnerability of the subject population, the witness should be someone who is not listed on the IRB Application and ICF as study personnel. A witness may be a clinic nurse from an unrelated area, a protocol coordinator involved in other studies, or a relative of the subject.

F. Each element of informed consent must be explained to the LAR, and the LAR’s comprehension must be assessed. The investigator/designee must also explain the subject’s rights as a research subject. The LAR must be given the opportunity to have all of his/her questions answered.

G. If the LAR has no further questions and allows permission for the subject to participate in the research, the LAR is instructed to sign and date the ICF and return the signed document to the investigator/designee by fax or a scanned copy via email.

H. No research procedures can be conducted until a signed copy of the ICF has been received by the investigator/designee via email or fax.

I. The ICF must be signed and dated by the investigator/designee upon receipt of the document with a note added on the form which explains the lapse in time between signatures (for example, “received in the mail 10/30/08”, “telephone consent obtained 10/27/08”).

J. A copy of the signed ICF must be provided to the LAR.

K. In addition to the requirements for documentation of the process of informed consent described in HRPP policy #5.1, the telephone consent documentation must also include:
   1) The rationale for use of telephone consent.
   
   2) The date and time of telephone consent.
   
   3) Identification of all personnel involved in obtaining, witnessing and documenting the informed consent.

4.0 Procedures for Use of Telephone Consent in Non-Clinical Research

4.1 With appropriate justification, the IRB, under certain circumstances, may approve the use of a telephone consent procedure. The study must be no more than minimal risk and the subjects/LARs are not required nor expected to come into personal contact with the researchers at any time during the conduct of the research (e.g., the research involves obtaining of data from medical records and the subjects are asked to complete a questionnaire and mail it back to the researcher).

4.2 The ICF and a copy of Rights of Research Subjects and What do I need to know? must be provided to the subject/LAR for review prior to the telephone consent process. The ICF can be provided to the subject/LAR by mail, fax or email. An extra copy must be provided for the subject/LAR to keep for his/her records.

4.3 A telephone call is scheduled for after the subject has received the ICF and has time to review it.
4.4 The minimum required participants in the informed consent process are: 1) the subject/LAR and 2) the investigator/designee.

4.5 Each element of informed consent must be explained to the subject/LAR, and the subject/LAR’s comprehension must be assessed. The investigator/designee must also explain the subject’s rights as a research subject. The subject/LAR must be given the opportunity to have all of his/her questions answered.

4.6 If the subject/LAR has no further questions and agrees to participate in the research, the subject/LAR is instructed to sign and date the ICF and return the signed document to the investigator/designee by mail, fax or a scanned copy via email.

4.7 No research procedures can be conducted until a signed copy of the ICF has been received by the investigator/designee by fax, email or mail.

4.8 The ICF must be signed and dated by the investigator/designee upon receipt of the original document with a note added on the form which explains the lapse in time between signatures (for example, “received in the mail 10/30/08”, “telephone consent obtained 10/27/08”).

4.9 In addition to the requirements for documentation of the process of informed consent described in HRPP policy #5.1, the telephone consent documentation must also include:

A. The rationale for use of telephone consent.

B. The date and time of telephone consent.

C. Identification of all personnel involved in obtaining and documenting informed consent.

ADMINISTRATIVE APPROVAL:
Ernest D. Prentice, PhD.  Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce Gordon, M.D.  IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s process for obtainment of an IRB waiver of the requirement to obtain a signed ICF.

2.0 Policy
2.1 It is the policy of the Organization that a waiver of the requirement to obtain a signed ICF for some or all subjects may be approved provided that the IRB finds and documents the criteria specified in HHS regulations at 45 CFR 46.117(c), equivalent sections of the Common Rule as adopted by other Federal Departments or Agencies, and FDA regulations at 21 CFR 56.109(c), as applicable, are satisfied.

2.2 Unless the IRB has granted a waiver of informed consent, even if the IRB has granted a waiver of documentation of informed consent, the PI/authorized study personnel must still perform an adequate informed consent process in accordance with HRPP policy #5.1.

3.0 Criteria for IRB Approval of a Waiver of Requirement to Obtain a Signed ICF Under 45 CFR 46.117(c)(1)
The following are the IRB requirements that must be met in order to approve a waiver of the requirement for the investigator to obtain a signed ICF for some or all subjects.

Note: Waivers under 45 CFR 46.117(c)(1) are not limited to minimal risk research. Examples of research which may qualify for a waiver would include studies of domestic violence and illegal behavior.

3.1 The only record linking the subject and the research would be the ICF and the principle risk would be potential harm resulting from a breach of confidentiality.

Note: The signed (as well as unsigned) ICF could create a link between the subject and the research that would not otherwise exist and there are no other links between the subject and the research (e.g., investigator notes with subject identifiers).

3.2 In assessing risk, the IRB will take into consideration the sensitivity of the research data and the stringency of the protections for confidentiality which will be in place.

Note: In studies where the principal risk to the subject is a breach of confidentiality, the investigator must have in place all measures necessary to minimize the possibility of this risk materializing.

3.3 Each subject will be asked whether he/she wants documentation linking the subject with the research and the subject’s wishes will govern. Documentation of the subject’s decision will be maintained in the research record.

Note: If a subject elects to have documentation of his/her informed consent, he/she will be asked to agree to documentation in the form of a written notation in the secure research record maintained by the investigator. The subject must be advised of the potential harm which may result from a breach of confidentiality before making the decision concerning documentation.

3.4 In accordance with 45 CFR 46.117(c), the IRB may require that each subject be provided with a written statement regarding the research which would generally be a summary of the research.

Note: The existence of a written summary or an unsigned ICF could potentially present a risk to the subject if someone else gains access to the summary or ICF and can link
the subject with the research. Therefore, it is unlikely that the IRB would require such a statement or ICF be provided to the subject when a waiver is granted under 45 CFR 46.117(c)(1). However, if the subject requests the written summary/unsigned ICF they must be advised of the potential harm which may result from a breach of confidentiality before making the decision concerning documentation.

4.0 Criteria for IRB Approval of a Waiver of Requirement to Obtain a Signed ICF Under 45 CFR 46.117(c)(2)

The following are the IRB requirements that must be met in order to approve a waiver of the requirement for the investigator to obtain a signed ICF for some or all subjects:

4.1 The research presents no more than minimal risk.
   
   Note: In order for the IRB to waive the requirement for the investigator to obtain a signed ICF for some or all subjects under 45 CFR 46.117(c)(2), the research must be no more than minimal risk and involve no procedures for which written informed consent would normally be required outside of the research context. Minimal risk means "The probability (of occurrence) and magnitude (seriousness) of harm or discomfort (e.g., psychological, social, legal, economic) associated with the research are not greater than those ordinarily encountered in daily life (of the average person in the general population) or during the performance of routine physical or psychological examinations or tests." Minimal risk, therefore, is used to define a threshold of anticipated harm or discomfort associated with the research that is low.

4.2 The research involves no procedures for which written informed consent is normally required outside of the research context.

   Note: Examples of procedures that would normally meet the requirements of 46.117(c)(2) include 1) routine diagnostic procedures such as venipuncture, magnetic resonance imaging, electrocardiography, and vital sign measurements; and 2) routine psychological assessments or tests.

4.3 The subject will be provided with a written statement regarding the research. This statement can be in the form of a ICF without signature blanks or a narrative.

   Note: All the elements of informed consent required by the IRB that are contained in the ICF template must be included unless some elements are waived under the provisions of 45 CFR 46.116(d).

   Note: The circumstances must be compelling in order for the IRB to grant a waiver under 45 CFR 46.117(c)(2). In most cases there is no reason why a signed ICF cannot be obtained from subjects.

5.0 Criteria for IRB Approval of a Waiver of Requirement to Obtain a Signed ICF Under 21 CFR 56.109(c)

The following are the IRB requirements that must be met in order to approve a waiver of the requirement to obtain a signed ICF for some or all of the subjects in FDA-regulated research:

5.1 The research presents no more than minimal risk.

   Note: In order for the IRB to waive the requirement for the investigator to obtain a signed ICF for some or all subjects under 21 CFR 56.109(c) the research must be no more than minimal risk and involve no procedures for which written informed consent would normally be required outside of the research context. Minimal risk means "The probability (of occurrence) and magnitude (seriousness) of harm or discomfort (e.g., psychological, social, legal, economic) associated with the research are not greater
than those ordinarily encountered in daily life (of the average person in the general population) or during the performance of routine physical or psychological examinations or tests.” Minimal risk, therefore, is used to define a threshold of anticipated harm or discomfort associated with the research that is low.

5.2 The research involves no procedures for which written informed consent is normally required outside of the research context. 

Note: Examples of procedures that might meet the requirements of 21 CFR 56.109(c) include routine diagnostic screening procedures to determine eligibility such as venipuncture, magnetic resonance imaging, electrocardiography, and vital sign measurements.

5.3 The subject will be provided with a written statement regarding the research. This statement can be in the form of an ICF without signature blanks or a narrative. Note: All the elements of informed consent required by the IRB that are contained in the ICF template must be included.

Note: The circumstances must be compelling in order for the IRB to grant a waiver under 21 CFR 56.109(c). In most cases there is no reason why a signed ICF cannot be obtained from subjects.

6.0 Process of Review

6.1 The investigator must complete and submit the Addendum M: Waiver of Requirement to Obtain Signed Consent Form together with the appropriate IRB application.

6.2 The process of IRB review will be conducted in accordance with the classification of the study: 1) Exempt research (HRPP policy #2.6); 2) Expedited review of research (HRPP policy #2.3); or 3) Full Board review (HRPP policy #2.2).

6.3 The IRB will review and approve any statements regarding the research required by federal regulations in accordance Sections 3.4, 4.3, and 5.3 of this policy.

6.4 Documentation of IRB approval of waiver of requirement to obtain signed ICF will appear in the IRB review letter.

ADMINISTRATIVE APPROVAL:
Ernest D. Prentice, PhD. Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for use of a short form written consent document for enrollment in clinical research.

2.0 Policy
2.1 It is the policy of the Organization that use of a short form written consent document is permissible in accordance with HHS regulations at 45 CFR 46.117(b)(2) and FDA regulations at 21 CFR 50.27(b)(2) when:

A. A subject/LAR who cannot understand English is unexpectedly encountered.

B. There is not sufficient time to develop and obtain IRB approval for a complete ICF written in language understandable to the subject/LAR.

C. There is prospect of direct therapeutic benefit if the individual is permitted to enroll in the research (as determined by the IRB at the time of approval of the research).

2.2 The short form is not a substitute for a complete fully translated ICF when it is anticipated that a significant number of subjects will be non-English speaking.

2.3 The short form is restricted to enrollment of no more than three (3) subjects per language in a given protocol. (e.g., the Laotian short form has been used three times in the same protocol). In order to enroll more than three subjects, the PI is required to translate the complete ICF into the appropriate language and submit to the IRB for review and approval.

2.4 The enrollment of a minor under circumstances which satisfy the criteria specified above is permitted using the short form signed by the minor’s parent/guardian. There is no requirement that the minor be provided with a study information sheet. However, minors, age 13 and above, must sign the short form. Minors between the ages of 7-12 must be verbally assented with documentation in the research or medical record.

3.0 Procedure
3.1 IRB-approved short forms are available on the IRB website (www.unmc.edu/irb) in the following languages: Arabic, Croatian, French, Hmong, Khmer, Laotian, Oromo, Russian, Somali, Spanish, and Vietnamese.

3.2 If an IRB-approved short form is not available on the IRB website in a language understandable to the subject/LAR, the investigator must develop an appropriate short form based upon the IRB-approved English version of the short form (found on the IRB website at www.unmc.edu/irb). The completed form and translated Short Form must be submitted electronically to IRBORA@unmc.edu for expedited review and approval before use, provided that the protocol and the English version of the complete ICF have already been approved by the convened IRB.

3.3 Investigators who wish to use an IRB-approved short form must complete a Short Form Request, available on the IRB website at www.unmc.edu/irb. The completed form must be submitted to the ORA.

Note: Each Short Form Request applies to only one subject.
3.4 The IRB Executive Chair/designee must approve each Short Form Request prior to use of the requested short form.

3.5 The IRB number and title of the protocol (in English) must be typed in the spaces provided at the top of the short form. In addition contact information must be typed in the spaces provided within the body of the short form.

3.6 The duration of IRB-approval of a short form (IRB stamped) will be no more than two weeks without justification provided to the IRB Executive Chair/designee for extended approval period.

3.7 An Official Interpreter who is fluent in both English and the language of the subject/LAR must be identified and can be any of the following in order of priority listing:

A. A Nebraska Medicine, CH&MC or study site hospital staff or contracted person who is a specifically trained interpreter/translator. This individual must be fluent in both languages and have a basic understanding of the medical or other scientific terminology related to the research.

B. A commercial interpretation/translation service (such as CyraCom).

3.8 If a prospective subject/LAR/parent insists on designating his/her own interpreter:

A. This must be documented in the medical/research record.

B. The Official Interpreter that qualifies under 3.7A-B above must also be present to ensure the quality and accuracy of the interpretation and this must also be documented.

C. Minors cannot be used as the Official Interpreter.

3.9 A witness who is fluent in both English and the language of the subject/LAR must be identified and can be any of the following in order of priority listing:

A. An official Nebraska Medicine, CH&MC, or study site hospital interpreter/translator.

B. A commercial interpretation/translation service (such as CyraCom).

C. With the exception of study personnel, if the Official Interpreter qualifies under 3.5A-B above, then they may also serve as the witness.

3.10 The interpreter must be involved in the process of consent as follows:

A. The subject/LAR should be given a copy of the short form.

B. The person obtaining consent, with the assistance of the interpreter, should explain the use of the short form.

C. The person obtaining consent, with the assistance of the interpreter, should carry out the process of consent using the IRB-approved English version of the complete ICF as a guide. The complete ICF (which serves as the summary required by federal regulations) need not be translated word-for-word.
D. The person obtaining consent, with the assistance of the interpreter, should obtain frequent feedback from the subject/LAR and ensure there is an acceptable level of understanding of the research and the rights of the subject.

3.11 Interpreters should be provided with a copy of the short form and the IRB-approved English version of the ICF. Whenever possible, these forms should be provided at least 24 to 48 hours in advance of initiating the consent process with the subject/LAR.

3.12 Upon conclusion of the consent process the subject/LAR must sign and date the short form.

3.13 The person obtaining consent must sign and date the English version of the complete ICF.

3.14 A witness to the oral presentation of the ICF (per Section 3.9 above) must sign both the short form, as well as the English version of the complete ICF.

3.15 A copy of the signed and dated short form and the English version of the complete ICF must be given to the subject/LAR.

3.16 Depending on the nature and duration of the research, the IRB Chair/designee may determine that the English version of the complete ICF must be translated into a language understandable to the subject with a copy given to the subject as soon as possible after enrollment in the research using the short form. In general, this may be required for studies which are significant risk and of long duration.

3.17 The process of consent using the short form must be fully documented and maintained on file which includes the following:

   A. The time over which the process of consent was conducted.
   B. The name and contact information of the interpreter.
   C. The name and contact information of the witness.

3.18 Both the investigator and interpreter must document the informed consent process utilizing the short form in the medical/research record.

ADMINISTRATIVE APPROVAL:
Ernest D. Prentice, PhD.  Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD  IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for IRB review and approval of an exception from informed consent requirements for emergency research.

2.0 Policy
It is the policy of the Organization that an exception from informed consent requirements for emergency research must be in full compliance with the requirements of 21 CFR 50.24 for FDA-regulated research. For non-FDA regulated research, the IRB will determine that the research is in full compliance with HHS regulations at 45 CFR 46.101(i); (OPRR Report 97-01, and FR Vol. 61, pp. 51531-51533).

