# 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 that the HRPP will: 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 affiliated entities:
   3.1.1 University of Nebraska Medical Center (UNMC)
   3.1.2 Nebraska Medicine consisting of:
      3.1.2.1 Nebraska Medical Center and all affiliated clinics (including, but not limited to, Nebraska Medicine - Village Pointe)
      3.1.2.2 UNMC Physicians
      3.1.2.3 Bellevue Medical Center (BMC)
   3.1.3 Children’s Hospital & Medical Center (CHMC)
   3.1.4 University of Nebraska at Omaha (UNO)

   3.2 As specified in HRPP policy 1.2 (Authority Granted to the IRB by the Organization) and the associated IRB authorization agreements, these 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 (“Research Protection(s)”).

   3.4 All HRPP policies are made available to all investigators and research staff through the IRB website (https://net.unmc.edu/irb) and the online application system – Research Support System (RSS) (https://net.unmc.edu/rss).

      3.4.1 When modifications are made in HRPP policies, a Summary of Changes will be appended to the updated policy manual found on the IRB website and RSS.

4.0 HRPP Mission
4.1 The mission of the HRPP is to:
   4.1.1 Safeguard and promote the health and welfare of human research subjects by ensuring that their rights, safety and well-being are fully protected.
   4.1.2 Facilitate excellence in human subject research in accordance with the highest ethical standards in full compliance with all applicable regulatory and organizational requirements.
4.1.3 Provide research personnel with high quality education on the ethics and regulation of human subjects research.

4.1.4 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.

4.1.5 Engage in community outreach activities designed to educate the public about research.

4.2 To ensure compliance with the stated mission, the HRPP will:

4.2.1 Exercise oversight of research protection through the Office of Regulatory Affairs (ORA).

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

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

4.2.4 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.

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

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

4.2.7 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.

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

4.2.9 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.

4.2.10 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 Nuremburg Code, the World Medical Association Declaration of Helsinki (2013), the ethical guidelines put forth by the Council for International Organizations of Medical Sciences (CIOMS), and the International Council for Harmonization (ICH) Guideline for Good Clinical Practice.

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 and the Organization will comply with the following:

6.1.1 The Federal Policy for the Protection of Human Subjects (hereinafter referred to as the Common Rule) for all research conducted, supported, or otherwise subject to regulation by the Common Rule departments and agencies:

6.1.1.1 For convenience, this and other HRPP policies will refer to specific regulations using the HHS regulatory designation. For example, the designation 45 CFR 46.111 will be used rather than (for example) 34 CFR 97.111 for Department of Education funded research, or the more generic §_.111.

6.1.1.2 The Common Rule was revised on January 19, 2017 (FR 82:7149, 2017). For convenience, this will be referred to as the Revised Rule. The Common Rule prior to the revision is referred to as the pre-2018 Rule.

6.1.1.3 Regulatory citations which are based on the Revised Rule will be noted with the prefix “rev” (for example, “rev 45 CFR 46.116(f)” refers to requirements for waiver or alteration of consent under the Revised Rule, as opposed to “45 CFR 46.116(d)” for the pre-2018 Rule).

6.1.1.4 Research initially approved by the IRB, or for which a determination was made that the research was exempt, before the effective date of the Revised Rule, shall comply with the pre-2018 Rule.

6.1.1.5 Research initially approved by the IRB, or for which a determination was made that the research was exempt, on or after the effective date of the Revised Rule, shall comply with the Revised Rule.

6.1.1.6 The Institution will not apply any of the Burden-Reducing Provisions” (per 83 FR 28497) during the delay in the general compliance date of the Revised Rule.

6.1.2 Applicable subparts to HHS regulations at 45 CFR 46, including Subparts A, B, C, D and Subpart E for all research conducted, supported, or otherwise subject to regulation by HHS.

6.1.3 FDA regulations at 21 CFR 50 including Subpart D (as required), 21 CFR 56, and other regulations as required.

6.1.4 Additional regulations and requirements of the other Common Rule agencies (as required).

6.1.5 The HIPAA Privacy and Security Rules at 45 CFR 160, 164 (as required)

6.1.6 Applicable federal, state and local laws.

6.1.7 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, or the General Counsel for CHMC as appropriate.

6.3 The Organization will apply equivalent protections to all research not subject to the Common Rule.

6.3.1 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.
6.3.2 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 1.13 (Compliance with ICH-GCP Guidelines).

7.0 Federalwide Assurance (FWA)

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

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

7.2.1 IRB-01 (IRB00000670) - primarily reviews research involving adult subjects

7.2.2 IRB-02 (IRB00000671) - primarily reviews research involving adult subjects

7.2.3 IRB-03 (Rapid Response) (IRB00002686) - utilized on an as-needed basis for research requiring expeditious IRB review (per HRPP policy 1.30: Use of Rapid Response IRB).

7.2.4 IRB-04 (Joint Pediatric IRB) (IRB00007222) - primarily reviews research involving pediatric subjects

Note: In all of the HRPP policies hereafter, “the IRB” will refer to all boards (IRB-01, IRB-02, IRB-03, and IRB-04) unless otherwise indicated.

8.0 Written Policies and Procedures

The HRPP Policies detail the policies of the Organization and regulations governing conduct of research involving human subjects under the auspices of the Organization. Review and revision of these policies and procedures will be conducted in accordance with HRPP policy 1.18 (Review and Approval of HRPP Policies and Procedures).

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 Clinical Research 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:

9.1.1 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 4.0, 5.0 and 6.0 of this policy.

9.1.2 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:

9.1.2.1 Ensure HRPP and IRB staffing is commensurate with the size and complexity of the research enterprise.
9.1.2.2 Ensure there is adequate HRPP and IRB space, equipment, materials, and technology.

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

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

9.1.2.5 Ensure there is access to legal counsel.

9.1.2.6 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).

9.1.2.7 Ensure there are sufficient resources to support the HRPP Post-Approval Monitoring (PAM) program (per HRPP Policy 1.21: Post-Approval Monitoring of Research).

9.1.2.8 Ensure there are adequate resources to support community outreach programs related to Human Research Protections.

9.1.2.9 Support educational opportunities related to Human Research Protections for IRB members, ORA staff, research personnel, and other members of the research community.

9.1.3 Oversee of the IRB within the Organization and ensuring the IRB functions independently.

9.1.4 Appoint and oversee of the IRB Executive Chair.

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

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

9.1.7 Remain informed of the activities and decisions of the IRBs.

9.1.7.1 The IO will receive copies of the IRB minutes, meet with the IRB Executive Chair and the Assistant Vice-Chancellor for Regulatory Affairs on a regular basis, attends ORA staff meetings and convened IRB meetings periodically. In addition, the IO will be promptly advised of all compliance problems, complaints, or any other significant concerns regarding human subject protection.

9.1.8 As necessary, further review and approve or disapprove research as it relates to the Organizations mission and priorities; however, the IO may not approve research that has not been approved or has been disapproved by the IRB.