3.0 Definition
3.1 Emergency Research: A clinical investigation (research) that is conducted in an emergency setting which may be in a hospital emergency room, ambulance, life-flight, or any other setting.

4.0 Requirements
4.1 For research which is subject to the FDA regulations at 21 CFR 50.24, the IRB may approve the investigation without requiring that informed consent for all research subjects be obtained if the IRB (with the concurrence of a licensed physician who is an IRB member or consultant to the IRB and who is not otherwise participating in the clinical investigation) finds and documents that each of the conditions under Section 4.3 (A-G) below have been satisfied.

4.2 For research not subject to FDA regulations, the IRB may approve the research without requiring that informed consent for all research subjects be obtained if the IRB (with the concurrence of a licensed physician who is a member of or consultant to the IRB and who is not otherwise participating in the research) finds and documents 1) that the research is not subject to regulations codified by the FDA at 21 CFR Part 50, and (2) that the conditions under Section 4.3 (A-G) below have been satisfied. In addition, this documentation must be submitted to OHRP.

4.3 Conditions for granting an exception from informed consent for emergency research are as follows:
A. The human subjects are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.

B. Obtaining informed consent is not feasible because:
1) The subjects will not be able to give their informed consent as a result of their medical condition, and

2) The intervention under investigation must be administered before informed consent from the subjects’ legally authorized representatives is feasible, and

3) There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation or research.
C. Participation in the research holds out the prospect of direct benefit to the subjects because:
   1) Subjects are facing a life-threatening situation that necessitates intervention, and
   2) Appropriate animal and other pre-clinical studies have been conducted, and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the individual subjects, and
   3) Risks associated with the investigation are reasonable in relation to what is known about the medical condition of the potential class of subjects, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.

D. The clinical investigation could not practicable be carried out without the waiver.

E. The protocol defines the length of the potential therapeutic window based on scientific evidence.

F. The PI will attempt to contact a LAR for each subject within the therapeutic window and, if feasible, ask the LAR for informed consent within that window rather than proceeding without informed consent.

G. The PI will summarize efforts made to contact LARs and make this information available to the IRB at the time of continuing review.

H. The IRB has reviewed and approved informed consent procedures and an ICF consistent with 21 CFR 50.25/45 CFR 46.116 and 46.117. These procedures and the ICF are to be used with subjects or their LAR in situations where use of such procedures and documents is feasible.

I. The IRB has reviewed and approved procedures and information to be used when providing an opportunity for a family member to object to a subject’s participation in the clinical investigation.

J. Additional protections of the rights and welfare of the subjects will be provided, including, at least:
   1) Consultation (including, where appropriate, consultation carried out by the IRB), with representatives of the communities in which the clinical investigation will be conducted and from which the subjects will be drawn.
   2) Public disclosure to the communities in which the clinical investigation will be conducted and from which the subjects will be drawn, prior to initiation of the clinical investigation, of plans for the investigation and its risks and expected benefits.
   3) Public disclosure of sufficient information following completion of the clinical investigation to apprise the community and researchers of the study, including the demographic characteristics of the research population, and its results.
4) Establishment of an independent data monitoring committee to exercise oversight of the clinical investigation.

5) If obtaining informed consent is not feasible and a LAR is not reasonably available, the PI has committed, if feasible, to attempting to contact within the therapeutic window the subject’s family member who is not a LAR, and asking whether he or she objects to the subject’s participation in the clinical investigation.

6) The PI will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review.

4.4 The IRB is responsible for ensuring that procedures are in place to inform, at the earliest feasible opportunity, each subject, or if the subject remains incapacitated, a LAR of the subject, or if such a representative is not reasonably available, a family member, of the subject’s inclusion in the clinical investigation, the details of the investigation and other information contained in the ICF.

A. The IRB shall also ensure that there is a procedure to inform the subject, or if the subject remains incapacitated, a LAR of the subject, or if such a representative is not reasonably available, a family member, that he or she may discontinue the subject’s participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

B. If a LAR or family member is told about the clinical investigation and the subject’s condition improves, the subject is also to be informed as soon as feasible.

C. If a subject is entered into a clinical investigation with waived informed consent and the subject dies before a LAR or family member can be contacted, information about the clinical investigation is to be provided to the subject’s LAR or family member, if feasible.

4.5 Protocols subject to FDA regulations and involving an exception to the informed consent requirement must be performed under an FDA approved separate investigational new drug application (IND) or investigational device exemption (IDE) that clearly identifies such protocols as protocols that may include subjects who are unable to informed consent. The submission of those protocols in a separate IND/IDE is required even if an IND for the same drug product or an IDE for the same device already exists.

4.6 If the IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in the exception, or because of other relevant ethical concerns, the IRB will document its findings and provide these findings promptly in writing to the PI and to the sponsor of the clinical investigation.

4.7 The IRB determinations are to be retained by the IRB for at least 7 years after completion of the clinical investigation, and the records shall be accessible for inspection and copying by FDA.
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for research involving the use of investigational and marketed drugs.

2.0 Policy
It is the policy of the Organization that: a) the IRB will review all research involving the use of investigational drugs, biologics, and marketed drugs (test articles) in full accordance with the following: 21 CFR 50, 56; 21 CFR 312, 314; 45 CFR 46; and b) investigators will conduct such research in full accordance with the above cited regulations and HRPP policies.

3.0 Definitions
3.1 **Investigational Drug:** An investigational drug means: a) a drug or a biologic that is used in a clinical investigation under an Investigational New Drug (IND) Application, or b) a marketed drug that is being studied for an unapproved or approved use in a controlled, randomized, or blinded clinical trial.

3.2 **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.

3.3 **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).

3.4 **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.

3.5 **Investigational New Drug (IND) Application:** An IND application is an application submitted to FDA to conduct a clinical investigation with an investigational drug that is subject to 21 CFR 312.2(a). The IND is submitted by the sponsor of the research. The FDA will provide a written authorization to conduct a clinical investigation within 30 days after FDA receives the IND.

3.6 **Marketed Drug:** A marketed drug is a drug or biologic approved by FDA for marketing and is generally in use for treatment purposes.

3.7 **Sponsor:** The sponsor is a person who takes responsibility for and initiates a clinical investigation. The sponsor may be a pharmaceutical company, governmental agency, academic institution, private organization or an individual investigator.

3.8 **Sponsor-Investigator:** A sponsor-investigator is an individual that both initiates and conducts an investigation. Additionally the sponsor-investigator directs the administration or dispensing of the investigational drug. An investigator who also
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serves as a sponsor must comply with all FDA requirements applicable to both an investigator as well as a sponsor.

3.9 **New Drug Application (NDA):** A New Drug Application is an application submitted to FDA for approval to market a new drug after the clinical investigation has been completed.

3.10 **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.

4.0 **Procedures**

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

4.2 The Organization requires all clinical investigations involving drugs to be reviewed by the full IRB in accordance with **HRPP policy #2.2**. Clinical investigations involving drugs are not eligible for expedited review in accordance with **HRPP policy #2.3**.

4.3 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 Q: Investigational New Drugs or Biologic Drugs**. If the PI has an investigator-initiated IND, **Addendum O: Principal Investigator Responsibilities: Investigator-Initiated Drug Trials** must also be submitted.

4.4 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 312.60-69 and ensure that the research is conducted in full compliance with the requirements of 21 CFR 50,56 and 45 CFR 46.

4.5 If the PI indicates on **Addendum Q**, or SPA informs the ORA that the contract agreement requires compliance with ICH GCP, the IRB will review the submission in accordance with **HRPP policy #1.12**.

4.6 The IRB will review the information in **Addendum Q** to ensure that investigational drugs are securely stored and dispensed in accordance with FDA regulations at 21 CFR 312.60-62.

A. For research conducted at UNMC and Nebraska Medicine investigational drugs must be stored and dispensed in accordance with Investigational Drug Policies (I380 and MS05) which describe in-patient and out-patient requirements.

B. For research conducted at CH&MC the applicable policy is **CH&M Policy 204.00**.

C. For research conducted at an external site, a copy of the policy of external site(s) can be submitted which satisfies the requirements in accordance with FDA regulations.

4.7 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 312.50-59.
4.8 Any PI who has a study that will be audited by the sponsor, a CRO or FDA must immediately notify the designated IRB Administrator and the UNMC Chief Compliance Officer. The IRB must be provided with a copy of the report following the audit.

4.9 When a 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.

4.10 The PI must promptly inform the IRB and Investigational Drug Pharmacist when a study involving investigational drugs has been terminated.

5.0 IND Studies

5.1 The IRB will ensure that a valid IND is in effect for any drug study subject to 21 CFR 312.2(a). Documentation of the IND could include any of the following depending upon the study:

A. Industry sponsored protocol with the IND number

B. Written determination from the FDA

C. Other documentation or communication verifying the IND number

D. If a study involves an investigator-initiated IND, it is the expectation of the Organization that the PI will also comply with the FDA-mandated sponsor requirements (21 CFR 312.50) and certify compliance by submitting Addendum O: Principal Investigator Responsibilities: Investigator-Initiated Drug Trials which specifies all of the responsibilities of the PI/Sponsor.

E. For studies involving marketed drugs for potential new indications or changes in dose, an IND is required in accordance with 21 CFR 312.2(b)(1).

F. All protocol-related documents, including FDA notification, must contain matching IND numbers.

5.2 A clinical investigation involving an exception from informed consent under 21 CFR 50.24 is not exempt.

5.3 If the IRB has any question or concern about whether an IND is required, the PI will be instructed to contact the Food and Drug Administration (FDA) Center for Drug Evaluation and Research (CDER) or the Center for Biologics Evaluation and Research (CBER) to obtain a written determination.

Note: If FDA regulated research involving an investigational drug is conducted outside of the US an IND is not required provided the study is conducted in accordance with GCP guidelines and FDA is able to validate the data from the study through an on-site inspection if FDA deems it necessary.

5.4 Exemptions from FDA Requirements Under 21 CFR 312.2(b)(1)

A. For studies involving marketed drugs for potential new indications or changes in dose, the IRB will require an IND in accordance with 21 CFR 312.2(b), unless all of the following conditions are met:
1) The investigation is not intended to be reported to FDA as a well-controlled study in support of a new indication for use or not intended to be used to support any other significant change in the labeling for the drug.

2) If the drug that is undergoing investigation is lawfully marketed as a prescription drug product, the investigation is not intended to support a significant change in the advertising for the product.

3) The investigation does not involve route of administration or dosage level or use in a patient population or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product.

4) The investigation is conducted in compliance with the requirements for institutional review set forth in part 56 and with the requirements for informed consent set forth in 21 CFR 50.

5) The investigation is conducted in compliance with the requirements of 21 CFR 312.7.

6) The research does not intend to invoke FDA regulations for planned emergency research at 21 CFR 50.24.

5.5 Exemptions from FDA Requirements Under 21 CFR 312.2(b)(2)

A. For studies involving the following products which are exempt from FDA requirements, the IRB will not require an IND:

1) A clinical investigation involving an in vitro diagnostic biological product listed in Section A2 below is exempt if:

   a) It is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established, diagnostic product or procedure, and

   b) It is shipped in compliance with 21 CFR 312.160.

2) In accordance with Section A1 above, the following products are exempt:

   a) blood grouping serum
   b) reagent red blood cells
   c) anti-human globulin

3) A drug intended solely for tests in vitro or in laboratory research animals is exempt if shipped in accordance with 21 CFR 312.160.

4) A clinical investigation involving use of a placebo if the investigation does not otherwise require submission of an IND.

5.6 Expanded Access of Investigational Drugs

A. FDA regulations at 21 CFR 312 allow certain individuals not enrolled in clinical trials to obtain expanded access to investigational drugs through the following methods:

1) Compassionate Use:

   a) The term “compassionate use” is erroneously used to refer to the provision of investigational drugs outside of an ongoing clinical trial to a limited
number of patients who are desperately ill and for whom no standard alternative therapies are available. The term “compassionate use” does not, however, appear in FDA or HHS regulations. It is preferable, instead, to use the names of the specific access programs when discussing the use of investigational articles outside of formal clinical trials.

b) Prospective IRB review and approval is required.

2) **Group C Treatment Investigational New Drug (IND):**
   a) A means for the distribution of investigational drugs, agents, or biologics to oncologists for the treatment of cancer under protocols outside controlled clinical trials. Group C drugs, agents, or biologics usually have shown evidence of relative and reproducible efficacy in a specific tumor type.

b) Although the FDA typically grants a waiver for most drugs used in Group C Treatment IND protocols, the IRB requires prospective IRB review and approval.

3) **Open – Label Protocol:**
   a) A study designed to obtain additional safety data, typically done when the controlled trial has ended and treatment continues. The purpose of such a study is to allow subjects to continue to receive the benefits of the investigational drug, agent, or biologic until marketing approval is obtained.

b) Prospective IRB review and approval is required.

4) **Parallel Track:**
   a) A method approved by the FDA that expands the availability of investigational drugs, agents, or biologics as quickly as possible to persons with AIDS and other HIV-related diseases. These drugs, agents or biologics are utilized in separate protocols that “parallel” the controlled clinical trials and are essential to establish the safety and effectiveness of these new drugs, agents, or biologics.

b) Although the Secretary of the Department of Health and Human Services may, on a protocol-by-protocol basis, waive the provisions of 45 CFR Part 46 where adequate protections are provided through other mechanisms, prospective IRB review and approval is required.

5) **Treatment IND or Biologics:**
   a) Under FDA regulations at 21 CFR 312, FDA has a mechanism for providing eligible subjects with investigational drugs (as early in the drug development process as possible) for the treatment of serious and life-threatening illnesses for which there are no satisfactory alternative treatments. The FDA defines an immediately life-threatening disease as a stage of a disease in which there is a reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment. The FDA will permit an investigational drug to be used under a treatment IND after sufficient data have been collected to show that the drug “may be effective” and does not have unreasonable risks.
b) Prospective IRB review and approval is required.

c) There are four requirements that must be met before a treatment IND can be issued:
   i) The drug is intended to treat a serious or immediately life-threatening disease.
   ii) There is no satisfactory alternative treatment available.
   iii) The drug is already under investigation or trials have been completed.
   iv) The trial sponsor is actively pursuing marketing approval.

d) The FDA identifies two special considerations when a patient is to be treated under a Treatment IND:
   i) Informed Consent. Informed consent is especially important in treatment use situations because the subjects are desperately ill and particularly vulnerable. They will be receiving medications which have not been proven either safe or effective in a clinical setting. Both the setting and their desperation may work against their ability to make an informed assessment of the risk involved. Therefore, the IRB will ensure that potential subjects are fully aware of the risks involved in participation.

   ii) Charging for Treatment INDs. The FDA permits charging for the drug, agent, or biologic when used in a Treatment IND. Therefore, the IRB will pay particular attention to Treatment INDs in which the subjects will be charged for the cost of the drugs. If subjects will be charged for use of the test article, economically disadvantaged persons will likely be excluded from participation. Charging for participation may preclude economically disadvantaged persons as a class from receiving access to test articles. The IRB will balance this interest against the possibility that unless the sponsor can charge for the drug, it will not be available for treatment use until it receives full FDA approval.