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

9.1.10 Oversee the development and implementation of an educational plan for IRB members, staff, and investigators.

9.1.11 Attain and maintain current CITI (Collaborative Institutional Training Initiative) Human Subjects Research Program certification as per HRPP policy 1.23 (HRPP Training Requirements and Opportunities for Research Personnel), and participate in other training in Human Subject Protection as appropriate.
9.1.12 Assure all IRB members are CITI certified and are appropriately knowledgeable to review research in accordance with ethical standards and applicable regulations.

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

9.1.14 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.

9.1.15 Ensure that any investigator, research personnel, or IRB member has free and direct access to the IO in order to express any concerns.

9.1.16 Implement the Organization’s HRPP policies and procedures.

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

9.1.18 Oversee the finances of the HRPP.

9.1.19 Perform an annual evaluation of the HRPP in accordance with HRPP policy 1.22 (Assessment of the Effectiveness and Efficiency of the HRPP).

9.2 Institutional Review Boards:

9.2.1 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 or students or others within the Organization’s facilities or under auspices of the Organization.

9.2.2 The IRB is responsible for the protection of the rights and welfare of human research subjects through assuring compliance with HRPP policies and Sections 4.0, 5.0, and 6.0 of this policy. A description of the IRB membership and qualifications is found in HRPP policy 1.6 (IRB Composition, Leadership, Qualifications, & Responsibilities).

9.2.3 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 1.4 (UNMC Ceding Review to an External Central IRB).

9.2.4 The HRPP may utilize selected independent commercial IRBs or other IRBs associated with universities, academic medical centers or hospitals for review and approval of applicable protocols in accordance with HRPP policy 1.4 (UNMC Ceding Review to an External Central IRB).

9.2.5 The IRB may serve as the IRB of record for external organizations in accordance with HRPP policy 1.3 (UNMC Serving as Central IRB).

9.3 Legal Counsel

The Organization relies on Legal Counsel for interpretations and applications of law, as described in HRPP policy 1.11 (HRPP Access to Legal Counsel).

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: Resources Necessary to Protect Subjects).
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 1.26 (PI Qualifications and Responsibilities)*.

9.6 *Other Review Committees*

9.6.1 Other Organizational review committees have specific responsibilities to review proposed or continuing research, as defined by HRPP and other Organizational Policies. These committees include: 1) Fred & Pamela Buffett Cancer Center Scientific Review Committee (SRC), 2) Pharmacy & Therapeutics Committee (P&T&C), 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 1.10 (Scientific and Other Committee Review of Research)*.

9.6.2 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*

9.7.1 Sponsored Programs Administration and UNeHealth

9.7.1.1 Sponsored Programs Administration (SPA) and/or UNeHealth staff review all research agreements with federal, non-federal (foundation and private), and commercial sponsors, as specified in *HRPP policy 1.12 (Sponsored Research)*.

9.7.1.1.1 UNMC SPA reviews federal and non-federal grant research agreements, and industry sponsored non-clinical research agreements, involving UNMC, Nebraska Medicine, BMC and CHMC.

9.7.1.1.2 UNeHealth reviews industry sponsored clinical research agreements, involving UNMC, Nebraska Medicine, BMC and CHMC.

9.7.1.1.3 UNO SPA reviews research agreements involving UNO.

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

9.7.2 Research Subject Advocate

9.7.2.1 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.

9.7.2.2 The Research Subject Advocate is listed on all consent forms as another contact for current, former, and prospective research subjects or others, in the event there are problems, concerns, and questions concerning the research.

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

9.7.2.4 The Research Subject Advocate works with the IRB and other Organizational Officials to resolve issues, obtain information, or offer input.

9.7.3 Pharmacy

9.7.3.1 Nebraska Medical Center Pharmaceutical & Nutrition Care Department:
9.7.3.1.1 This department oversees the use of pharmaceutical and investigational agents in human subject research conducted at Nebraska Medicine and affiliated clinics, UNMC, and BMC in compliance with hospital policy.

9.7.3.1.2 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.

9.7.3.1.3 The Pharmacy & Therapeutics (P&T) Committee reviews all clinical protocols conducted at UNMC, Nebraska Medicine, or BMC, which involve the use of investigational or marketed drugs in accordance with HRPP policy 1.10 (Scientific and Other Adjunct Review of Research).

9.7.3.1.4 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.

9.7.3.2 CHMC Pharmacy Department:

9.7.3.2.1 This department oversees the use of pharmaceutical and investigational agents in human subject research conducted at CHMC in compliance with hospital policy.

9.7.3.2.2 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.

9.7.3.2.3 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.

9.7.4 Health Information Management

9.7.4.1 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.

9.8 Relationship Between Components

9.8.1 The IRB functions independently of, but in coordination, with other Organizational regulatory committees (see HRPP policy 1.10: Scientific and Other Committee Review of Research). The IRB, however, makes an independent determination whether to approve or disapprove a protocol.

9.8.2 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 or has been disapproved by the IRB.

9.8.3 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

9.9.1 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 4.0, 5.0 and 6.0 of this policy. The ORA reports to the Assistant Vice-Chancellor for Regulatory Affairs and has a close working relationship with the IRB Executive Chair and the committees specified above.

9.9.2 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.

9.9.3 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 1.22 (Assessment of Effectiveness and Efficiency of the HRPP).

9.9.3.1 IRB Administrator Qualifications and Training

9.9.3.1.1 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, or equivalent qualifications. 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.

9.9.3.1.2 IRB Administrators must complete, and keep current CITI certification. IRB Administrators are expected to attend national or regional IRB conferences, and otherwise stay informed of new regulations and guidance issued by relevant authorities, and to review pertinent articles related to human subject protection.

9.9.3.2 ORA Staff Qualifications and Training

9.9.3.2.1 The IRB Staff are supervised on a daily basis by an IRB Administrator and/or the Assistant Vice-Chancellor for Regulatory Affairs. IRB staff must have relevant skills and experience including computer word processing and data management skills. A Bachelor’s degree is preferred but not required.

9.9.3.2.2 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.

9.9.3.2.3 IRB Staff must complete, and keep current CITI certification.

9.9.4 Training Records

9.9.4.1 The ORA is responsible for maintaining all initial and continuing education training records. The ORA will monitor the status of CITI certification for all IRB administrators and staff and notify them when it is time for renewal.
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
It is the policy of the Organization that:

2.1 All research involving human subjects conducted at the Organization or conducted by faculty, students, staff or other representatives of the Organization at external sites must receive approval by a designated IRB before the research may commence.

   2.1.1 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 1.4 (UNMC Ceding Review to an External Central IRB).

   2.1.2 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 1.4 (UNMC Ceding Review to an External Central IRB).

2.2 The IRB shall review and approve all non-exempt human subject research before such research is initiated, as per Section 2.1.

   2.2.1 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 (Full IRB Review).

   2.2.2 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 or IRB Chair has 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 (Expedited Review).

2.3 When IRB approval of non-exempt human subject research expires, or is terminated by the IRB or the Organization, or when the research is classified as completed by the investigator or the IRB, no further research activities may occur. This includes collection of existing or additional identifiable private information, or analysis existing identifiable private information.

2.4 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 (Exempt Research). The ORA will accept approval of exempt research by an external institution on a case-by-case basis.