6) Single-Patient Use:
   a) The use of an investigational drug outside of a controlled clinical trial for a patient, usually in a desperate situation, who is unresponsive to other therapies or in a situation where no approved or generally recognized treatment is available. There is usually little evidence that the proposed therapy is useful, but may be plausible on theoretical grounds or anecdotes of success.

   b) Access to investigational drugs for use by a single, identified patient may be gained either through the sponsor under a treatment protocol, or through the FDA, by first obtaining the drug from the sponsor and then submitting a treatment IND to the FDA requesting authorization to use the investigational drug for treatment use.

   c) Prospective IRB review and approval is required (See Section 5 above).

7) Emergency IND: The emergency use of an unapproved investigational drug, agent, or biologic requires an emergency IND. The FDA has established
mechanisms and guidance for obtaining an Emergency IND for the use of investigational drugs, agents, or biologics.

5.7 Emergency Waiver of an IND
A. FDA regulations at 21 CFR 312.34, 312.35, and 312.36 address the need for an investigational drug to be used in an emergency situation that does not allow time for submission of an IND. The FDA may authorize shipment of the drug for a specific use in such a circumstance in advance of submission of an IND. The IRB will assist the investigator in obtaining an emergency waiver of an IND.

B. Prospective IRB review is required unless the conditions for exemption are met (21 CFR 56.104(c) and 56.102(d)). Informed consent is required unless the conditions for exemption are met (21 CFR 50.23). All applicable regulations must be met including those at 21 CFR Parts 50 and 56, and 21 CFR 312.34 and 312.35.

5.8 Emergency Use of Investigational Drugs
Emergency use of an investigational drug will be administered to subjects in accordance with HRPP policy #6.4.

5.9 Waiver of Informed Consent for Planned Emergency Research
A waiver of informed consent for planned emergency research will be reviewed and approved by the full IRB in accordance with HRPP policy #5.7.

ADMINISTRATIVE APPROVAL:
Ernest D. Prentice, PhD  Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD  IRB Executive Chair
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 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 21 CFR 56.109(c).

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 A(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 and the rationale for the classification 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 and *TNMC Policy #MI29*. 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 Fred & Pamela Buffett 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.

ADMINISTRATIVE APPROVAL:
Ernest D. Prentice, PhD. Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, M.D. IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for the use of a medical device that has a Humanitarian Use Device (HUD) designation.

2.0 Policy
It is the policy of the Organization that all uses of a HUD will be reviewed and approved in accordance with FDA regulations at 21 CFR 50, 56 and 814 Subpart H, as well as HHS regulations at 45 CFR 46.

3.0 Definitions
3.1 **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 US per year. Requests for HUD designation must be submitted to the FDA Office of Orphan Products Development.

3.2 **Humanitarian Device Exemption (HDE):** HDE is an application that is similar to a Pre-Market Approval (PMA) application, but is not required to contain efficacy results from clinical trials. FDA will grant or deny an HDE application within a total of 75 days from the date of receipt.

4.0 IRB Review Procedures
4.1 In accordance with FDA regulations at 21 CFR 814.124(a), the full IRB will review and approve the use of a HUD before it is used by a physician to treat or diagnose patients.

4.2 The IRB HUD application should be submitted to the ORA for all proposed uses of a HUD under an HDE. The application is designed to provide the IRB with all information necessary to determine that use of the device is justified and the rights and welfare of the patients will be fully protected.

4.3 If the HUD is the subject of a clinical investigation in which safety and effectiveness data is being collected to support a pre-marketing approval application, the IRB Application for Biomedical Research should be used instead along with submission of Addendums R and P as necessary.

4.4 The IRB HUD application will be submitted to the full Board for review and approval. Expedited review will not be used.

4.5 The IRB will normally not review and approve individual patient uses of a HUD within the IRB-approved HUD Application. However, on a case-by-case basis, the IRB may decide to require such approval.

4.6 An HUD may be used in an emergency situation without prior IRB approval in accordance with the applicable sections of HRPP policy #6.4.

4.7 The UNMC IRB requires that written informed consent be obtained from patients who will be recipients of HUDs. 

*Note: The ICF for use of an HUD must reflect the standard IRB template titled Clinical Consent for Use of a Humanitarian Use Device which is available on the IRB website*
at www.unmc.edu/irb. It should be noted that this is not the standard “Biomedical Research consent form template” because the use of the HUD does not constitute research or an investigation.

4.8 The IRB HUD Continuing Review application will be submitted to the full IRB for review and approval. Expedited review will not be used. The full IRB will determine the continuing review date which will be no less often than annually.

ADMINISTRATIVE APPROVAL:
Ernest D. Prentice, PhD. Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, M.D. IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the requirements for utilization of a test article under emergency circumstances where there is not sufficient time to obtain full IRB approval at a convened meeting of the IRB.

2.0 Policy
2.1 It is the policy of the Organization that emergency use of a test article (investigational drug, biologic, or device) must be conducted in full compliance with the requirements of FDA regulations at 21 CFR 56.102(d), 21 CFR 56.104(c), and FDA information sheets which address such use. In addition, it is the organization’s policy that in an emergency use situation, if time permits, the treating physician who is proposing to use the test article must obtain concurrence from the IRB Chair/designee through the Office of Regulatory Affairs (ORA) that the emergency use meets all FDA requirements.

2.2 Nothing in the policy is intended to limit the authority of a physician to provide emergency medical care, to the extent the physician is permitted to do so under applicable federal, state, or local law.

2.3 If the emergency use involves administration of a test article and the activity is DHHS funded, the patients cannot be classified as human subjects. The outcome of such care cannot be included in any report (e.g., research article in a journal) subject to DHHS regulations. However, data obtained during emergency use of the test article is subject to FDA inspection and may be required to be submitted to FDA.

3.0 Definitions
3.1 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 [21 CFR 56.102(d)].

A. Life-threatening: Diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted.

B. Severely debilitating: Diseases or conditions that would likely cause major irreversible morbidity (e.g. loss of a limb, paralysis or stroke).

Note: A life-threatening and/or severely debilitating condition does not necessarily mean that the condition is immediately life-threatening or may imminently result in death or irreversible morbidity. Rather, the patient must be in a situation requiring prompt administration of the test article before review at a convened meeting of the IRB is feasible and any treatment delay will have a significant deleterious effect on the patient. Consequently, premature death and/or persistent morbidity are likely.

4.0 Emergency Use Circumstances
4.1 The need for emergency use of a test article in a life-threatening or severely debilitating situation could occur under the following circumstances:

A. An IND/IDE exists for the test article but a protocol has never been submitted to the IRB.
Note: Emergency use should never be construed as a mechanism to avoid submitting a protocol to the IRB for review and approval. Therefore, utilization of a test article under the FDA Emergency Use provisions should be uncommon.

B. An IND/IDE exists for the test article. A protocol has been submitted to the IRB, but has not yet been approved by the IRB.

C. An IND/IDE does not exist for the test article.
   Note: FDA may authorize shipment of the test article in advance of the IND/IDE submission upon requests.

D. The intended patient is in the life-threatening or severely debilitating situation is ineligible to participate in an existing IRB-approved protocol.

   Note: FDA allows physician requests for a single patient IND for compassionate or emergency use in accordance with 21 CFR 312.300. This is referred to as “expanded access use” and requires approval of both the drug manufacturer and FDA. The patient or patients to be treated must have a serious or immediately life-threatening disease or condition and there is no comparable or satisfactory alternative therapy.

   Expanded access, however, requires prospective IRB review and approval before use of the drug or biologic. Expanded access use is, therefore, an option when: 1) the patient(s) medical condition warrants treatment with the investigational drug/biologic, 2) the treating physician obtains FDA approval of an expanded access submission, and 3) prospective IRB review and approval can and will be obtained.

5.0 IRB Requirements

5.1 Physicians intending to use a test article under emergency circumstances should have carefully assessed the potential for therapeutic benefit to the patient and be assured that all of the following criteria are met:

A. The test article has not been used at the Organization to date under the FDA emergency use provisions.

B. The patient is suffering from a life-threatening or severely debilitating condition.

C. There is no available alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the patient’s life and/or alleviating a debilitating condition.

D. When possible and/or required, the holder of the IND or IDE (sponsor or device developer) has authorized the emergency use.

E. When the test article is a medical device, an independent assessment, as appropriate, has been obtained from an uninvolved physician that use of the test article is necessary.

F. There is not sufficient time to obtain full IRB approval of a protocol.

6.0 FDA Notification

6.1 When there is an industry sponsor who is the holder of the IND/IDE, the sponsor will notify FDA as required.
6.2 When the investigator is the holder of the IND/IDE, the investigator will notify FDA as required.

6.3 When no IND/IDE exists, the treating physician will notify the drug/device developer who, in turn, will notify FDA.

*Note: The FDA should be provided with a written summary of the conditions constituting the emergency use, patient protection measures, and clinical results.*

7.0 Procedures for emergency use of a test article

7.1 If time is sufficient, the treating physician should contact the ORA during normal work hours at 402-559-6463.

7.2 The IRB administrator(s) responsible for emergency use coordination (Emergency Use Coordinator) will obtain pertinent information about the proposed emergency use and access the IRB database to determine whether the test article has been used previously in an emergency situation.

7.3 The Emergency Use Coordinator will document the call concerning the proposed emergency use and will notify the IRB Executive Chair/designee of any issues.

7.4 The Emergency Use Coordinator will direct the physician to contact the IRB Executive Chair/designee to obtain a determination whether the proposed emergency use of the test article meets the conditions specified in Section 5.0 of this policy.

7.5 If the emergency occurs outside of normal business hours, the physician should contact the IRB Executive Chair/designee by phone, page, or through the hospital operator.

7.6 The treating physician should be prepared to verbally justify the emergency use of the test article to the IRB Executive Chair/designee.

7.7 The IRB Executive Chair/designee must verbally concur that the proposed emergency use has met all the requirements of 21 CFR 56.102(d) and 21 CFR 56.104(c). The IRB database will be accessed and the Emergency Use Coordinator will be consulted as necessary.

7.8 The IRB Executive Chair/designee will notify the Emergency Use Coordinator of his/her concurrence concerning the proposed emergency use and the coordinator will electronically issue an IRB acknowledgement of emergency use. The IRB database will be updated accordingly.

7.9 If a test article involves an investigational drug or biologic, if time permits, the physician must contact the Chair of the P&T Committee/designee and obtain a one-time only P&T emergency use approval. In addition, the Executive Director of the Pharmacy or Investigational Drug Pharmacist must be notified of the emergency use, as well as provided information concerning financial responsibility for the pharmacy costs of the test article.

7.10 The IRB Executive Chair/designee will complete the *Emergency Use Notification Report* and forward it electronically to the ORA as soon as possible.
7.11 The treating physician should be prepared to obtain written informed consent from the patient or the patient’s legally authorized representative (LAR) unless this is not possible given the emergency circumstance.

7.12 An ICF should be developed utilizing the standard IRB template for emergency use of a test article. Alternatively, if appropriate, the sponsor’s ICF with an addendum containing local information can be used.

A. The ICF must comply with the requirements of 21 CFR 50.25 and include all the basic elements of informed consent as well as appropriate additional elements of consent.

B. The elements of informed consent should be worded to reflect the nature of the emergency situation (i.e., the patient is being treated for a life-threatening or severely debilitating condition and there are no alternative therapeutic methods that provide an equal or greater likelihood of saving the patient’s life.).

C. The ICF must include HIPAA required information and a clear disclosure of the financial obligations of the patient.

7.13 If there is sufficient time, the ICF should be reviewed by the IRB Executive Chair/designee before consent is obtained.

7.14 It is the expectation of the IRB that emergency use of the test article will not be delayed unless there are clinical reasons for doing so.

7.15 The Emergency Use of a Test Article Report must be submitted by the treating physician to the IRB within five (5) business days following initiation of the treatment. [21 CFR 56.104(c)].

7.16 The Emergency Use of a Test Article Report will be reviewed by the Emergency Use Coordinator for completeness and then provided to the IRB as a notification at the next full IRB meeting. IRB members are expected to review the reports and raise any questions or concerns.

7.17 Any subsequent use of the test article must have prospective IRB review and approval. Note: As previously indicated in Section 5.0, FDA acknowledges that it would be inappropriate to deny emergency treatment to a second individual if the only obstacle is the IRB has not had sufficient time to convene a meeting to review a protocol (reference “1998 FDA Information Sheets”).

7.18 If there is not sufficient time, therapeutic privilege prevails and the physician should use the test article in accordance with the conditions specified in Section 5.0 of this policy.

7.19 If the physician decides not to use the test article the emergency use coordinator must be promptly notified.

8.0 Exceptions to the Informed Consent Requirement for Emergency Use of a Test Article

8.1 Emergency use of a test article without obtaining informed consent from the patient or their LAR is permissible providing both the investigator and an independent physician who is not otherwise participating in any clinical investigation involving the test article certify in writing all of the following in accordance with the requirements of 21 CFR 50.23(a):
A. The human patient is confronted by a life-threatening or severely debilitating situation necessitating the use of the test article.

B. Informed consent cannot be obtained from the patient because of an inability to communicate with, or obtain legally effective consent from the patient.

C. Time is not sufficient to obtain consent from the patient’s LAR.

D. There is available no alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the patient’s life.

Note: The IRB Executive Chair/designee can provide the required certification if they are not participating in any clinical investigation involving the test article. Alternatively, another independent physician can provide certification. The independent assessment of the inability to obtain informed consent should be carried out if possible in advance of the use of the test article.

8.2 If time is not sufficient to obtain the independent physician determination before use of the test article, the actions of the investigator must be reviewed and evaluated in writing by an independent physician within 5-6 working days. The IRB must be notified within 5 working days when an emergency waiver is used. This notification must not be construed as an approval for the emergency waiver by the IRB. The IRB Executive Chair/designee will review the report to verify that circumstances of the emergency waiver conformed to FDA regulations.

9.0 The full IRB will be provided with a copy of the Emergency Use of a Test Article Report and ICF for the purpose of notification.

Administrative Approval:
Ernest D. Prentice, PhD.  Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD  IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for IRB approval of placebo controlled randomized clinical trials.

2.0 Policy
It is the policy of the Organization that all placebo controlled randomized clinical trials must be justified in accordance with this policy.

3.0 Definition
3.1 Placebo: Placebo is “a chemically inert substance given in the guise of medicine for its psychologically suggestive effect; used in controlled clinical trials to determine whether improvement and side effects may reflect imagination or anticipation rather than actual power of a drug” (OHRP Institutional Review Board Guidebook Glossary.)

3.2 Randomization: Randomization is an “assignment of subjects to different treatments, interventions, or conditions according to chance rather than systematically (e.g., as dictated by the standard or usual response to their condition, history, or prognosis, or according to demographic characteristics). Random assignment of subjects to conditions is an essential element of experimental research because it makes it more likely the probability that differences observed between subject groups are the result of the experimental intervention” (OHRP Institutional Review Board Guidebook Glossary.)

4.0 Justification of a Placebo
4.1 To approve use of a placebo control in a clinical trial, the IRB must find that all of the following are met:
   A. The use of a placebo is scientifically necessary to answer the research question.
   B. The risk of no treatment associated with placebo is not significant or irreversible.
   C. The risk of placebo is minimized (e.g., monitoring, withdrawal, treatment).
   D. Possible assignment to the active study drug offers the prospect of at least equivalent direct subject benefit compared to standard treatment.

4.2 The following are not required, but should also be considered by the IRB in determining the acceptability of a placebo control:
   A. There is no standard treatment with proven efficacy.
   B. The standard treatment has significant toxicity compared to the active study drug.
   C. The study employs a cross-over design.
   D. The predicted placebo response is high.
   E. The standard treatment has a high rate of non-compliance.
   F. The randomization scheme allows more than 50% of subjects to be assigned to the active study drug by requiring three doses of study drug versus placebo.
G. The use of a placebo is added to a standard therapeutic arm.

H. The standard treatment is very expensive or not readily available.

I. There is no treatment available.

5.0 Informed Consent Requirements

The IRB must find that the ICF clearly discloses the following:

5.1 That a placebo is used in the study and defines what a placebo is.

5.2 That the subject may be randomized to the placebo group.

5.3 The risks of non-treatment associated with placebo.

5.4 The monitoring plan.

5.5 Stopping rules for withdrawal from the study due to ineffective therapy (i.e., clinical status worsens or fails to improve to a pre-defined level.)

Administrative Approval:
Ernest D. Prentice, PhD. Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for
banking human biological material (HBM) for future research.

2.0 Policy
It is the policy of the Organization that excess HBM, also referred to as “specimens” or “samples”,
may be collected as part of an addendum study attached to a clinical protocol, or as a free
standing tissue banking protocol thereby providing a resource for future, unspecified research, in
accordance to HHS regulations at 45 CFR 46, HIPAA Privacy Rule, other applicable HRPP
policies and Organizational requirements.

3.0 Definitions

3.1 Human Biological Materials: This includes the full range of human biological
specimens: sub-cellular structures (e.g., DNA); cells; tissues (e.g., blood, bone,
muscle, connective tissue, teeth, and skin); organs (e.g., liver, bladder, heart, kidney,
and placenta); gametes (e.g., sperm and ova); and waste (e.g., hair, nail clippings,
urine, feces, saliva, and sweat, which often contains shed skin cells).

3.2 Human Biological Material Collections: HBM in the form of slides, paraffin blocks,
formalin-fixed, frozen, tissue culture, or extracted DNA may be accumulated for years
and be found in:
A. Large tissue banks, repositories, and core facilities
B. Materials collected as part of longitudinal studies
C. Research collections requiring unique tissue specimens
D. Pathology specimens initially collected for clinical purposes
E. Newborn screening tests accumulating in various laboratories
F. Forensic DNA banks
G. Umbilical cord blood banks
H. Organ banks
I. Blood banks
J. Individual investigators’ collections

3.3 Centralized Human Biological Material Bank: A centralized HBM bank (also referred
to as a biorepository) is defined as a non-local HBM bank, a cooperative group
associated HBM bank, or a bank operated out of another University. The IRB
recognizes that the investigators at UNMC will not have control over what studies are
performed utilizing HBM obtained through these banks. Therefore, particular attention
will be paid to what, if any, subject identifiers will be maintained.

3.4 Commercial Human Biological Material Bank: A commercial HBM bank is defined
as a non-local HBM bank maintained by a corporate sponsor. These banks are often
associated with a specific commercially sponsored clinical trial, or may be an
independent bank.

3.5 Local Human Biological Material Bank: A “local” HBM bank is defined as a
repository located within the Organization or operated entirely, or in part, by an
investigator affiliated with the Organization. Local HBM banks may be established for
one of the following reasons:
A. The HBM bank is associated with specific IRB-approved protocol(s) and will involve only that group of subjects participating in the associated trial(s).

B. The HBM bank is not associated with a specific IRB-approved clinical protocol and is designed as a free-standing specimen bank. In many cases the bank is based on a specific disease or condition and specimens may be collected from many subjects in multiple trials.

4.0 IRB Review

4.1 The IRB will review the clinical research and/or proposed HBM bank in accordance with all applicable federal regulations and HRPP policies.

4.2 When excess or additional HBM is collected for the purpose of storage in a biorepository, the subject or participant must provide consent to the banking of the biological material.

A. Subject participation cannot be required in an unrelated addendum study in order to enroll in the main study.

B. If the HBM to be banked will be collected in conjunction with subject participation in an IRB-approved study, separate informed consent must be obtained from the subject.

C. The bank will be classified and reviewed in accordance with HRPP policy #2.6 for exempt research; HRPP policy #2.3 for banking which qualifies for expedited review; and HRPP policy #2.2 for banking which requires review by the full IRB.

5.0 Commercialization of banked human biological material

5.1 If the research includes an element of commercialization of the banked HBM, the ICF must disclose this information and not contain any exculpatory language.

A. If the bank will be housed within the Organization, the ICF must contain the standard statement indicating that the donated HBM is the property of the Organization, and the Organization has no plans to compensate the participant if products are commercialized.

B. If the bank will be housed outside the Organization, the ICF must address both the property and the compensation issues.

C. The ICF is not meant to serve as a commercial contract where subject compensation and/or subject waiver of future revenue sharing is presented.

D. Commercial negotiations must be separate from the ICF and are negotiated by the researcher, representatives of the Organization, the subject, and their legal counsel.

5.2 If the research does not initially include the element of commercialization, but at a later point in time a commercial product appears likely to develop from the subject’s donated HBM and additional samples from the subject are necessary, the IRB requires submission of a protocol amendment and re-negotiation of informed consent.

5.3 If the research does not initially include the element of commercialization, but at a later point in time a commercial product appears likely to develop from a subject’s donated
HBM, the IRB does not require re-negotiation of informed consent providing no additional samples from the subject are necessary.

**Administrative Approval:**
Ernest D. Prentice, PhD. Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for the use of human biological material (HBM) in research.

2.0 Policy
It is the policy of the Organization that HBM, also referred to as “specimens” or “samples”, may be collected and used in research in accordance with HHS regulations at 45 CFR 46; FDA regulations at 21 CFR 50, 56; HIPAA Privacy Rule, applicable HRPP policies, and Organizational requirements.

3.0 Definitions

3.1 Human Biological Materials: HBM includes the full range of human biological specimens: sub-cellular structures (e.g., DNA); cells; tissues (e.g., blood, bone, muscle, connective tissue, teeth, and skin); organs (e.g., liver, bladder, heart, kidney, and placenta); gametes (e.g., sperm and ova); and waste (e.g., hair, nail clippings, urine, feces, saliva, and sweat, which often contains shed skin cells).

3.2 Identifiable Human Biological Material: HBM that is linked to any of the 18 HIPAA identifiers (e.g., medical record number, dates) so that the subject or participant from whom the sample was obtained can be identified (refer to HRPP policy #3.4).

3.3 De-identified Human Biological Materials: HBM that is stripped of any of the 18 HIPAA identifiers before any research testing has taken place. Samples may be coded so that clinical information that has already been obtained from a medical record or questionnaire can be linked to the sample. However, the identity of the subject from whom the sample was obtained, cannot be readily ascertained (refer to HRPP policy #3.4).

4.0 Source of HBM
Specimens may be obtained from:

4.1 Extra/additional HBM obtained at the time of a clinically indicated procedure (e.g., an extra tube of blood).

4.2 Excess HBM that would ordinarily be discarded following a clinically indicated procedure (e.g., left over tissue following a biopsy procedure after all diagnostic tests have been completed).

4.3 Samples collected specifically for purposes of the research protocol (e.g., cheek swab to obtain DNA).

4.4 An existing HBM repository (bank).

4.5 Pathology samples stored for purposes of clinical care.

5.0 IRB Review
5.1 The IRB will review research protocols involving the use of HBM in accordance with all applicable federal regulations, HRPP policies and Organizational requirements.

A. When the purpose of the research relates only to the use of HBM, the application for Human Biological Materials Research must be submitted for IRB review.
B. When the HBM is obtained as part of a clinical trial, the application for Biomedical Research must be submitted for IRB review.

C. The research will be classified and reviewed in accordance with HRPP policy #2.6 for exempt research; HRPP policy #2.3 for research which qualifies for expedited review; and HRPP policy #2.2 for research which requires review by the full IRB.

D. If the HBM will not have any subject identifiers attached to the sample, or if there is a one-way code that will not be released to the investigator, the research is classified as “not human” and an application would not have to be submitted for IRB review and approval.

ADMINISTRATIVE APPROVAL:
Ernest D. Prentice, PhD.  Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD  IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for creation and operation of a data registry (repository).

2.0 Policy
2.1 It is the policy of the Organization that internal registries, as defined by Section 3.1 below, utilized either wholly, or in part, for human subject research (as defined by 45 CFR 46.102(d)(f)) must be reviewed and approved by the UNMC IRB. All IRB approved registries must comply with the following requirements.

A. The purpose and goals of the registry are clearly justified.

B. The registry complies with all applicable requirements of HHS regulations at 45 CFR 46.

C. The minimum amount of PHI necessary to accomplish the purpose and goals of the registry is entered into the registry.

D. There is acceptable security to safeguard the confidentiality, integrity and availability of data in the registry.

E. There are procedures in place for release of Protected Health Information (PHI) from the registry that comply with Organization privacy policies.

F. As necessary, a Data Use Agreement (DUA), Data Transfer Agreement (DTA), or a Business Associate Agreement (BAA) is in place before release of data.

2.2 It is the policy of the Organization that External Data Registries (as defined in Section 3.3 below) must be reviewed by the ORA.

2.3 It is the policy of the Organization that Clinical Data Registries (as defined in Section 3.2 below) are exempt from UNMC IRB review. Therefore an application to the IRB is not required.

3.0 Definitions
3.1 Internal Data Registry: An Internal Data Registry is a repository of clinical or other data housed and administered within the Organization under the oversight of the UNMC IRB. The data may be used for: a) human subject research, b) assessment of patient outcomes; c) improve healthcare delivery; d) develop policies; or e) other non-research purposes.

Note: A Human Subject is defined at 45 CFR 46.102(f) as, “a living individual about whom an investigator (whether professional or student) conducting research obtains: 1) Data through intervention or interaction with the individual, or 2) Identifiable private information” (i.e., PHI).

Research is defined at 45 CFR 46.102(d) as, “any systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge.”
3.2 **Clinical Data Registry:** A Clinical Data Registry (internal or external) is an organized repository of clinical or other data which is used solely to assess patient outcomes, improve healthcare delivery, or develop policies and is not used for human subject research.

*Note:* As indicated in Section 2.3 above, a clinical data registry is exempt from UNMC IRB review and, therefore, cannot be used for research purposes.

3.3 **External Data Registry:** An External Data Registry is a repository of clinical or other data which is housed and administered at an external site normally under the oversight of an external IRB or other oversight body. The data may be used for: a) human subject research, b) assessment of patient outcomes; c) improve healthcare delivery; d) develop policies; or e) other non-research purposes.

*Note:* If an UNMC investigator accesses data from an external data registry for human subject research purposes, the Institution is engaged in research per OHRP guidance (Guidance on Engagement of Institutions in Human Subjects Research, dated 10/16/2008 [http://www.hhs.gov/ohrp/policy/engage08.html]). Therefore, submission of a Medical Records Application to the UNMC IRB is required.

*Note:* If the external registry is not under the oversight of an external IRB, the UNMC IRB may choose to require submission of information about the external registry.

3.4 **Protected Health Information (PHI):** PHI is individually identifiable health information, whether oral or recorded in any medium, that:

A. Is created or received by the Covered Entity (i.e., UNMC, Nebraska Medicine, CH&MC)

B. Relates to the past, present, or future physical or mental health or condition of an individual; the provision of health care to an individual; or the past, present, or future payment for the provision of health care to an individual.

3.5 **HIPAA Identifiers:** PHI that includes the following direct identifiers of the individual or of relatives, employers, or household members of the individual:

1) Names
2) All geographic subdivisions smaller than a state, including street address, city county, precinct, zip code, and their equivalent geocodes, except for the initial three digits of a zip code, if, according to the current publically available data from the Bureau of the Census:
   a) The geographic unit formed by combing all zip codes with the same three initial digits contains more than 20,000 people, and
   b) The initial three digits of a zip code for all such geographic units containing 20,000 or fewer people are changed to 000.
3) All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death; and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older;
4) Telephone numbers
5) Fax numbers
6) Electronic mail addresses
7) Social security numbers
8) Medical record numbers
9) Health plan beneficiary numbers
10) Account numbers  
11) Certificate/license numbers  
12) Vehicle identifiers and serious numbers, including license plate numbers  
13) Device identifiers and serial numbers  
14) Web Universal Resource Locators (URLs)  
15) Internet Protocol (IP) address numbers  
16) Biometric identifiers, including finger and voice prints  
17) Full face photographic images and any comparable images  
18) Any other unique identifying number, characteristic, or code  
19) The Organization does not have actual knowledge that the information could be used alone or in combination with other information to identify an individual who is the subject of the information.  

Note: Per 45 CFR 164.514(b)(2)(ii), this is not a “19th” individual identifier; rather it is in addition to removing the 18 individual identifiers indicated above.

3.6 Limited Data Set (LDS):  
A. PHI that includes only the following individual identifiers:  
   1) Dates such as admission, discharge, treatment dates, date of birth, date of death.  
   2) Town, City, State, 5 digit or more Zip Code  
   3) Age in years, months, days, or hours  

B. A covered entity may use or disclose a LDS for the purposes of research under HRPP policy #3.4. Workforce members can release a LDS for public health and healthcare operations in accordance with other Organizational policies.

4.0 Procedures  
4.1 Healthcare professionals who develop or maintain an Internal Data Registry as defined in Section 3.2 must submit a Data Registry Application to the UNMC IRB.  

Note: If the registry also includes collection of excess or additional human biological material (HBM) the Human Biological Material Banking Application must be completed instead (as specified in HRPP policy #7.1).

4.2 Investigators who access data from any data registry (e.g., internal or external) for the purpose of conducting human subject research as defined in Section 3.1 above must submit a Medical Records Research Application to the UNMC IRB.

4.3 Data Registry Applications and Medical Record Research Applications will be classified and reviewed in accordance with HRPP policy #2.6 for exempt research; HRPP policy #2.3 for expedited review, and HRPP policy #2.2 for full IRB review.

4.4 Clinical data (that is, data collected solely for clinical purposes) by representatives of the Organization which is submitted to an external data registry does not constitute engagement in human subject research by the Organization, and is, therefore, not subject to UNMC IRB approval.

A. Healthcare professionals who submit clinical data to external data registries must submit the External Data Registry Form or the Data Registry Application to the ORA. The information will be entered into the IRB database for tracking purposes.
B. If the clinical data contains PHI, an ICF must be submitted unless the external IRB has waived informed consent and the waiver is determined by the ORA to be acceptable.

C. In consideration of such factors as sensitivity of the data collected, the subject population, whether the registry is under the oversight of an external IRB or government entity, and Organizational requirements, the ORA, in consultation with the IRB Executive Chair, may require submission of additional information regarding administration of the registry, data security, and processes for release of data.

4.5 The appropriate agreements (e.g., Data Use Agreement, Data Transfer Agreement) must be fully executed prior to final release of the Data Registry or Medical Records Research.

**ADMINISTRATIVE APPROVAL:**
Ernest D. Prentice, PhD  Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD  IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements and procedures for approval of a single subject protocol deviation.

2.0 Policy
2.1 It is the policy of the Organization that investigators must request IRB approval prior to the initiation of a single subject protocol deviation.

2.2 Deviations that are minor are eligible for expedited review under the provisions of HHS regulations at 45 CFR 46.110(b)(2) and FDA regulations at 21 CFR 56.110(b)(2), as applicable.

2.3 Deviations that are more than minor do not qualify for expedited review and therefore must be reviewed by the full IRB.

2.4 Deviations must be approved by the IRB in advance of implementation, except under the provisions of 45 CFR 46.103(b)(4); 21 CFR 56.108(a)(4):

A. When it is necessary to eliminate apparent immediate hazards to the human subject.

B. There is not sufficient time to obtain IRB approval.

2.5 IRB approval of single subject deviations only applies to the subject for which the request was made. If it is anticipated that the same deviation will be necessary in the future for other subjects a standard request for change should be submitted.