2.5 The IRB has the authority to review research involving the use of fetal tissue (FT) and human embryonic stem cells (hESC), as per HRPP policy 7.4 (Research Involving Human Embryonic Stem Cells (hESC) and Fetal Tissue).
2.6 The IRB has the authority to approve a waiver or an alteration of the Authorization requirement of the HIPAA Privacy rule per 45 CFR 165.512.

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

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

2.9 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.

2.10 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 HRPP policy, or that has been associated with unexpected serious risk or harm to subjects or others.

2.11 The IRB Executive Chair/designee, in consultation with the IO and others as necessary, has the authority to suspend research that is not being conducted in accordance with the IRB’s requirements or HRPP policy, or that has been associated with unexpected serious risk or harm to subjects or others.

2.12 Research approved by the IRB may be subject to further review by an authorized official of the involved component of the Organization. Approval by the IRB can be overturned by those authorized individuals. However, no official of the Organization may approve research that has not been approved by or has been disapproved by the IRB.

2.12.1 The reason(s) for administrative disapproval of research by the authorized official shall be provided in writing to the PI and the IRB.

2.12.2 The PI may appeal the administrative decision to overturn IRB approval by submitting a written justification. The authorized official, in consultation with the IO as appropriate, will make the final determination.

2.13 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 including but not limited to notifying the supervisor of the individual who attempted to influence the IRB, the Chief Compliance Officer and other appropriate officials of the Organization. A thorough investigation will be undertaken and corrective action including counseling or other disciplinary action will be taken as necessary.

**Administrative Approval:**

BRUCE G. GORDON, MD  IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS

CHRISTOPHER KRATOCHVIL, MD  INSTITUTIONAL OFFICIAL

**Policy History:**

- **Initial** - April 4, 2016
- **Amended** - March 9, 2018
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for the UNMC IRB to serve as the Central IRB (CIRB) for multisite research.

2.0 Policy
2.1. It is the policy of the Organization that the UNMC IRB may serve as the CIRB for multisite research as permitted by HHS regulations at 45 CFR 46.114 and FDA regulations at 21 CFR 56.114.

2.2. It is the policy of the Organization that the IO has the sole authority to determine whether or not to allow the UNMC IRB to serve as the Central IRB for multisite research.
   2.2.1. For all non-exempt research, the Organization requires execution of a Reliance Agreement.
   2.2.2. For exempt research, the Organization does not normally require execution of a Reliance Agreement.

2.3. It is the policy of the Organization that the UNMC IRB may serve as the IRB of record as permitted by HHS regulations at 45 CFR 46.114 and FDA regulations at 21 CFR 56.114 for NIH-funded research, in accordance with the NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research (NOT-OD-16-094).
   2.3.1. The following requirements must be met for NIH funded research
      2.3.1.1. The requirement for single IRB review applies to awardees in the United States and participating research sites in the United States.
      2.3.1.2. The requirement for single IRB review does not apply to organization as outside the United States.
      2.3.1.3. Awardee organizations are responsible for ensuring authorization agreement are in place, and that documentation is maintained.
      2.3.1.4. The reviewing IRB is responsible for determining the additional requirements of the NIH Genomic Data Sharing Policy have been appropriately addressed.
   2.3.2. Participating sites are expected to rely on the single IRB, though they may conduct their own review in accordance with NIH policy on exceptions from single IRB review.

3.0 Definitions
3.1. Ceded Review: An institution agrees to transfer IRB review and oversight authority for specified research to another institution’s IRB.
3.2. Local Context: Unique legal requirements, cultural or religious values, or other site-specific variables that exist at a site where subjects are enrolled in research.
3.3. Reliance Agreement (also known as an Authorization Agreement): An agreement between two Organizations engaged in human subject research that documents respective
authorities, roles, responsibilities, and communication between an organization providing the ethical review and a participating organization relying on a reviewing IRB.

3.4. **Relying Institution:** A participating Institution that cedes IRB review to the IRB of record designated under a Reliance Agreement.

3.5. **Site Principal Investigator (SPI):** The lead investigator at each institution participating in multisite research usually responsible for the conduct of the research at the participating institution.

3.6. **Study-Wide Principal Investigator (PI):** The lead Principal Investigator with ultimate responsibility for the conduct and integrity of multisite research.

4.0 Responsibilities

4.1. **Responsibilities of the UNMC IRB**

4.1.1. Determining if the relying organization(s) apply their FWA to some or all of the research and ensuring the IRB review is consistent with the requirements of the Relying Institutions FWA (as applicable per DHHS and FDA regulations).

4.1.2. Provide the Site PIs/Relying Institutions with template informed consent form(s) which indicate areas where the Relying Institutions must add information related to local context.

4.1.3. Assume responsibility for IRB review of the research in full accordance with applicable federal and state regulations, and all relevant HRPP policies (including, but not limited to, initial review, continuing review, review of amendments, noncompliance, unanticipated problems involving risk to subject or others, deviations, adverse events, study holds, suspensions, and terminations).

4.1.3.1. The UNMC IRB is responsible for obtaining any additional approvals from DHHS when the research involves pregnancy women, fetuses, and neonates; or children; or prisoners.

4.1.3.2. The UNMC IRB is responsible for reporting all determinations of serious or continuing noncompliance, unanticipated problems involving risk to the subject or others, and suspensions or terminations to the Relying Institution, Institutional Officials and Federal Agencies (HRPP policy #8.7: Reporting Incidents to Institutional Officials and Federal Agencies)

4.1.4. Notify the Investigator and the Relying Institution (when applicable) of the IRB’s determinations.

4.1.5. Ensure HRPP policies are readily accessible to Relying Institutions through the IRB website (http://www.unmc.edu/irb) and there is a mechanism for communicating updates to the policies.

4.1.6. Provide the Relying Institution’s investigators and research staff with the Point of Contact (POC) to obtain answers to questions, express concerns, and convey suggest regarding the IRB.

4.1.7. Upon written request, provide Relying Institutions with access to relevant records related to IRB review (including, but not limited to minutes, approved protocols, consent forms, and other records that document the IRBs determinations to the Relying Institution).

4.1.8. Notify the Relying Institution within three business days, in the event that the FDA or other governmental agency issues the Organization any “Notice of Inspectional Observations”, “Warning Letters”, or other communications citing improper or inadequate research practices.
4.1.9. Maintain all research records for at least three years after completion of the research and make available for inspection or copying by the HHS Office of Human Research Protection (OHRP) and/or FDA upon request in accordance with federal regulations.

4.1.10. Ensure compliance with UNMC’s OHRP-approved FWA.

4.2. Responsibilities of the Relying Institution

4.2.1. Advise the UNMC IRB of any applicable state or local laws which govern research conducted at the site.

4.2.2. Advise the UNMC IRB of the results of additional reviews conducted at the Relying Institution, including but not limited to biosafety review, radiation safety review, recombinant DNA research review, human stem cell research review and conflict of interest.

4.2.2.1. Educate the investigators and research personnel at the Relying site of any requirements resulting from the additional reviews.

4.2.3. Advise the UNMC IRB of any circumstances when the review must take into account additional regulatory requirements.

4.2.4. Ensure that all investigators participating in the research are members of the Institution’s medical staff in good standing and are credentialed and privileged to perform the procedures outlined in the studies.