2.6 Investigators may request approval of the same deviation for a second subject without having obtained approval of a request for change if there is sufficient justification.

2.7 Protocol deviations which occur for reasons of subject convenience or unforeseen circumstances (e.g. weather or transportation problems which delay a scheduled clinic visit) need not be reported to the IRB unless the deviation represents an unanticipated problem involving risk to the subject or others as described in HRPP policy #8.4.

3.0 Definitions
3.1 Single subject protocol deviation: A change in an IRB-approved protocol which is permitted for an individual subject when it is in the best interest of that subject and/or is necessary for research purposes (e.g., data completion). Protocol deviations are classified as either “minor” or “more than minor”.

A. Minor deviation: A deviation that presents no more than minimal risk to the subject and is often in the best interest of the subject.

Example: Upon review of the medical record of a patient referred to Nebraska Medicine, the physician determined that participation in IRB protocol #600-09 would be in the best interest of the patient. However, the patient’s blood cell counts deviated slightly from the protocol-specified values. The PI requested approval of the deviation prior to obtaining consent. (Minor deviation)
Example: The subject signed an ICF to participate in an IRB-approved sponsored clinical trial which involved screening. During the course of screening, the PI noted that the subject’s blood sugar values deviated slightly from the protocol-specified values. However, the PI determined that participation in the study would be in the best interest of the subject. The sponsor approved the deviation. (Minor deviation)

Example: As part of screening the subject underwent an ultrasound for research purposes. The results came back inconclusive. The PI requested that the ultrasound be repeated. The sponsor approved the deviation. (Minor deviation)

Example: A patient lives a long distance away from Nebraska Medicine. The PI wants to use an unapproved telephone consent process in order to have the patient’s private physician perform an EKG for research-related screening (i.e., determination of eligibility). In this example, the use of the patient’s private physician to perform the EKG and use of telephone consent are both deviations. (Minor deviation)

B. More than minor deviation: A deviation that presents more than minimal risk to the subject.

Example: An IRB-approved protocol included two (2) routine follow-up CT scans performed at 6 month intervals, and one (1) scan performed for research purposes only at 18 months. A technical failure occurred and the PI requested the CT scan at 18 months be repeated. In this example the subject is exposed to increased radiation related risk associated with the CT scan. (More than minor deviation)

4.0 Procedures

4.1 A single subject protocol deviation request form must be submitted to the ORA and be approved by either the IRB Executive Chair/designee or the full IRB prior to the initiation of the deviation.

4.2 The PI/authorized study personnel should request approval for the single subject protocol deviation from the study sponsor (if appropriate) in advance of submission to the ORA.

4.3 The IRB Executive Chair/designee will obtain any additional information required for the review.

4.4 Single subject protocol deviation requests that are more than minor cannot be approved by the IRB Executive Chair/designee and will be referred to the full IRB by the designated IRB Administrator for review and approval.

4.5 Single subject protocol deviation requests that are minor will be reviewed and approved by the IRB Executive chair/designee under the provisions of 45 CFR 46.110(b)(2) and 21 CFR 56.110(b)(2) as applicable.

4.6 Under compelling circumstances when there is not sufficient time to obtain IRB approval of the single subject protocol deviation, the PI could elect to initiate the change under the provisions of 45 CFR 46.103(b)(4) and 21 CFR 56.108(a)(4) per section 2.4 of this policy.
4.7 If the PI implements a single subject protocol deviation under Section 2.4 above, the subject must be verbally informed as of the nature of the deviation and any associated risks. This disclosure must be documented in the medical/research record.

4.8 Implementation of the deviation exercised under Section 2.4 above must be reported to the ORA within five (5) working days and will be submitted to the full IRB for their notification. All IRB members are expected to review the report and raise any questions or concerns.

4.9 All minor single subject protocol deviation requests approved by IRB Executive Chair/designee will be submitted to the IRB for their notification. All IRB members are expected to review the requests and raise any questions or concerns.

4.10 Single subject protocol deviations approved by the IRB via Expedited review or full IRB review in advance of implementation and deviations implemented in accordance with Section 2.4 above are not considered incidents of noncompliance.

4.11 If a single subject protocol deviation is initiated without IRB approval the incident will be classified as noncompliance and addressed in accordance with HRPP policy #8.5.

ADMINISTRATIVE APPROVAL:
Ernest D. Prentice, PhD.  Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD  IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe: 1) the procedure to ensure prompt reporting of Adverse Events (AEs) and Adverse Device Effects (ADEs) to the IRB, and 2) the IRB’s process for review.

2.0 Policy
It is the policy of the Organization to comply with: a) HHS regulations at 45 CFR 46.103(b)(5)(i), b) any additional requirements of Common Rule agencies (as applicable), and c) FDA regulations at 21 CFR 56.108(b)(1), 21 CFR 312.32(a), and 21 CFR 812.3(s) (as applicable).

3.0 Definitions
3.1 Adverse Event (AE): An AE in the broad context of human subject research is any untoward or unfavorable occurrence in a human subject (e.g., physical, psychological, social, legal, or economic harm) temporally associated with the subject’s participation in the research (whether or not related to participation in the research). This means that the AE may be expected or unexpected, and related or unrelated to the subject’s participation in the research. Most AEs involve physical harm. Note: This policy does not make a differentiation between medical and non-medical AEs. However, for clarity, FDA regulations at 21 CFR 312.32(a) define an AE as any untoward medical occurrence in a patient or clinical investigation subject administrated a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. An AE can, therefore, be any unfavorable and unintended sign, symptom, or disease temporally associated with use of the product, whether or not it is considered related to the product.

3.2 Unanticipated Adverse Device Effect (UADE): Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects. Note: The FDA device 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 312.32(a).

3.3 Unexpected AE/Unexpected UADE: An AE/UADE that is unexpected is one in which the specificity, severity, or frequency of the AE/UADE is not consistent with any of the following:
A. IRB application and detailed protocol
B. Risk information in the ICF
C. Current investigator’s brochure
D. Investigational plan or application
E. The reasonably expected natural history and progression of the underlying disease or condition.
Note: For clarity, FDA regulations at 21 CFR 312.32(a) defines “Unexpected Adverse Drug Experience” as any adverse drug experience, the specificity of severity of which is not consistent with the current investigator brochure; or, if an investigator brochure is not required or available, the specificity of severity of which is not consistent with the risk information described in the general investigational plan or elsewhere in the current
application. “Unexpected”, as used in this definition, refers to an adverse experience that has not been previously observed (e.g., included in the investigator brochure) rather than from the perspective of such experience not being anticipated from the pharmacological properties of the pharmaceutical product.

Example: A subject on a drug study is hospitalized and diagnosed with renal failure. There are no previous descriptions of renal failure occurring in pre-clinical animal models, or in patients treated with the drug to date.

3.4 Related AE/Related UADE: An AE/UADE that is related to (associated with) the research intervention or procedure is one for which there is clear causality or at least a reasonable possibility (e.g., strong temporal relationship) that the AE/UADE may have been caused by the research intervention or procedure.

Example: The subject that experienced renal failure in the example above recovered after discontinuation of the drug, and subsequently developed the same AE when re-challenged.

3.5 Possibly Related AE/Possibly Related UADE: An AE/UADE that is possibly related (associated with) is one that may have been caused by the research intervention or procedure; however there is insufficient information to determine the likelihood of this possibility.

Example: Upon further review, the subject that experienced renal failure in the example above was found to have also undergone treatment with other potentially nephrotoxic drugs. The rapid onset of renal failure following administration of the investigational drug suggests, but now does not prove, causality.

3.6 Unrelated AE/Unrelated UADE: An AE/UADE that is unrelated to the drug, device, or intervention is one where there is no information or reason to attribute the AE/UADE to the research intervention or procedure.

Example: The subject that experienced renal failure in the example above had a prior history of renal toxicity with aminoglycoside antibiotics, which he was receiving when he received the investigational drug. Subsequent challenge with the investigational drug was not associated with any nephrotoxicity.

3.7 Serious AE/Serious UADE: An AE/UADE that is serious is one which results in any of the following outcomes:

A. Death
B. A serious threat to life, health, safety or welfare of subjects
C. Inpatient hospitalization or prolongation of existing hospitalization
D. Required intervention to prevent permanent impairment or damage
E. Persistent or significant disability or incapacity
F. Congenital anomaly or birth defect
G. Other serious important medical events
H. Any medical event in an investigational drug study that requires treatment to prevent one of the outcomes listed above
I. The rights, safety, or welfare of subjects is seriously jeopardized

Example: The subject that experienced renal failure in the example above was admitted to the hospital and required dialysis until recovery of an acceptable level of renal function.
Example: A subject treated with an investigational drug developed neutropenia much more severe than expected based on the investigator’s brochure. The patient required treatment to increase the white blood count in order to prevent a potentially serious or fatal infectious complication.

3.8 **Non-Serious AE/Non-Serious UADE:** An AE/UADE that is *not serious* is one that does not meet the criteria for serious events.

3.9 **Internal AE/Internal UADE:** An AE/UADE experienced by a subject in a study conducted at the Organization or at an external site under the jurisdiction of the UNMC IRB.

3.10 **External AE/External UADE:** An AE/UADE experienced by a subject in a study conducted at an external site (a site not under the jurisdiction of the UNMC IRB).

3.11 **AEs/UADEs that are Unanticipated Problems (UPs):** An AE or UADE may also require classification as an unanticipated problem involving risk to the subject or others (UP) in compliance with reporting requirements under HHS and FDA regulations. The following are events that qualify as UPs (refer to **HRPP policy #8.4**):

   A. A single occurrence of a serious, unexpected event that is uncommon and strongly associated with the drug or device intervention.

   B. A single occurrence or more often a small number of occurrences, of a serious, unexpected event that is not commonly associated with the drug or device intervention but uncommon in the subject population.

   C. Multiple occurrences of an event that, based on an aggregate analysis, is determined to be a UP. There should be a determination that a series of events represents a signal that the events were not just isolated occurrences and involve risk to human subjects.

   D. An event that is described or addressed in the Investigators Brochure, protocol, investigational plan, or ICF, but occurs at a specificity or severity that is inconsistent with prior observations.

   E. A serious event that is described or addressed in the Investigator’s Brochure, protocol, investigational plan, or ICF, but for which the rate of occurrence in the study represents a clinically significant increase in the expected rate of occurrence (ordinarily, reporting would only be triggered if there were a credible baseline rate for comparison).

   F. Any other event or safety finding (e.g., based on animal or epidemiological data) that would cause the sponsor to modify the Investigator’s Brochure, protocol, investigational plan or ICF, or would prompt other action by the IRB to ensure protection of human subjects.

4.0 **Procedures for Reporting AEs/UADEs**

4.1 **Internal AEs/UADEs**

   A. Internal AEs/UADEs must be reported to the IRB if the PI determines that all of the following conditions are met:

      1) The AE/UADE is *unexpected*. 
2) The AE/UADE is related to, or possibly related to, the research intervention or procedures.

B. All internal AEs/UADEs that meet the conditions listed above must be reported promptly to the IRB (in no case later than two (2) business days following PI notification that the event occurred). In addition, if the internal AE/UADE involves a fatal event and it meets the conditions listed above, the IRB must also be notified by either telephone or email within 24 hours.

C. Internal AEs that meet the criteria listed above must be reported for 30 days after the subject has completed study interventions.

D. Internal UADEs must be reported while the subject is on study and for as long as the device is classified as investigational.

E. Internal AEs/UADEs are reported to the IRB on-line through the electronically through RSS (https://net.unmc.edu/rss).

Note: The PI must report the event to the IRB and the study sponsor.

4.2 External AEs
A. External AEs which occur at other institutions must be promptly reported to the UNMC IRB, in no case later than five (5) business days following PI notification (in a safety or other report) that the event occurred ONLY if the sponsor or PI determines that all of the following conditions are met:
   1) The external AE is unexpected
   2) The external AE is related or possibly related to the research intervention or procedure.
   3) The external AE is serious.
   4) The external AE requires a change to the protocol and informed consent form and reconsent of subjects is required.

B. The PI is responsible for keeping up-to-date on all information which impacts risk(s) or subject safety and submitting to the IRB changes in the protocol and the ICF as necessary.

C. The IRB will not accept, acknowledge or review external safety reports if there are no changes required in the protocol, IRB application and/or ICF.

D. The external site’s IRB is responsible for dealing with events which qualify as UPs and reporting those events to OHRP, FDA, and sponsors as required.

4.3 External UADEs
A. External UADEs which occur at other institutions must be reported to the UNMC IRB (in no case no later than five (5) business days following PI notification from the sponsor that the event occurred) in accordance the requirements of 21 CFR 812.150(b)(1).

B. The PI should submit the report received from the sponsor along with any required Request for Change.
C. Once the status of a study is changed to “completed”, the IRB will no longer accept external UADE reports except under circumstances where the report involves important new risk information.

5.0 ORA Procedures for Pre-Review of Internal AEs and UADEs

5.1 The IRB administrator will conduct a pre-review of the report, identify any missing or incomplete information, and obtain a revised report and/or supporting documents, as necessary.

5.2 Once the report is accepted, it is forwarded to an IRB Executive Chair/designee for review.

5.3 The IRB Chair/designee corresponds with the IRB Administrator to obtain additional information as necessary from the PI.

5.4 The IRB Executive Chair/designee will take all actions necessary to protect human subjects including, if warranted, immediate halting of the study.

5.5 Upon completion of the IRB Executive Chair/designee review, further IRB review will occur as follows:
   A. Full IRB review of internal AEs and UADEs that meet the conditions specified in Section 4.1.
   B. Full IRB review of all external UADEs.

6.0 IRB Review of Internal AEs and UADEs

6.1 The full IRB will review the reports in accordance with HRPP policy #2.2.

6.2 To approve the AE report, the IRB must ensure the following criteria are met:
   A. The risk/benefit relationship of the research remains acceptable.
   B. No additional changes in protocol are necessary to further minimize risk.
   C. No additional monitoring of data is necessary to ensure the safety of subjects.
   D. The consent document(s) as written/revised are acceptable.
   E. Currently enrolled subjects will be provided new information related to the AE per requirements at 45 CFR 46.116(b)(5) and/or 21 CFR 50.25(b)(5).
   F. Currently enrolled subjects will be re-consented as necessary.
   G. Currently enrolled subjects may continue on study.
   H. Further subject accrual is permitted.
   I. Additional information must be provided to past participants
   J. The current continuing review schedule is appropriate.

6.3 The IRB will determine if the AE/UADE is a UP and the action plan is appropriate in accordance with HRPP policy #8.4.

Note: Any AE/UADE which meets all of the criteria specified below is considered a UP:
1) The event is unexpected in terms of specificity, severity, or frequency, considering:
   a) the nature of the research,
   b) the characteristics of the subject population, and
   c) the information contained in the protocol, protocol-related documents, and the ICF.

2) The event is related, or possibly related to, participation in the research or procedures involved in the research. This means there is a reasonable possibility based
upon available information that the event may have been caused by procedures involved in the research or resulted from participation in the research by the subject(s).

3) The subject or others suffered harm, or were placed at greater risk of harm (including physical or psychological, economic, social, or legal) than was previously known or recognized when the IRB approved the research either initially, at continuing review, or at the time of approval of a Request for Change.

AEs/UADEs which are classified as UPs likely warrant substantive changes in the research protocol, informed consent process/document, or investigator’s brochure, or other corrective action in order to protect the safety, welfare or rights of subjects.

However, it should be noted that the vast majority of AEs/UADEs are not unanticipated problems involving risk to the subject or others (UPs) and are, therefore, not reportable to the IRB.

7.0 Reporting AEs/UADEs that are UPs to Institutional Officials, OHRP, FDA, and Department or Agency Heads

All required reports will be submitted in accordance with HRPP policy #8.8.

ADMINISTRATIVE APPROVAL:
Ernest D. Prentice, PhD. Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the: 1) definition and classification of complaints, 2) procedures for reporting complaints to the IRB, 3) process for review of complaints, and 4) possible actions in response to a complaint.

2.0 Policy
2.1 It is policy of the Organization that any complaints involving the human research protection program must be promptly reported to the IRB and appropriate Organizational officials.

2.2 All complaints will be promptly investigated in order to ensure ongoing adequate protection of the rights and welfare of research participants.

2.3 Findings of serious or continuing noncompliance and suspensions or terminations of IRB approval as a result of a complaint will be promptly reported to OHRP, FDA and sponsors or funding agency heads in accordance with 45 CFR 46.103(b)(5); 21CFR56.108(b)(2) and HRPP policy #8.8, as required

3.0 Definitions
3.1 Complaint: A complaint is defined as an accusation, an expression of concern, or a grievance which is directly related to research under the oversight of the UNMC IRB or related to the operation of the IRB. Complaints may be filed by subjects, LARs, study personnel, and others.

Note: Misunderstandings on the part of the subject which are quickly resolved through communication with study personnel are not considered reportable complaints.

3.2 Minor Complaint: A minor complaint is one which does not impact human subject protection.

Note: Examples of minor complaints includes incorrect billing and failure to provide compensation in a timely manner.

3.3 Significant Complaint: A significant complaint is one which impacts human subject protection and constitutes a violation of the subject’s rights and/or welfare.

Note: Examples of significant complaints includes conducting a flawed consent process or failure to follow the protocol thereby increasing risk.

4.0 PI Reporting Requirements
4.1 The PI must be promptly notified of all complaints received by his/her study personnel.

4.2 Minor complaints should normally be reported to the ORA within five (5) business days after receipt of the complaint.

4.3 Significant complaints should be reported to the ORA promptly and immediately in some cases.

4.4 Reports of complaints should include: 1) a description of the complaint, 2) the date the complaint was received, 3) other relevant information, and 4) any actions taken by the PI or other study personnel.
4.5 Complaints about the conduct of IRB members or IRB staff and the IRB operation which relate to human subject protection should be reported in compliance with HRPP policy #8.6.

5.0 Mechanism for Reporting Complaints to the ORA

5.1 A complaint received by the PI, or other study personnel, from subjects, LARs, or other individuals must be promptly reported in writing (email or letter).

5.2 A complaint can be reported the IRB Executive Chair, IO, UNMC Chief Compliance Officer, the Research Subject Advocate, or other Organizational officials. The complainant should choose the most appropriate recipient of the complaint.

5.3 A complaint can be reported via a letter, e-mail (to irbora@unmc.edu or ORA staff), or telephone call from any source (e.g., subjects, LARs, PIs, other study personnel and other individuals).

5.4 A complaint may be reported through the IRB website (http://www.unmc.edu/irb), utilizing the “Report a Problem or Complaint” tab. This reporting system provides access to “Solv-Anon”, a commercial site providing a mechanism for reporting totally anonymous complaints.

6.0 ORA Procedures for Reviewing Complaints

6.1 All complaints should be forwarded to the IRB Administrator/Compliance Coordinator.

6.2 Receipt of the complaint will be documented and maintained on file. Complaints received by phone will be summarized in writing.

6.3 The IRB Administrator/Compliance Coordinator will obtain additional information as necessary.

6.4 The IRB Administrator/Compliance Coordinator will initiate all necessary actions to resolve minor complaints.

6.5 The IO, IRB Executive Chair/designee and the UNMC Chief Compliance Officer will be given all pertinent information concerning any complaints judged to be significant. Other institutional officials will be notified as necessary.

6.6 The PI and other involved individuals will be promptly notified of the concerns expressed in the complaint, unless such notification would compromise handling of the complaint.

6.7 If a complaint is determined to be significant, the IRB Executive Chair/designee, IRB Administrator/Compliance Coordinator, the Chief Compliance Officer, and other representatives of the Organization will take all necessary actions to ensure that human subjects are fully protected. Depending upon the circumstances, these actions could include the following:

A. A meeting with the complainant and/or the investigator.

B. Immediate audit of the investigator’s research records.

C. Immediate halt of research in accordance with HRPP policy #8.7.
D. Convene a meeting of the UNMC IRB Compliance Subcommittee in order to investigate the complaint and/or decide on additional actions necessary to protect human subjects.

E. Convene an emergency meeting of the IRB.

F. Other actions as necessary to protect human subjects.

6.8 All actions will be documented in the record.

7.0 IRB Review of Complaints

7.1 The full IRB will be notified of all minor complaints and action(s) taken. The IRB may take further action as necessary.

7.2 The full IRB will review all significant complaints and any action(s) taken under Section 6.7 above.

A. The IRB may take further action as necessary under Section 9.0 below to protect human subjects.

B. The IRB will determine whether or not the complaint constitutes:

1) Serious or continuing noncompliance per HRPP policy #8.5.

2) An unanticipated problem involving risk to the subject or others (UP) per HRPP policy #8.4.

7.3 The PI will be notified of the IRB’s action in writing.

8.0 IRB Review Criteria

The IRB must ensure the approval criteria under 45 CFR 46.111, 21 CFR 56.111, and HRPP policy #2.5 as required to continue to be satisfied.

9.0 IRB Actions

The IRB will take one or more of the following actions when reviewing complaints:

9.1 No action or no further action
9.2 More information is required.
9.3 Modification of the research protocol
9.4 Modification of the consent document
9.5 Notification of current participants (required when such information may relate to participants’ willingness to continue to take part in the research)
9.6 Requirement that current participants re-consent to participation
9.7 Additional information must be provided to past participants
9.8 Modification of the continuing review schedule
9.9 Monitoring of the research
9.10 Monitoring of the consent process
9.11 A study hold
9.12 Suspension of the research
9.13 Termination of the research
9.14 Referral to other organizational entities (e.g., legal counsel, risk management)
9.15 The IRB may recommend to the IO that additional whistleblower protection is needed for the complainant.
ADMINISTRATIVE APPROVAL:
Ernest D. Prentice, PhD.  Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD  IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe: 1) the procedure to ensure prompt reporting to the IRB any event or outcome that may be an unanticipated problem involving risk to the subject or others (UP), and 2) the IRB’s process for determining when an event or outcome is, in fact, a UP reportable to OHRP and FDA (as applicable).

2.0 Policy
2.1 It is the policy of the Organization to comply with: a) HHS regulations at 45 CFR 46.103(b)(5)(i); b) any additional requirements of Common Rule agencies (as applicable); and c) FDA regulations at 21 CFR 56.108(b)(1), 21 CFR 312.32(a), and 21 CFR 812.3(s) (as applicable).

2.2 Any AE, UADE, noncompliance incident, unexpected incident, unexpected outcome, or complaint, regardless of the level of associated or potential risk, which appears to meet the criteria for classification as a UP will be submitted to the full IRB for review.

2.3 The full IRB is responsible for determining whether the event, incident, outcome, or complaint meets the criteria for classification as a UP under Section 3.1 below.

3.0 Definitions
3.1 Unanticipated Problems Involving Risk to Subjects or Others (UP):
A. Any event (incident, experience, or outcome) which meets all of the criteria specified below:
   1) The event is unexpected in terms of specificity, severity, or frequency, considering: 1) the nature of the research, 2) the characteristics of the subject population, and 3) the information contained in the protocol, protocol-related documents, and the ICF.

   2) The event is related, or possibly related to subjects’ participation in the research or procedures involved in the research. This means there is a reasonable possibility based upon available information that the event may have been caused by procedures involved in the research or resulted from participation in the research by the subject.

   3) The subject or others suffered harm, or were placed at greater risk of harm (including physical, psychological, economic, social, or legal) than was previously known or recognized when the IRB approved the research either initially, at continuing review, or at the time of approval of a Request for Change.

Note: A UP may only involve exposure of a subject or others to an unexpected risk or the risk may culminate in a subject or another individual actually experiencing a harm which is generally described as an adverse event (AE) in clinical research or an adverse outcome (AO) in behavioral or social science research.

Note: As indicated in Section 2.2 above, a UP may arise from an AE, UADE, noncompliance incident, unexpected incident, unexpected outcome, or a complaint. Classification as a UP, however, requires the criteria specified under Section 3.1.A to be met.
Note: An event which meets the three criteria specified above will generally warrant substantive changes in the research protocol or informed consent process/document or other corrective actions in order to protect the safety, welfare, or rights of subjects or others.

Note: UPs may occur in research other than clinical trials, for example social and behavioral research (e.g., stolen laptop or thumb drive containing identifiable information), and may involve risks other than physical harm (e.g., loss of confidentiality).

4.0 Procedures for reporting events that are potential UPs to the IRB

4.1 Reports of AEs/UADEs are submitted in accordance with HRPP policy #8.2 which provides definitions, reporting requirements, and the time frame for reporting AEs/UADEs.

4.2 Reports of complaints are submitted in accordance with HRPP policy #8.3 which provides definitions, reporting requirements, and the time frame for reporting complaints.

4.3 Reports of noncompliance are submitted in accordance with HRPP policy #8.5 which provides definitions, reporting requirements, and the time frame for reporting noncompliance.

4.4 IND safety reports, DSMB reports, or other outcome information on risk is submitted in accordance with HRPP policy #3.2 which specifies reporting requirements and the time frame for reporting.

4.5 Reports of other unanticipated events related to the research that either expose subjects or others to potential risk or result in harm, but do not fall under the reporting requirements above (Sections 4.1-4.4 above) are reported to the IRB via letter or email.

A. These reports must be submitted no later than two (2) business days following PI notification that the event occurred.

B. The report must include the following:

1) IRB number, title of the protocol, and PI name.

2) Detailed information about the event including date(s) of occurrence.

3) Any action, planned or already taken to ensure that the event is appropriately managed and reoccurrence is minimized.

4) An assessment of whether any subjects or others were placed at risk as a result of the event or suffered any harm and a plan to address the consequences.

5) Any other relevant information.

5.0 IRB Review

5.1 The IRB administrator will conduct a pre-review of the report, identify any missing or incomplete information, and obtain a revised report, as necessary.
5.2 The report will be submitted to full IRB for review as soon as possible in consideration of the nature and seriousness of the event.

5.3 The IRB will review reports under Section 4.1 - 4.5 above in accordance with the criteria specified in HRPP policies #2.2, 8.2, 8.3, and 8.5.

5.4 The IRB will determine whether or not the event is a UP in accordance with Section 3.1 of this policy.

5.5 The IRB may determine that an event has multiple classifications. For example, a protocol violation may be classified as both a UP and noncompliance. On the other hand, an AE/UADE may not be related to any protocol violations and may be classified only as a UP.

5.6 The IRB will ensure all necessary steps will be taken in order to protect the rights and welfare of human subjects and maintain compliance with applicable federal regulations and HRPP policies. Therefore, the IRB may require any of the following actions:

1) Revision of inclusion/exclusion criteria.
2) Provision of additional information about newly recognized risk(s) to currently enrolled subjects via the most expedient and appropriate method (refer to HRPP policy #5.1).
3) Revision of the ICF to address the newly recognized risk(s)
4) Additional or different safety monitoring
5) Change in operating procedure (e.g., drug dispensing)
6) More frequent continuing review by the IRB
7) Interim reporting to the IRB
8) Change in the risk classification of the protocol (i.e., minimal risk to greater than minimal risk)
9) Halt enrollment of new subjects by either the IRB Executive Chair or the full IRB
10) Suspension of research procedures by the IRB
11) Termination of research by the IRB
12) Provision of additional information about newly recognized risks to previously enrolled subjects

6.0 Reporting UPs to Institutional Officials, OHRP, FDA, and Department or Agency Heads
All required reports will be submitted in accordance with HRPP policy #8.8.

ADMINISTRATIVE APPROVAL:
Ernest D. Prentice, PhD.  Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD  IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the: 1) definitions and classifications of noncompliance involving the PI and other study personnel; 2) procedures for reporting allegations of noncompliance, 3) procedures for reporting documented incidents of noncompliance; 4) the process for review; 5) possible actions in response to noncompliance; and 6) procedures for reporting noncompliance to OHRP, FDA, and Organizational officials.

2.0 Policy
It is the policy of the Organization that:

2.1 Any allegations or reports of noncompliance with: a) HHS regulations at 45 CFR 46 (Subparts A, B, C, D), the Model Federal Policy (Common Rule) as adopted by other federal departments and agencies, b) FDA regulations at 21 CFR 50, 56; 21 CFR 312, 21 CFR 600, 21 CFR 812, c) HRPP policies, or d) the requirements or determinations of the IRB, must be promptly reported to the IRB and the IO.

2.2 The PI and other study personnel (e.g., secondary investigators, participating personnel, study coordinators, data managers) will be proactive in identifying noncompliance and minimizing repeat occurrences and for implementing any required corrective action plan.

2.3 All Organizational personnel including study personnel specified above in Section 2.2 and others (e.g., Organizational administrators or other support personnel) shall ensure prompt reporting to the IRB any noncompliance with applicable requirements in Section 2.1 above.

2.4 The PI is ultimately responsible for the proper conduct of research and for assuring that both incidents and allegations of noncompliance are promptly reported in accordance with this policy and for implementing any required corrective action plan.

2.5 All allegations or incidents of noncompliance will be promptly addressed by the ORA/IRB and appropriate action taken in order to ensure ongoing adequate protection of the rights and welfare of research subjects.

2.6 Findings of serious or continuing noncompliance and suspensions or terminations of IRB approval as a result of noncompliance will be promptly reported to OHRP, FDA and sponsors or funding agency heads in accordance with the requirements of 45 CFR 46.103(b)(5), the corresponding section of the Common Rule adopted by other federal departments or agencies, and 21 CFR 56.108(b)(2) as specified in HRPP policy #8.8.

3.0 Definitions
3.1 Noncompliance is defined as the lack of compliance by PI and other study personnel with the applicable requirements specified in Section 2.1 above.

Findings of noncompliance are classified as non-serious, serious, continuing, or combinations of these. It should be noted that noncompliance may also be classified as an unanticipated problem involving risk to the subject or others (UP) as defined in HRPP policy #8.4.
3.2 **Serious noncompliance** is defined as an incident that represents a violation of applicable federal regulations, HRPP policies, or the determinations of the IRB which include one or more of the following consequences: a) significantly increases the risk to subject(s); b) appreciably decreases the potential direct benefit to the subject(s); c) compromises the scientific integrity of the research; or d) otherwise compromises the rights and welfare of the research subjects.

3.3 **Non-serious noncompliance** is defined as an incident that does not satisfy the definition of serious noncompliance in Section 3.2 of this policy.  
*Note: Protocol violations may occur which: a) are not a violation of federal regulations or HRPP policies, and b) do not impact protection of human subjects. These violations do not have to be reported unless they increase the risk to which the subject was exposed.*

3.4 **Continuing noncompliance** is defined as repeated incidents of the same or substantially similar noncompliance that clearly indicates an inability or unwillingness to comply with federal regulations, HRPP policies, or requirements of the IRB despite appropriate retraining and/or specific corrective action as directed by the IRB.  
*Note: Continuing noncompliance may also be a pattern of noncompliance involving different kinds of more than minor violations that indicates an inability or unwillingness to comply with federal regulations, HRPP policies, or requirements of the IRB.*

IRB classification of noncompliance as “continuing” will depend upon the circumstances.