4.2.5. Ensure that all investigators participating in the research understand their responsibilities under applicable federal regulations (45 CFR 46 including subparts as applicable, 21 CFR 50, 56, 312, 812, and HIPAA Privacy Rule), state laws, institutional policies, and the protocol.

4.2.6. Ensure that all research personnel involved in the process of consent or assent are properly trained and are fully aware of their responsibilities relative to the obtainment of informed consent/assent according to institutional policies, applicable federal regulations, and state law.

4.2.7. Notify the UNMC IRB within three business days of the termination, suspension, or modification of any clinical privileges of members of its Medical Staff who are participating in the studies authorized by the UNMC IRB.

4.2.8. Inform the UNMC IRB of any contact by the FDA, HHS, or any other persons or entities regarding any of the research specified above within three business days of contact. The Local Institution will also notify the UNMC IRB within three business days, in the event that the FDA or other governmental agency issues the Local Institution any “Notice of Inspectional Observations”, “Warning Letters”, or other communications citing improper or inadequate research practices with respect to the research specified above.

4.2.9. Maintain a copy of the signed informed consent document in the subject’s medical record for each subject participating in studies approved by the UNMC IRB.

4.2.10. Maintain all research records for at least three years after completion of the research and made available for inspection or copying by OHRP and/or FDA upon request in accordance with federal regulations.

4.2.11. Ensure compliance with its OHRP approved FWA (if applicable).

4.2.12. Permit the UNMC IRB, or its authorized representatives, the FDA, and OHRP to the extent permitted by law, to conduct the following:
4.2.12.1. Examine and inspect the Relying Institution facilities used for the performance of the studies, including storage and use of any investigational products.

4.2.12.2. Observe the conduct of the studies.

4.2.12.3. Inspect and copy all documents relating to the studies, including research records, patient medical records, informed consent documents, Investigational Product logs, and other study specific data.

4.2.12.4. Interview, as necessary, all necessary personnel involved in patient care for the studies.

4.2.13. Modify their FWA to designate the UNMC IRB as the IRB of record for the research.

4.3. Responsibilities of the Study-Wide PI

4.3.1. Serve as the primary contact with the UNMC IRB. The Study-Wide PI assumes primary responsibility for notifying the relying sites of all UNMC IRB actions.

4.3.2. Promptly respond to questions or request for information from Site PIs and/or study teams at relying institutions or the Relying Institution IRBs.

4.3.3. Assure the Site PIs have access to the HRPP policies.

4.3.4. Ensure all site consent forms/information sheets follow the UNMC IRB approved template and include applicable site-specific required language provided by each relying institution.

4.3.5. Provide the Site PIs and study teams with the IRB approved versions of all study documents.

4.3.6. Promptly report to all Site PI's any unanticipated problems involving risks to subjects or others, research related subject injuries, or significant subject complaints that are related to or may affect subject's willingness to continue participation in the study.

4.3.7. Notify Site PIs of all UNMC determinations and communications, including initial review, continuing review, Requests for Change, and reportable events.

4.3.8. Ensure Site PIs submit in a timely manner the Continuing Review Worksheet in order for the information to be included in the formal Continuing Review Application submitted to the UNMC IRB for review.

4.3.8.1. If a Site PI does not provide the Study-Wide PI with the required information in a timely manner, the Continuing Review application must report the absence of this information.

4.3.8.2. The Study-Wide PI must notify the Site PI of the lapse in IRB approval of their site and any applicable corrective action plans.

4.3.8.3. Provide access, upon request, to all study records by audit by any Relying Institution, the UNMC IRB, and other regulatory or monitoring entities.

4.3.8.4. Further description of PI responsibilities are defined in HRPP policy 1.26 (PI Qualifications and Responsibilities).

5.0 Procedures

5.1. A request that the UNMC IRB serve as the CIRB for multisite research must:
5.1.1. Identify the research network (if applicable) and the participating sites.

5.1.2. Provide rationale for use of the UNMC IRB as the CIRB for the research.

5.1.3. Specify if this request applies to one, or multiple, research proposals.

*Note: If the request applies to multiple research proposals specify if a UNMC PI will serve as the Lead Study Site for all research proposals or if Lead Study Site will vary according to the research.*

5.1.4. Provide any relevant deadlines or funding agency requirements.

5.2. The UNMC IO must agree to allow the UNMC IRB to serve as the CIRB.

5.3. An *IRB Reliance Agreement* must be executed between the respective institutions. The fully executed IRB Reliance Agreement must be maintained as documentation verifying the responsibilities of each organization to ensure compliance with the requirements of the Common Rule.

*Note: The Organization prefers to utilize the “SMART IRB Master Common Reciprocal Institutional Review Board Authorization Agreement” platform. However, if the External Site cannot use that platform, a separate Reliance Agreement will be initiated between the Organization and the Relying Institution/IRB.*

5.4. Each Relying Institution IRB must agree to cede IRB review to the UNMC IRB for each specific research proposal by completion of the *Relying Institution Agreement to Cede IRB Review to the UNMC IRB*.

*Note: All local institutional requirements regarding ceding review to the UNMC IRB must be complete before study activation at the Relying Institution.*

5.5. Once the Organization has agreed to serve as the CIRB, the Study-Wide PI will complete the appropriate UNMC IRB applications throughout the life of the research through in RSS ([https://net.unmc.edu/rss](https://net.unmc.edu/rss)) in compliance with HRPP policy 2.1 (*Submission of Items for Review by the IRB*).

*Note: Section I of the IRB application must clearly identify the external site(s) requiring UNMC IRB oversight.*

5.6. The research will be reviewed by the IRB in accordance with the criteria for approval specified in HRPP policy 2.5 by either full IRB review (HRPP policy 2.2), or expedited review (HRPP policy 2.3) as applicable.

*Note: All research conducted at participating sites will be subject to all relevant UNMC HRPP policies.*

5.7. The UNMC-approved consent forms and information sheets will serve as the template for the relying sites. The template consent forms/information sheets to be used for the external sites will be created by the ORA/IRB Administrator.

5.8. Each Site PI must complete and submit for IRB review the *CIRB Site Specific Application* for the research. This application provides local context information specifically related to the research proposal. The application must include:

5.9. Verification of human subject protection training for all personnel listed on the CIRB Site Specific Application.

5.10. Information related to financial conflict of interest for personnel listed on the CIRB Site Specific Application.
5.11. Consent form(s)/information sheets(s) for that site based upon the template consent form/information sheet templates provided by the IRB Administrator.

Note: The Site Specific Application may be submitted at the time of initial submission of the protocol for IRB review, or at a later date to be reviewed as a Request for Change. The IRB has determined that addition of sites may be handled under expedited review (see HRPP policy 2.3), as applicable.

ADMINISTRATIVE APPROVAL:
BRUCE G. GORDON, MD IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS
CHRISTOPHER KRATOCHVL, MD INSTITUTIONAL OFFICIAL

POLICY AMENDED:
- APRIL 4, 2016
- MARCH 27, 2018
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for the UNMC IRB to cede review to an external IRB.

2.0 Policy
2.1. It is the policy of the Organization that selected independent commercial IRBs may serve as the IRB of record as 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 2.5 below.