3.5 **Allegation of noncompliance** is defined as an accusation or unproved assertion of noncompliance.

3.6 **Incident of noncompliance** is defined as a proven noncompliance.

4.0 **Procedures for reporting an allegation of noncompliance**

4.1 Allegations of noncompliance can be submitted by letter, email, telephone call, or web report to:
   A. ORA
   B. IRB Executive Chair or any IRB member
   C. IO
   D. UNMC Chief Compliance Officer
   E. Research Subject Advocate
   F. Any other appropriate Organizational official
   G. OHRP or FDA

4.2 Allegations of noncompliance can be submitted by accessing the UNMC IRB website ([http://www.unmc.edu/irb](http://www.unmc.edu/irb)), utilizing the “Report a Problem or Complaint” tab.  
*Note: This reporting system provides access to “Solv-Anon”, a commercial site providing totally anonymous comments to the IRB.*

5.0 **ORA procedures for reviewing allegations of noncompliance**

5.1 All allegations of noncompliance are administratively processed by the ORA.

5.2 ORA receipt of the allegation of noncompliance will be documented and maintained on file by the IRB Administrator/Compliance Coordinator.
5.3 If an allegation describes an incident which, if substantiated, is non-serious noncompliance, the IRB Administrator/Compliance Coordinator will take action as necessary to determine if the allegation is substantiated and take action as necessary. The incident will forwarded to the full IRB as a notification item on the next IRB agenda.

5.4 If an allegation appears to be serious or continuing, the IRB Administrator/Compliance Coordinator will give the IO, IRB Executive Chair/designee and the UNMC Chief Compliance Officer all pertinent information concerning the allegation.

5.5 The IRB Administrator/Compliance Coordinator will notify the PI (and other involved individuals), by email or other written communication, that there has been an allegation. The details of the allegation will be provided. In some circumstances, pertinent records will be immediately sequestered. The PI, as the individual ultimately responsible for the research, will be invited to provide any relevant information and/or records that should be considered.

5.6 The PI (and other involved individuals) will be afforded due process.

5.7 Whistleblower protection will be provided in accordance with UNMC Policy 8003.

5.8 The IRB Executive Chair, the UNMC Chief Compliance Officer, and the IRB Administrator/Compliance Coordinator will promptly review all available information including pertinent records and make one or more of the determinations listed below in consideration of the need to protect human subjects. The PI, other individual(s) and the complainant, will be notified accordingly.
   A. The allegation of noncompliance has no basis in fact and does not merit further investigation.
   B. The allegation is, in fact, noncompliance but does not require further investigation.
   C. The allegation of noncompliance merits further investigation.
   D. The research protocol in which the noncompliance occurred will be immediately halted in accordance with HRPP policy #8.7.
      Note: The IRB Executive Chair is authorized to immediately halt research at any time before or during an investigation in order to protect human subjects.
   E. An emergency meeting of the IRB will be convened as soon as possible.
   F. Other action(s) as necessary to protect human subjects.

5.9 A record of the actions taken under Section 5.8 of this policy will be maintained on file and the IRB will be notified.

6.0 Procedures for IRB Compliance Subcommittee Investigations

6.1 If the allegation of noncompliance merits further investigation, it will be referred to an IRB Compliance Subcommittee by the IRB Executive Chair. The Committee will be formally charged with conducting an investigation of the allegation:
   A. The IRB Compliance Subcommittee will be comprised of:
      1) IRB Executive Chair/designee
      2) UNMC Chief Compliance Officer
3) IRB Administrator/Compliance Coordinator
4) Other IRB members as necessary
5) Internal consultants as necessary

B. A written record of the on-going investigation conducted by the IRB Compliance Subcommittee will be maintained on file by the IRB Administrator/Compliance Coordinator.

C. Minutes of the IRB Compliance Subcommittee meetings will be recorded by the IRB Administrator/Compliance Coordinator and maintained on file.

D. The IRB Compliance Subcommittee will take all necessary actions to protect human subjects.

E. The Research Integrity Officer (RIO) will notified if the noncompliance indicates possible research misconduct.

Note: If, at any time during the investigation, possible evidence of research misconduct is identified the RIO should be notified and the IRB/RIO investigations will be coordinated.

F. The IRB Compliance Subcommittee will make one or more of the determinations listed below:
   1) The allegation, in fact, substantiates noncompliance.
   2) The protocol in which the allegation of noncompliance occurred should be immediately halted in accordance with HRPP policy #8.7.
   3) An emergency meeting of the IRB will be convened as soon as possible.

G. The IRB Executive Chair/designee will keep the IO up-to-date on the status of the investigation.

H. The IO will brief other Organizational officials, as appropriate, on the status of the investigation.

6.2 Upon conclusion of an investigation of noncompliance the IRB Administrator/Compliance Coordinator will prepare a written report of the results of the investigation.

7.0 IRB Procedures for Reviewing Allegations of Noncompliance

7.1 If the IRB Compliance Subcommittee determines that the allegation is not substantiated:

A. The IRB Administrator/Compliance Coordinator will provide a copy of the results of the investigation to the PI and other involved study personnel.

B. The report will be provided to the IRB as a notification item.

C. The matter will be considered closed and no further action will be taken unless the IRB raises concerns and further investigation is warranted.

D. The IO will brief other Organizational officials as necessary.
E. The complainant will be notified that the allegation was not substantiated.

7.2 If the IRB Compliance Subcommittee determines that the allegation is substantiated:

A. The IRB Administrator/Compliance Coordinator will provide a copy of the results of the investigation to the PI and other involved study personnel.

B. The PI is directed to respond in writing to the report within thirty (30) days or sooner as directed by the Subcommittee. This response must include a corrective action plan as required.

C. After a response is received, all documents will be forwarded to the full IRB for review in accordance with this policy.

D. The IRB may request additional information or refer the matter for further investigation.

E. The full IRB is responsible for reviewing the determination of the IRB Compliance Subcommittee and deciding if additional actions are necessary to protect human subjects in accordance with Section 10.5 of this policy.

F. The complainant will be notified that the allegation was substantiated.

8.0 Procedures for Reporting a Verified Incident of Noncompliance to the ORA

Incidents of noncompliance that have a basis in fact must be reported to the ORA by submission of a Noncompliance Report via RSS (https://net.unmc.edu/rss). The PI is responsible for ensuring that the required reports are submitted within five (5) business days following discovery of the incident.

9.0 ORA Procedures for Reviewing Verified Incidents of Noncompliance

9.1 The IRB Administrator/Compliance Coordinator will review the Noncompliance Report and obtain any additional information or clarification as necessary.

9.2 The IRB Administrator/Compliance Coordinator, in consultation with the IRB Executive Chair/designee as necessary, will determine if the incident of noncompliance can be classified as non-serious noncompliance in accordance with Section 3.3 above or requires review by the IRB for other reasons.

A. The Noncompliance Reports are reviewed by expedited review in accordance with HRPP policy #2.3.

B. The Noncompliance Reports are forwarded to the full IRB as a notification item on the next IRB agenda. The IRB may question the noncompliance classification or require modification of the corrective action plan.

9.3 The IRB Executive Chair/designee and the IRB Administrator/Compliance Coordinator will promptly review Noncompliance Reports that potentially represent serious or continuing noncompliance.

A. The IRB Executive Chair/designee will immediately take any necessary action to protect the rights and welfare of currently enrolled subjects including imposing a study hold on the research in accordance with HRPP policy #8.7.
B. The IRB Executive Chair/designee may convene an emergency meeting of the IRB as necessary.

C. The IRB Executive Chair/designee will inform the IO of the noncompliance

D. The IRB Executive Chair/designee will consult the UNMC Chief Compliance Officer as necessary.

E. Noncompliance Reports which may represent serious or continuing noncompliance are forwarded to the full IRB for review at the next meeting.

10.0 IRB Review of Incidents of Noncompliance

10.1 Incidents of noncompliance referred to the full IRB will be reviewed in accordance with HRPP policies #2.2 and #2.5.

10.2 All documents which are relevant to the incident of noncompliance will be provided to the full IRB.

10.3 The IRB will determine whether the noncompliance is serious and/or continuing.

10.4 The IRB will determine whether the PI’s corrective action plan is acceptable.

10.5 The IRB will determine if any of the following actions are warranted:

A. The involved study personnel will be provided with additional education and training.

B. Modification of the protocol and/or ICF(s).

C. Human subjects currently enrolled in the study will be notified of noncompliance determined by the IRB to potentially affect their willingness to continue participation in the research.

D. Human subjects currently enrolled in the research will be required to reconsent to continue participation in the research.

E. Human subjects who have completed the research will be notified of noncompliance determined by the IRB to have an associated latent risk.

F. Increased monitoring of the research.

G. Increased frequency of continuing review.

H. The IRB Administrator/Compliance Coordinator will audit the study(s) related to the noncompliance.

I. The IRB Administrator/Compliance Coordinator will audit all of the PI’s active and/or completed studies.

J. Observations of a set number of consent processes will be required.

K. HRPP policies will be revised as necessary, in consideration of the noncompliance in order to minimize the possibility of future occurrences.
L. If the research does not satisfy the required approval criteria, the IRB will suspend the protocol in accordance with HRPP policy #8.7.

M. If the circumstances of the noncompliance are sufficiently serious, the IRB will terminate the research in accordance with HRPP policy #8.7.

N. The Organization’s general counsel will be informed of the noncompliance and the IRBs actions.

O. The noncompliance will be referred to Nebraska Medicine or CHMC Risk Management for further action as necessary.

P. The IRB may recommend to the IO one or more of the following actions:
   1) The involved study personnel be reprimanded by their supervisors and a note (if appropriate) placed in their personnel file.

   2) There be an immediate halt of all pending publications, presentations, or uses of the research data in question.

   3) Any associated research data or biological materials cannot be used for research purposes and must be destroyed.

   4) The involved study personnel’s privilege to conduct human subject research be revoked for a specified period.

   5) The incidence of noncompliance be referred to the scientific misconduct committee for investigation.

Q. The IO will consult with appropriate senior Organizational officials in deciding which, if any, of the IRB recommended actions should be implemented.

11.0 Appeal of Sanctions/Penalties

11.1 The involved study personnel have the right to appeal any actions imposed by the IRB (in accordance with HRPP policy #8.7) by submitting a written appeal within thirty (30) days.

11.2 The involved study personnel have the right to appeal any actions imposed by the IO by submitting a written appeal with thirty (30) days. The IO will convene an Appeals Panel to consider the appeal and make recommendations to the IO.

12.0 Reporting Noncompliance to Organizational Officials, OHRP, FDA and Department or Agency Heads
All required reports will be submitted in accordance with HRPP policy #8.8.

ADMINISTRATIVE APPROVAL:
Ernest D. Prentice, PhD.  Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD  IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the: 1) definitions and classifications of noncompliance involving members of the IRB, ORA staff, and others involved in the HRPP; 2) procedures for reporting noncompliance, 3) possible actions in response to noncompliance; and 4) procedures for reporting noncompliance to OHRP, FDA, and Organizational officials.

2.0 Policy
It is the policy of the Organization that:

2.1 Any noncompliance by members of the IRB, ORA staff, or others involved in the HRPP with: a) HHS regulations at 45 CFR 46 (Subparts A, B, C, D), the Model Federal Policy (Common Rule) as adopted by other federal departments and agencies, b) FDA regulations at 21 CFR 50, 56; 21 CFR 312, 21 CFR 600, 21 CFR 812, or c) HRPP policies must be promptly reported to appropriate Organizational officials.

2.2 The ORA administration and staff, IRB members and others involved in the HRPP will be proactive in identifying noncompliance, minimizing repeat occurrences, and implementing any corrective action plan required by the Organization.

2.3 All allegations or incidents of noncompliance will be promptly addressed by the UNMC Chief Compliance Officer and appropriate action taken in order to ensure ongoing adequate protection of the rights and welfare of research participants.

2.4 Findings of serious or continuing noncompliance will be promptly reported to OHRP, FDA and sponsors or funding agency heads in accordance with the requirements of 45 CFR 46.103(b)(5), the corresponding section of the Common Rule adopted by other federal departments or agencies, and 21 CFR 56.108(b)(2) as required in accordance with HRPP policy #8.8.

3.0 Definitions

3.1 **Noncompliance** is defined as the lack of compliance by IRB members, ORA staff, or others involved in the HRPP with the applicable requirements specified in Section 2.1 above.

*Note:* Noncompliance that is attributable to study personnel is covered in HRPP policy #8.5.

Findings of noncompliance are classified as non-serious, serious, continuing, or combinations of these. It should be noted that noncompliance may also constitute an unanticipated problem involving risk to the subject or others (UP) as defined in HRPP policy # 8.4.

3.2 **Serious noncompliance** is defined as an incident that represents a violation of applicable federal regulations, HRPP policies, or the determinations of the IRB which include one or more of the following consequences: a) significantly increases the risk to subject(s); b) appreciably decreases the potential direct benefit to the subject(s); or c) otherwise compromises the rights and welfare of the research subjects.

*Note:* An example of serious noncompliance would include failure of the IRB to ensure that all of the criteria for IRB approval have been satisfied and because of the
noncompliance subjects were placed at risk and their rights and welfare were compromised. A second example would be failure of the IRB to perform continuing review of a greater than minimal risk study and the study continued without IRB approval.

3.3 **Non-serious noncompliance** is defined as an incident that does not satisfy the definition of serious noncompliance in section 3.2 of this policy.

3.4 **Continuing noncompliance** is defined as repeated incidents of the same or substantially similar noncompliance that indicates an inability or unwillingness to comply with federal regulations, HRPP policies, or requirements of the IRB despite corrective action as directed by the IO or other appropriate Organizational officials. *Note: Continuing noncompliance may also be a pattern of noncompliance involving different kinds of more than minor violations that indicates an inability or unwillingness to comply with federal regulations or HRPP policies.*

Classification of noncompliance as “continuing” will depend upon the circumstances.

3.5 **Allegation of noncompliance** is defined as an accusation or unproved assertion of noncompliance.

3.6 **Incident of noncompliance** is defined as a proven noncompliance.

4.0 **Procedures for Reporting an Allegation or Incident of Noncompliance**

4.1 Allegations of noncompliance can be submitted by letter, email or telephone call to:

   A. UNMC Chief Compliance Officer
   B. IO
   C. Research Subject Advocate
   D. Any other appropriate Organizational official
   E. OHRP or FDA

4.2 Allegations of noncompliance can be submitted by accessing the UNMC IRB website (http://www.unmc.edu/irb), utilizing the “Report a Problem or Complaint” tab. *Note: This reporting system provides access to “Solv-Anon”, a commercial site providing totally anonymous comments.*

5.0 **Procedures for Reviewing Noncompliance**

5.1 Allegations or incidents of noncompliance are reviewed by the UNMC Chief Compliance Officer.

5.2 Any involved individual(s) will be afforded due process.

5.3 Whistleblower protection will be provided in accordance with **UNMC Policy 8003**.

5.4 The UNMC Chief Compliance Officer will determine whether: a) the allegation of noncompliance clearly lacks merit; b) the allegation merits further investigation; c) an incident of noncompliance merits further investigation; and d) an ad hoc subcommittee should be convened to carry out the investigation. The IO and other Organizational officials will be consulted as necessary.