2.2. It is the policy of the Organization that the National Cancer Institutes (NCI) Central IRBs (CIRBs) may serve as the IRB of record for pediatric and adult research sponsored by the National Cancer Institute (NCI) National Cooperative Groups as permitted by HHS regulations at 45 CFR 46.114 and FDA regulations at 21 CFR 56.114.

2.3. It is the policy of the Organization that other external IRBs may serve as the IRB of record as permitted by HHS regulations at 45 CFR 46.114 and FDA regulations at 21 CFR 56.114 on a case-by-case basis, with the exceptions specified under Section 2.5 below, provided that the external IRB:

   2.3.1. Is part of an accredited HRPP (or has completed the OHRP QA Self-Assessment Tool if the research constitutes no more than minimal risk)

   2.3.2. The research is conducted in association with a consortium requiring use of a Central IRB, or the research is federally funded and requires the use of a Central IRB.

   2.3.3. The external Institution has a valid FWA, and their IRB(s) is registered with OHRP and FDA (as applicable).

2.4. It is the policy of the Organization that an external IRB, including selected independent commercial IRBs, may serve as the IRB of record as permitted by HHS regulations at 45 CFR 46.114 and FDA regulations at 21 CFR 56.114 for NIH-funded research, in accordance with the NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research (NOT-OD-16-094).

   2.4.1. The following requirements must be met for NIH funded research

      2.4.1.1. The requirement for single IRB review applies to awardees in the United States and participating research sites in the United States.

      2.4.1.2. The requirement for single IRB review does not apply to organization as outside the United States.

      2.4.1.3. Awardee organizations are responsible for ensuring authorization agreement are in place, and that documentation is maintained.

      2.4.1.4. The reviewing IRB is responsible for determining the additional requirements of the NIH Genomic Data Sharing Policy have been appropriately addressed.

2.4.2. Participating sites are expected to rely on the single IRB, though they may conduct their own review in accordance with NIH policy on exceptions from single IRB review.
2.5. It is the policy of the Organization that if the external IRB is not AAHRPP accredited, the Organization must be assured:

2.5.1. The external IRB reviews the research appropriately, in compliance with all federal, state, and local regulations.

2.5.2. The review criteria utilized by the external IRB is in compliance with the Organization’s ethical standards and with applicable laws and regulations. The extent of review will vary depending on the level of risk to participants in the research.

2.6. It is the policy of the Organization that, unless funded by NIH and required to use an external IRB, the use of an external IRB is not permitted for:

2.6.1. Phase I clinical trials
2.6.2. Clinical trials initiated by a UNMC investigator
2.6.3. Use of a Humanitarian Use Device (HUD) subject to 21 CFR 814.124(a)
2.6.4. Emergency research subject to FDA regulations at 21 CFR 50.24.
2.6.5. Research that involves the use of vaccines developed or manipulated at UNMC.
2.6.6. Research involving gene transfer.
2.6.7. Emergency use of a test article subject to FDA regulations at 21 CFR 56.102(d) and 21 CFR 56.104(c).
2.6.8. Research involving prisoners as subjects.
2.6.9. Research involving fetal tissue or HESCs, or their derivatives

2.7. It is the policy of the Organization that the IO has the sole authority to determine whether or not to allow the UNMC IRB to cede review of research described in 2.1, 2.2 and 2.3, to an external IRB.

2.8. It is the policy of the Organization that the IO, in consultation with the IRB Executive Chair as appropriate, has the sole authority to allow exceptions to the exclusions under section 2.5 above.

2.9. It is the policy of the Organization that there must be an executed Reliance Agreement between UNMC and the external IRB’s institution or the commercial IRB, prior to utilization of the external or commercial IRB, for all non-exempt research.

2.9.1. The execution of the agreement should (but is not required to) precede submission of the application to utilize the external IRB.
2.9.2. For exempt research, the Organization does not normally require execution of the Reliance Agreement.

2.10. It is the policy of the Organization that all Organizational review requirements must be completed and the Reliance Agreement fully executed before the research will be released to the external or commercial IRB.

2.11. It is the policy of the Organization that the research may not commence until approval has been granted by the external IRB.

2.12. It is the policy of the Organization that all research conducted under an external IRB is subject to post approval monitoring per HRPP policy 1.21 (Post-Approval Monitoring of Research).

2.13. The status of studies where review is ceded to an external IRB are maintained in the Research Administration (RA) database and Research Support Services (RSS) application system.
3.0 Definitions

3.1. Cede Review: The Organization has agreed to transfer IRB review and oversight authority for specified research to another IRB.

3.2. Reliance Agreement (also known as an Authorization Agreement): An agreement between two Organizations engaged in human subject research that documents respective authorities, roles, responsibilities, and communication between an organization providing the ethical review and a participating organization relying on a reviewing IRB.

3.3. Relying Institution: A participating Institution that cedes IRB review to the IRB of record designated under a Reliance Agreement. In this policy, the UNMC IRB is ceding review to another Organization’s IRB.

4.0 External IRB, UNMC IRB and PI Responsibilities

4.1. It is the responsibility of the external IRB to:

4.1.1. Ensure all investigators and research staff have the appropriate qualifications and expertise to conduct the research, are knowledgeable about laws, regulations, codes and guidance governing their research, and are knowledgeable about the Institutions policies and procedures.

4.1.2. The external IRB is responsible for obtaining any additional approvals from DHHS when the research involves pregnant women, fetuses, and neonates; or children; or prisoners (as applicable per DHHS and FDA regulations).

4.1.3. The external IRB is responsible for reporting all determinations of serious or continuing noncompliance, unanticipated problems involving risk to the subject or others, and suspensions or terminations to the Relying Institution, Institutional Officials and Federal Agencies.

4.1.4. Provide a Point of Contact (POC) and contact information for UNMC researchers and research staff to obtain answers to questions, express concerns, and convey suggestions regarding the use of the external IRB.

4.1.5. Report to the UNMC IRB:

4.1.5.1. Any unanticipated problems involving risk to the subject or others associated with subjects enrolled at this site.

4.1.5.2. Any serious or continuing noncompliance.

4.1.5.3. Any serious complaints which impact the rights and welfare of research subjects.

4.1.5.4. The results of any external audits conducted by FDA, OHRP, sponsors, and CROs.

4.1.5.5. Any reports filed with the FDA or OHRP.

4.1.5.6. Any FDA 483 or warning letter pertaining to the study or IRB review.

4.2. It is the responsibility of the UNMC IRB to advise the external IRB of:

4.2.1. Any applicable state or local laws governing research conducted at this Organization.
4.2.2. Advise the external IRB of the results of additional reviews conducted at the Relying Institution, including but not limited to biosafety review, radiation safety review, recombinant DNA research review, human stem cell research review and conflict of interest.

4.2.2.1. Educate the investigators and research personnel at the Relying site of any requirements resulting from the additional reviews.

4.2.3. Advise the external IRB of any circumstances when the review must take into account additional regulatory requirements.

4.2.4. The termination, suspension, or modification of any clinical privileges of the Organizations investigators.

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

4.2.6. Any complaint directly from subjects or others. The Research Subject Advocate Office will assist in the resolution of the complaint as necessary.