5.5 The UNMC Chief Compliance Officer will promptly initiate all necessary action(s) to: 1) ensure that human subjects are fully protected, and 2) the interests of the Organization
are appropriately considered. Depending upon the circumstances, these actions could include one or more of the following:

A. Request the IRB Executive Chair convene an emergency meeting of the IRB.

B. Recommend the IO and/or the IRB Executive Chair immediately halt IRB approval of some or all research activities in accordance with HRPP policy #8.7.

C. Recommend the IO promptly notify OHRP and/or FDA of the allegation or incident of noncompliance.

D. Refer the allegation or incident of noncompliance for investigation by a specially appointed ad hoc Subcommittee.

E. Other action(s) as necessary.

5.6 A record of the actions taken under Section 5.5 of this policy by the Chief Compliance Officer will be maintained on file.

5.7 Upon conclusion of an investigation of noncompliance the UNMC Chief Compliance Officer will prepare a written report of the results of the investigation and submit it to the IO and other Organizational officials as appropriate.

5.8 The UNMC Chief Compliance Officer may recommend to the IO one or more of the following actions which are appropriate for the circumstances of noncompliance:

A. The Organization’s general counsel will be informed of the noncompliance and the IRBs actions.

B. The noncompliance will be referred to Nebraska Medicine or CHMC Risk Management for further action as necessary.

C. The involved personnel should be reprimanded by their supervisors and a note (if appropriate) placed in their personnel file.

6.0 Reporting Noncompliance to Organizational Officials, OHRP, FDA and Department or Agency Heads

All required reports will be submitted in accordance with HRPP policy #8.7.

ADMINISTRATIVE APPROVAL:
Ernest D. Prentice, PhD. Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the IRB’s authority to: a) disapprove research; b) accept a study hold by the PI or sponsor; c) impose a study hold by the IRB Executive Chair; d) suspend IRB approval of research; e) terminate IRB approval of research, and f) implement an Organizational directed termination of IRB approval of research.

2.0 Policy
It is the policy of the Organization that the IRB has the authority to:

2.1 Disapprove research in accordance with 45 CFR 46.109(a)(d); 21 CFR 56.109(a)(e).

2.2 Accept a study hold imposed by the PI, sponsor, DSMB, or FDA.

2.3 Suspend or terminate IRB approval of research that: 1) is not being conducted in accordance with IRB requirements, or 2) has been associated with unexpected serious harm to subjects, in accordance with 45 CFR 46.113; 21 CFR 56.113.

2.4 Implement institutional directed suspension or termination of IRB approval of research in accordance with 45 CFR 46.112; 21 CFR 56.112.

3.0 Definitions

3.1 **IRB Disapproval of Research:** The application has very serious design flaws and/or subjects will be placed at undue risk. The PI has the right to appeal to the IRB.

3.2 **Study Hold:** Study hold imposed by the PI, sponsor, DSMB, or FDA to temporarily halt:
   A. New subject accrual. Currently enrolled subjects are allowed to continue on study, **OR**
   B. New subject accrual and currently enrolled subjects are **not** permitted to continue on study.
   AND
   C. New subject accrual into a specific research arm and/or recruitment of a subset of subjects. Currently enrolled subjects are allowed to continue on study, **OR**
   D. New subject accrual into a specific research arm and/or recruitment of a subset of subjects. Currently enrolled subjects are **not** permitted to continue on study.
   **Note:** A study hold as described above in Section 3.2 which is not imposed by the IRB does not constitute a suspension or termination of IRB-approval of research under 45 CFR 46.113; 21 CFR 56.113.

3.3 **Study Hold Imposed by the IRB Executive Chair:** The IRB Executive Chair imposes a halt to subject accrual.
   **Note:** If human subjects are place at risk, the IRB Executive Chair is authorized to halt subject accrual.

3.4 **Complete Study Hold Imposed by the IRB Executive Chair/IO:** The IRB Executive Chair, in consultation with the IO, imposes a complete halt to research activities.
Note: If the risks to which subjects are exposed justifies a complete halt to research activities, the IRB Executive Chair, in consultation with the IO, is authorized to impose this halt. The IRB will be convened as soon as possible to review the situation and may decide to suspend the research.

3.5 **Suspension of IRB Approval:** A directive of the IRB at a convened meeting that all, or some, research activities in one or more protocols must be temporarily suspended because of subject safety or noncompliance concerns.

3.6 **Termination of IRB Approval:** A directive by the IRB at a convened meeting that one or more protocols must be terminated (all research activities must cease) because the research can no longer be conducted safely or the PI has not conducted the research in full compliance with the applicable federal regulations and HRPP policies.

3.7 **Organization Directed Termination of IRB Approval:** A directive by the Institutional Official (IO) that IRB approval of research be terminated.

Note: The terms “suspension” applies to a temporary interruption in research which is related to concerns regarding the safety, rights, or welfare of human research subjects, investigators, research staff, or others. They do not include interruptions in human research resulting solely from the expiration of the IRB approval period. The term “termination” does not imply a temporary interruption in research.

4.0 ** Procedures for IRB Disapproval of Research**

4.1 The IRB shall notify the PI and the IO in writing of the decision to disapprove the proposed research activity or of modifications required to secure IRB approval of the research activity. This written notification will contain a statement of the reasons for the IRBs decision.

4.2 The IRB shall give the PI an opportunity to appeal the IRBs decision in writing and also in person if so requested. The IRB is granted the final authority to act on any appeals and the decision of the Board cannot be overturned.

5.0 ** Procedures for PI/Sponsor/FDA Directed Study Holds**

5.1 The PI, sponsor, DSMB, or FDA may place a study hold by contacting the ORA by email or letter.

5.2 The ORA will acknowledge the study hold by email to the PI.

5.3 The PI will be responsible for notifying all study personnel that there is a study hold and subject accrual and/or research activities may be restricted.

5.4 The IRB will be notified at the next convened meeting that a study hold was placed on the protocol.

5.5 The IRB will take appropriate action(s) to protect the rights and welfare of currently enrolled subjects in accordance with Section 9.0 of this policy.

5.6 If the study hold involves permanently closing a particular study arm, or permanently changing inclusion or exclusion criteria, then the investigator must submit a Request for Change.
5.7 If the study hold was initiated for subject safety concerns only the full IRB may release the hold. If the study hold was initiated for other non-safety concerns, then the IRB Executive Chair/designee may release the study hold.

6.0 IRB Executive Chair Study Holds
6.1 The IRB Executive Chair/Vice Chair will halt a study if such action is warranted in accordance with Sections 3.4-3.5 of this policy.

6.2 The full IRB will review the study hold at the next convened meeting.

6.3 The IRB Executive Chair/Vice Chair will take appropriate action(s) to protect the rights and welfare of currently enrolled subjects in accordance with Section 10.0 of this policy.

6.4 The PI and all listed study personnel will be immediately notified by email that the study has been halted.

6.5 The IRB Executive Chair/Vice Chair will promptly notify the IO of all study holds.

6.6 The PI may petition the IRB Executive Chair/Vice Chair in writing to continue currently enrolled subjects on study because it is in their best interests. The IRB Executive Chair/Vice Chair is authorized to grant approval. 
*Note: In general, there should be compelling clinical justification to continue currently enrolled subjects on a study.*

6.7 The full IRB will review the decision of the IRB Executive Chair/Vice Chair to continue subjects on study and take any additional action as necessary.

6.8 The full IRB must approve the release of a study hold.

7.0 Suspension of IRB Approval
7.1 The full IRB may suspend IRB approval of research if such action is warranted in accordance with Section 3.6 of this policy.

7.2 The IRB will take appropriate action(s) to protect the rights and welfare of currently enrolled subjects in accordance with Section 10.0 of this policy.

7.3 The PI must report to the IRB any adverse events or outcomes associated with the suspension.

7.4 The PI must notify research subjects currently on study of suspension of IRB approval of research activities. Subjects should be advised of any follow-up necessary for safety reasons.

7.5 The IRB shall give the PI an opportunity to appeal the suspension in writing and also in person if so requested.

7.6 The IRB is granted the final authority to act on any appeals and the decision of the Board cannot be overturned.

7.7 The full IRB must approve the release of a study suspension.
8.0 Termination of IRB Approval

8.1 The full IRB may terminate IRB approval of research if such action is warranted in accordance with Section 3.5 of this policy.

8.2 The full IRB will take appropriate action(s) to protect the rights and welfare of currently enrolled subjects in accordance with Section 10.0 of this policy.

8.3 The IRB will provide the PI with written justification for termination of IRB approval of the research.

8.4 The PI will be afforded due process.

8.5 The IRB will promptly notify the IO of the termination of IRB approval of research.

8.6 The IO will notify other officials at the Organization as appropriate of the termination of IRB approval of the research.

8.7 The PI must report to the IRB any adverse events or outcomes associated with the termination.

8.8 The PI must notify research subjects of termination of IRB approval of research. Subjects must be advised of any follow-up necessary for safety reasons (i.e., arrange for appropriate medical care off study). No individual, however, can be compelled to participate in follow-up.

8.9 The PI may file a written appeal with the IRB within thirty (30) days of the termination.

8.10 The IRB shall give the PI an opportunity to appear before the Board. The PI will be afforded due process and may bring legal counsel who will be restricted to observation only.

8.11 The IRB is granted the final authority to act on any appeals and the decision of the Board cannot be overturned.

9.0 Organization Directed Termination of IRB Approval

9.1 The IO may terminate IRB approval of any, or all, of a PI’s research protocols in consultation with the IRB Executive Chair and appropriate administrative officials within the Organization.

9.2 The IO will notify the PI, and other organizational officials as appropriate, by email that the research has been terminated and the reason(s) for such action.

9.3 The IRB Executive Chair will provide notification of termination to the IRB.

9.4 The PI must report to the IRB any adverse events or outcomes associated with the termination.

9.5 The PI must notify research subjects of Organization directed termination of the research. Subjects must be advised of any follow-up necessary for safety reasons. No individual, however, can be compelled to participate in follow-up.

9.6 The PI may file a written appeal with the IO within thirty (30) days of the termination.
9.7 The IO has full authority to act on the appeal and may at his/her discretion convene an
Appeals Panel to make a recommendation regarding appropriate action.

9.8 The PI will be afforded due process and is entitled to meet with the IO and/or the
Appeals Panel. The PI may bring legal counsel who will be restricted to observation
only.

9.9 The decision of the IO with regard to any appeal is final.

10.0 Actions to Protect Subjects
One or more of the following actions, as appropriate, will be taken in order to protect the rights and
welfare of currently enrolled subjects when research is placed on study hold, suspended, or
terminated. Any action which requires subject approval must be obtained.

10.1 Arrange for appropriate medical care off study.
10.2 Transfer the subjects to another investigator.
10.3 Continue the research under independent monitoring.
10.4 Inform current subjects of the study hold, suspension, or termination.
10.5 Inform former subjects of the suspension or termination.
10.6 Require amendment of the protocol
10.7 Require implementation of a corrective action plan
10.8 Suspend or terminate the PI’s protocol
10.9 Suspend or terminate some or all of the PIs protocols where similar subject safety risks
have been identified or may be reasonably expected.
10.10 Suspend or terminate other investigator’s protocols where similar subject safety risks
have been identified or may be reasonably expected.
10.11 Other actions as necessary.

11.0 Reporting Suspensions and Terminations to OHRP, Department and Agency Heads,
and FDA
Suspensions and terminations are reported in accordance with HRPP policy #8.8.

ADMINISTRATIVE APPROVAL:
Ernest D. Prentice, PhD. Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD IRB Executive Chair
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements to ensure prompt reporting to Institutional Officials, OHRP, Department or Agency Heads (or designee), and the FDA the following: 1) unanticipated problems involving risk to the subject or others (UPs), 2) serious or continuing noncompliance, 3) suspensions of IRB approval, and 4) terminations of IRB approval.

2.0 Policy
It is the policy of the Organization that: 1) UPs, b) serious noncompliance, 2) continuing noncompliance, 3) suspension of IRB approval, and 4) termination of IRB approval must be promptly reported to the following in accordance with federal requirements:

   2.1 The Institutional Official (IO).
   2.2 The OHRP and the Department or Agency Head (or designee) in accordance with HHS regulations at 45 CFR 46.103(b)(5).
   2.3 Other Common Rule Department or Agencies.
   2.4 The FDA in accordance with 21 CFR 56.108(b)(5).

3.0 Definitions
3.1 **Unanticipated Problems Involving Risk to the Subject or Others:** A UP is defined as an event that meets the criteria specified in HRPP policy #8.5.

3.2 **Serious Noncompliance:** Serious noncompliance is defined as an incident that meets the criteria specified in HRPP policies #8.5 and #8.6.

3.3 **Continuing noncompliance** is defined as an incident that meets the criteria specified in HRPP policies #8.5 and #8.6.

3.4 **Suspension of IRB approval of research:** A directive that all or some research activities must be halted immediately because of serious subject safety or noncompliance concerns. Refer to HRPP policy #8.7 for additional information.

3.5 **Termination of IRB approval of research:** A directive by the IRB or the IO to the PI that all research activities are terminated immediately. Refer to HRPP policy #8.7 for additional information.

4.0 Procedures
4.1 The IRB Executive Chair/designee is responsible for the prompt submission of all required written reports to the IO within five (5) business days following the IRB’s determination that the event is a reportable incident in accordance with the requirements of this policy.

4.2 The IO may notify OHRP, FDA, and Department or Agency heads verbally in advance of a written report when the incident is particularly significant with respect to human subject protection.
4.3 The IO will submit all required written reports to the federal government agencies identified in Section 4.2 of this policy no later than ten (10) business days from the time the report is received from the IRB Executive Chair.

4.4 If an event occurs in non-federally funded research which is particularly serious, the IO, in consultation with the IRB Executive Chair and other senior administrators as appropriate, may choose to notify OHRP.

4.5 Reports to the IO, OHRP and FDA must include the following:
   A. Name of the institution conducting the research
   B. The IRB assigned IRB number and title of the research and/or grant proposal in which the noncompliance occurred; or for IRB or institutional noncompliance, the IRB or institution involved.
   C. Name of the PI (if applicable)
   D. Identification of the sponsor (federal, non-federal, commercial), number of any applicable federal grants award(s) (grant, contract, or cooperative agreement).
   E. Timeline and detailed description of the noncompliance or unanticipated problem involving risk to the subject or others.
   F. Applicable reports from IRB consultants.
   G. Other documentation pertaining to the event.
   H. Corrective action plan approved by the full IRB.

Note: Reports to the OHRP should be sent to the Division Director for Compliance Oversight, Office for Human Research Protections. The current mailing address may be found on the OHRP website (http://www.hhs.gov/ohrp/about/index.html#contact).

Note: Reports to the FDA should be sent to the appropriate division (i.e., drug products, biologic products, or medical devices.) Mailing addresses may be found on the FDA website (http://www.fda.gov/oc/gcp/irbterm.html).

4.6 Copies of the report and any necessary supporting documents will be provided to the PI.

4.7 Copies of the report may also be sent to other Organizational officials as determined by the IO (e.g., Chancellor; Dean; Department Chair).

4.8 For federally sponsored research, the PI will be instructed to notify the federal department, institute, or agency sponsoring the research. Any expenditure of federal funds during research which is not in compliance with federal regulations is prohibited. Verification of this notification must be provided to the IRB.

4.9 For commercially sponsored research, the PI will be instructed to notify the sponsor and the Contract Research Organization (as applicable) and provide verification of this notification to the IRB.
4.10 Reporting events which occur at institutions not under the jurisdiction of the UNMC IRB are the responsibility of the external institution.

**Administrative Approval:**
Ernest D. Prentice, PhD. Associate Vice Chancellor for Academic Affairs and Institutional Official
Bruce G. Gordon, MD IRB Executive Chair