4.2.7. Any contact by the FDA, HHS, or any other persons or entities regarding the research.

4.3. It is the UNMC PI’s responsibility to:

4.3.1. Complete all requirements for submission of request to utilize the CIRB to the ORA.

4.3.2. Complete all requirements for submission to the external IRB.

4.3.3. Comply with all determinations and requirements of the external IRB.

4.3.4. Comply with the external IRB’s requirements for initial and continuing review, record keeping, and reporting in a timely manner.

4.3.5. Promptly report the following to the external IRB (in accordance with their policies):

4.3.5.1. Any proposed changes to the research. The investigator cannot implement changes to the research (including changes in the consent form) without prior IRB approval except where necessary to eliminate apparent immediate hazard to subjects.

4.3.5.2. Conflict of interest management plans (in accordance with HRPP policy #1.25: Financial Conflicts of Interest). The UNMC PI and research staff must comply with all determinations.

4.3.5.3. Incidents of noncompliance. Copies of all reports to the federal government must be provided to the UNMC IRB administrator.

4.3.5.4. Protocol deviations.

4.3.5.5. Any complaints from subjects or others. The Research Subject Advocate Office will assist in the resolution of the complaint as necessary.

4.3.5.6. Data Safety Monitoring Reports

4.3.6. Promptly report to the external IRB (in accordance with their policies) and the ORA any internal adverse events and other events which qualify as an unanticipated problem involving risk to the subject.
4.3.7. Notify the ORA when there are changes in study personnel so that human subject protection training and conflict of interest may be reviewed in accordance with Organizational policy.

4.3.8. Ensure that all research personnel understand their responsibility in enrolling participants in the research; including obtainment, documentation, and maintenance of records of consent for each subject/LAR.

4.3.9. Conducting monitoring in addition to, or in cooperation with, the external IRB.

4.3.10. Notify the ORA when a study is completed. The date of completion will be entered into the IRB database and the study will be reclassified as “completed”.

4.4. There may be additional external IRB, UNMC IRB, and PI, responsibilities dictated by the IRB Reliance Agreement. The fully executed IRB Reliance Agreement must be maintained as documentation verifying the responsibilities of each organization to ensure compliance with the requirements of the Common Rule.

5.0 Procedures

5.1. The PI must submit the application CIRB Review of Research through RSS (https://net.unmc.edu/rss). The application must be accompanied by the following documents:

5.1.1. Full protocol
5.1.2. Sponsor’s template consent forms and/or information sheets
5.1.3. Clinical Trial Master Matrix
5.1.4. Pharmacy & Therapeutic Committee Drug Registry Forms, if applicable
5.1.5. Recruitment materials (such as fliers and brochures, text of radio and TV advertisements)

Note: It is recommended that the PI contact the ORA to determine if the proposed research will qualify for external IRB review prior to submission of the application. Acceptance of the application by the ORA does not signify that review will be ceded.

5.2. The IRB Administrator must determine that the request to utilize an external IRB satisfies the requirements of Sections 2.1, 2.2, 2.3 or 2.4, and not excluded by 2.5 above. The administrator, in consultation with the Executive Chair as appropriate, will then present to the IO the request to allow the UNMC IRB to cede IRB review to the external IRB.

5.3. If the IO approves the request, the UNMC IRB Administrator will review the “CIRB Review of Biomedical Research” application to determine that:

5.3.1. The research satisfies UNMC requirements including, but not limited to:

5.3.1.1. Subject payment; per HRPP policy 3.8 (Research Subject Compensation)
5.3.1.2. Contraception; per HRPP policy 3.9 (Contraception Requirements)
5.3.1.3. Subject identification and recruitment; per HRPP policies 3.5 (Subject Recruitment through Advertisements) and 3.6 (Subject Recruitment Through Direct Invitation), including ethical access (HRPP policy 3.12).
5.3.1.4. Investigator and research staff training; per HRPP policy 1.23: HRPP Training Requirements and Opportunities for Research Personnel)
5.3.1.5. Review and approval by other components of the HRPP (including, as appropriate, Conflict of Interest Committee, Fred & Pamela Buffett Cancer Center Scientific Review Committee, Pharmacy & Therapeutics Committee, Investigational Device Review Committee, Pathology, IT Security if SSNs maintained)

5.3.1.6. Contract review by Sponsored Programs Administration or UNeHealth

5.3.1.7. Coverage analysis and matrix/study calendar

5.3.2. Appropriate agreements are in place, including, but not limited to:

5.3.2.1. Executed sponsored agreement

5.3.2.2. Data Use, Data Transfer and/or Material Transfer Agreements

5.3.2.3. IRB Reliance Agreement between UNMC IRB and external IRB

5.3.3. The UNMC IRB Administrator will issue a conditional acceptance letter to the investigator, conditional on any required modifications based on Organizational requirements.

5.3.4. The UNMC Administrator will supply to the investigator the following items, to be provided to the external IRB:

5.3.4.1. UNMC CF letterhead

5.3.4.2. UNMC Addendum CF containing required language as per addendum to this policy. The external IRB may, at its discretion, merge the required UNMC CF language into the main CF.

5.3.4.3. Any COI management plan and the potential impact on the protocol (for example, prohibiting the PI from obtaining informed consent) or any requirements for disclosure in the informed consent form.

5.3.4.4. Additional information related to local context issues, including state, local or institutional regulations or policies that may impact IRB review.

5.3.4.5. Updates to all local context issues as applicable.

5.3.5. When the external IRB has completed its review, the approved CF language must be placed on UNMC letterhead. The UNMC IRB Administrator will review CF to assure inclusion of required language.

5.3.6. Once all Organizational requirements have been met (as specified in HRPP policy 2.2; Section 8.0: Full IRB Review and HRPP policy 2.3; Section 13.0: Expedited Review) and the IRB Reliance Agreement is fully executed, the IRB Administrator will provide the PI with an acceptance letter granting acceptance of IRB oversight by external IRB.

5.3.7. The study may not be initiated until the acceptance letter has been provided to the PI.

Note: 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 with the external IRB, except as specified in Sections 4.3.6, 4.3.7, and 4.3.8 above. UNMC IRB staff do not have the authority to respond to questions or concerns on behalf of the external IRB.

Note: The external IRB policies and procedures for stamping (or not stamping) consent forms with the approval dates take precedence. The UNMC IRB will not review or provide an approval stamp on any consent forms or information sheets approved by an external IRB.

5.3.8. The full UNMC IRB will be notified of the acceptance of the external IRB review and approval of the research as a special notification item in the IRB agenda and minutes.
5.3.9. The ORA, the IRB and the IO retain the authority to suspend research conducted within the organization which has been ceded to an external IRB, if the ORA, IRB or IO believes such action is necessary to protect the rights and welfare of human subjects of the research. The suspension will be promptly reported to the external IRB.

**Administrative Approval:**

Bruce G. Gordon, MD  IRB Executive Chair & Assistant Vice Chancellor for Regulatory Affairs
Christopher Kratochvil, MD  Institutional Official

**Policy Amended:**
- Revised February 28, 2018
- Revised May 30, 2017
Addendum: UNMC Required Consent Form Language

1. What will being in this research study cost you?
   [This section should describe the financial obligations the subject will incur as a result of participating in the study and whether any financial obligations will be increased as a result of procedures performed solely for research purposes.]

   You will be responsible for any applicable insurance deductibles and co-payments. If you wish to speak with a financial counselor about your insurance coverage and benefits, let the investigator or other study personnel know. A contact for personal assistance will be made available for you.

   [If there are no financial obligations, use only the following clause]
   There is no cost to you to be in this research study.

2. Who is paying for this research study?

   [For commercially supported studies]:
   The sponsor of the research is [name of sponsor]. [Name of Institution; Nebraska Medicine, UNMC, CHMC and/or UNO] receives money from the sponsor to conduct this study.

   [For studies supported by research grants]:
   This research is being paid for by [name of granting agency]. The Institution receives money from [name of granting agency] to conduct this study.

   [For NIH funded cooperative group studies]:
   The Institution receives money from [name of cooperative group] to conduct this study.

   [For studies without external support, include as applicable]:
   This research is being paid for by [for example, the Department of Internal Medicine, Section of Oncology of the University of Nebraska Medical Center].

   [If required by the institution, the PI will be directed to add any required financial conflict of interest statement here.]

3. What are the pregnancy risks associated with this study?
   Insert appropriate contraception language based on FDA Pregnancy and Lactation Labeling Rule and/or FDA Use-In-Pregnancy category, as per HRPP Policy 3.9 (Contraception Requirements)

4. What should you do if you are injured or have a medical problem during this research study?
   Your welfare is the main concern of every member of the research team. If you are injured or have a medical problem as a direct result of being in this study, you should immediately contact one of the people listed at the end of this consent form. Emergency medical treatment for this injury or problem will be available at Nebraska Medicine [or Children’s Hospital Medical Center]. If there is not sufficient time, you should seek care from a local health care provider.

   The Institution has no plans to pay for any required treatment or provide other compensation. If you have insurance, your insurance company may or may not pay the costs of medical treatment. If you do not have insurance, or if your insurance company refuses to pay, you will be expected to pay for the medical treatment.
Agreeing to this does not mean you have given up any of your legal rights.

5. **How will information about you be protected?**
   In addition to the information given to you in the main consent form, we may share information about you with other groups:
   - The UNMC Institutional Review Board (IRB)
   - Institutional officials designated by the UNMC IRB
   - [if the research involves patients with cancer]:
   - The Fred & Pamela Buffett Cancer Center Scientific Review Committee (SRC)

6. **What are your rights as a research subject?**
   You have rights as a research subject. These rights have been explained in this consent form and in "The Rights of Research Subjects" and "What Do I Need to Know" handout that you have been given. If you have any questions concerning your rights or want to discuss problems, concerns, obtain information or offer input, or make a complaint about the research, you can contact any of the following:
   - The investigator or other study personnel
   - [insert contact information for CIRB]
   - UNMC Institutional Review Board
     - (402) 559-6463
     - IRBORA@unmc.edu
     - UNMC Institutional Review Board, 987830 Nebraska Medical Center, Omaha, NE 68198-7830
   - UNMC Research Subject Advocate
     - (402) 559-6941
     - unmcrsa@unmc.edu

7. **What will happen if you decide to stop participating once you start?**
   You can stop participating in this research (withdraw) at any time. Please tell the Principal Investigator or any of the research staff if you want to withdraw. The investigator may ask you to have some additional tests done. You do NOT have to agree to do these tests.

   Deciding to withdraw will otherwise not affect your care or your relationship with the investigator or this institution. You will not lose any benefits or care that you would have gotten if you weren’t in the research study.

   OR

   You can stop participating in this research (withdraw) at any time. Please tell the Principal Investigator or any of the research staff if you want to withdraw. *They will advise you how to safely stop taking any study drugs or treatments.* If you withdraw the investigator may ask you to have some additional tests done. You do NOT have to agree to do these tests.

   Deciding to withdraw will otherwise not affect your care or your relationship with the investigator or this institution. You will not lose any benefits or care that you would have gotten if you weren’t in the research study.
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for research either (1) conducted by a faculty member, staff, student, or other representative of the Organization at an international site, or (2) conducted by external investigators under the direction of a faculty member, staff, student, or other representative of the Organization.

2.0 Policy
2.1. It is the policy of the Organization that 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 and regulations, local IRB (IEC, REB, REC) requirements and UNMC HRPP policies.

2.2. It is the policy of the Organization that non-exempt research conducted at an international site by the Organization’s faculty, staff, students, or other representative of the Organization, must be reviewed and approved by both the UNMC IRB, and by 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.

2.3. It is the policy of the Organization that exempt research conducted at an international site by the Organization’s faculty, staff, students, or other representative of the Organization, requires review and approval by both the ORA, and by any local IRB or official which has review and oversight jurisdiction. If there is no local IRB or official which has review and oversight jurisdiction, an exception may be granted by the Institutional Official upon recommendation by the IRB Executive Chair.

2.4. It is the policy of the Organization that, when reviewing research conducted entirely or in part in other countries, the IRB must have appropriate knowledge concerning the laws, regulations, guidance, and customs in that country either through the direct expertise by a member or by the use of consultants.

Note: The IRB may utilize as a resource the latest edition of the “OHRP International Compilation of Human Research Standards” as well as the information provided by the investigator in Addendum T of the IRB application.

2.5. It is the policy of the Organization that the investigator must have appropriate knowledge concerning the laws, regulations, guidance, and customs in that country either through the direct expertise or by the use of consultants.

2.6. It is the policy of the Organization that Protections of human subjects at the international site must be at least equivalent to HHS regulations at 45 CFR 46

2.7. It is the policy of the Organization that international research involving prisoners is not permitted.

3.0 Additional Requirements
3.1. When any international 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 or the UNMC Chemical and Radiation Safety Office.
3.2. When any international research is subject to US export control regulations, the PI must comply with UNMC policy 8005 (Export Control Policy). For more information contact the UNMC Export Control Compliance Office or the UNMC Chief Compliance Officer.

3.3. The PI is responsible for obtaining all appropriate host country permissions to conduct research (including as appropriate, institutional, governmental or ministerial, IRB or EC, local or tribal).

4.0 Procedures

4.1. **Non-Exempt International Research**

4.1.1. 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:

4.1.1.1. The appropriate IRB application

4.1.1.2. Addendum T: International Research

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

4.1.1.4. A copy of the ICF approved by the local IRB which has been translated into English.

4.1.1.5. A copy of the ICF approved by the local IRB in the native language.

4.1.1.6. An IRB Reliance Agreement which specifies the responsibilities of the local IRB which includes, but is not limited to, the following:

   4.1.1.6.1. Continuing review must be performed no less often than annually.

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

   4.1.1.6.3. 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.

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

4.1.2. In addition to the criteria for approval under 45 CFR 46.111, when conducting its review, the IRB will consider whether:

4.1.2.1. The PI and research personnel are qualified to conduct research in the specified country, including knowledge of relevant laws, regulations, guidance, and customs.

4.1.2.2. The consent process and consent documents are appropriate for the languages of the subjects and communication with the subject population, and whether appropriate arrangements are considered to communicate with the subjects throughout the research.

4.1.2.3. The PI has in place an adequate process for handling:

   4.1.2.3.1. Modifications to the research. The IRB and investigators should consider as many contingencies as possible when research is reviewed and approved.

   4.1.2.3.2. Complaints, noncompliance, protocol deviations, and unanticipated problems involving risk to subject or others.

   4.1.2.3.3. Post-approval monitoring of the research.
4.1.2.4. There is an adequate mechanism for communication between the IRB and the PI and research personnel when they are at the international site.

4.1.3. The UNMC IRB will review the protocol in accordance with HRPP policies 2.2 (Full IRB Review) and 2.3 ( Expedited Review).

4.1.4. Following the effective date of the Revised Rule, written documentation of informed consent may be waived by the IRB if the subjects or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not the norm, that the research presents no more than minimal risk of harm to subjects and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained (45 CFR 46.117(c)(1)(iii))

4.1.5. If a conflict arises between country specific laws/regulations and applicable US regulations, the IRB will consult with legal counsel (per HRPP policy 1.11: HRPP Access to Legal Counsel), other legal consultants, OHRP, and FDA as necessary.

4.2. Exempt International Research

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

4.2.1.1. The appropriate IRB application
4.2.1.2. Addendum T: International Research
4.2.1.3. A copy of the approval letter from the local IRB or authorized official
4.2.1.4. A copy of the ICF approved by the local IRB (if a consent form is required) which has been translated into English.
4.2.1.5. A copy of the ICF approved by the local IRB (if a consent form is required) in the native language.

4.2.2. The ORA will review the protocol in accordance with HRPP policy 2.6 (Exempt Research).

4.2.3. If a conflict arises between country specific laws/regulations and applicable US regulations, the IRB will consult with legal counsel (per HRPP policy 1.11: HRPP Access to Legal Counsel), other legal consultants, OHRP, and FDA as necessary.
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 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 Composition of the IRBs
3.1. Each IRB will have at least five members.
3.2. Each IRB shall be sufficiently qualified through the experience and expertise of its members (professional competence), and the diversity of its members, including race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects.
3.3. Each IRB shall include persons knowledgeable in terms of institutional commitments (including policies and resources) and regulations, applicable law, and standards of professional conduct and practice to be able to ascertain the acceptability of proposed research.
3.4. 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.
3.5. The IRB shall not consist entirely of members of one profession.
3.6. 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.
3.7. Each IRB will include at least one member that is not affiliated with the Institution.
   3.7.1. 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 patient or 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.
   3.7.2. 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.
   3.7.3. It is expected that at least one unaffiliated member will be present at each meeting of each IRB.
3.8. 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.

3.9. A member of the IRB may fill multiple membership position requirements (for example, an unaffiliated member may also serve as a non-scientist member).

3.10. 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.

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

3.12. 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 a prisoner representative with appropriate background and experience to serve in that capacity. This individual must have a reasonable working knowledge, understanding, and appreciation of prison conditions and be able to act in the best interests of the prisoners who will participate in the research.

3.13. 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 1.7 (IRB Member, Consultant, Staff COI Identification and Management).

3.14. When review of a proposal requires medical or 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:

3.14.1. 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) (or rev 45 CFR 46.107(e)) 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.

3.14.2. Consultants may be selected from within or from outside the Organization, based upon the required expertise.

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

3.14.4. Consultants must certify in writing that they do not have any conflict of interest as described in HRPP policy 1.7 (IRB Member, Consultant, Staff COI Identification and Management).

3.14.5. Consultants will produce written reviews upon request which will be provided to IRB members in advance of, or at the IRB meeting.

3.14.6. 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.

3.15. IRB alternate members are appointed according to discipline and membership category. They may represent more than one named IRB member. 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. Alternate members may
attend any IRB meeting; 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.

3.16. The UNMC Chief Compliance Officer will regularly attend IRB meetings as a consultant, but will not vote.

3.17. 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.

3.18. When the IRB membership changes, the HHS/FDA IRB registration will be modified by the IRB Administrator responsible for membership documentation, in accordance with 45 CFR 46.505(b) and FDA regulations.

3.19. A full listing of IRB members will be maintained by the ORA. This list will include for each IRB member:
   3.19.1. Name
   3.19.2. Earned degree(s)
   3.19.3. Representative capacity
   3.19.4. Scientific/nonscientific status
   3.19.5. Affiliation status of the IRB member with the organization, and, if an affiliation exists, the nature of the affiliation (e.g., employment or other relationship).
   3.19.6. Indications of expertise sufficient to describe the IRB member’s chief anticipated contribution to IRB deliberations.
   3.19.7. When applicable, identify alternate members and the IRB member or class of IRB member for whom the alternate member can substitute.

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

4.0 IRB Leadership

4.1. IRB Executive Chair

4.1.1. 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.

4.1.2. The IO will appoint an IRB Executive Chair to serve for renewable 3 year terms. Any change in appointment, including reappointment or removal, will require written notification.

4.1.3. The IRB Executive Chair reports directly to the IO on all matters pertaining to the IRB and related HRPP issues.

4.1.4. 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.

4.1.5. The IRB Executive Chair performs all the duties of the IRB Chair in section 5.2 B-E below.

4.1.6. 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.
4.1.7. The IRB Executive Chair is a signatory for correspondence in accordance with HRPP policy 1.19 (IRB Signature Authority).

4.1.8. The IRB Executive Chair appoints qualified IRB members to perform expedited review, in accordance with HRPP policy 2.3 (Expedited Review).

4.1.9. 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.

4.1.10. The performance of the IRB Executive Chair will be reviewed in accordance with HRPP policy 1.22 (Assessment of Effectiveness and Efficiency of the HRPP).

4.1.11. The IRB Executive chair must satisfy continuing education requirements per HRPP policy 1.24 (HRPP Training Requirements for IRB Members), section 5.0.

4.1.12. 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.

4.2. IRB Chairs

4.2.1. The IRB Chair(s) is appointed by the IO, in consultation with the IRB Executive Chair, for a renewable 3 year term. The Chair must:

   4.2.1.1. Have at least four years of IRB experience.
   
   4.2.1.2. Be knowledgeable about regulatory and institutional requirements for protection of human subjects.

   4.2.1.3. Be committed to serving in a leadership role

4.2.2. The IRB Chair conducts the IRB meetings, performs expedited reviews, reviews adverse events, unanticipated problems involving risk to the subject or others, protocol deviations, noncompliance, provides continuing education of IRB members and investigators, and participates in the development of policies, procedures, IRB forms and checklists.

4.2.3. If the IRB Chair is an MD (or equivalent) he/she will review requests for emergency use of a test article under 21 CFR 56.104(c)

4.2.4. The IRB Chair is a signatory for correspondence in accordance with HRPP policy 1.19 (IRB Signature Authority).

4.2.5. The IRB Chair appoints qualified IRB members to perform expedited review, in accordance with HRPP policy 2.3 (Expedited Review).

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

4.2.7. The performance of the IRB Chair will be reviewed in accordance with HRPP policy 1.22 (Assessment of Effectiveness and Efficiency of the HRPP).

4.2.8. The IRB Chair(s) must satisfy continuing education requirements per HRPP policy 1.24 (HRPP Training Requirements for IRB Members), section 5.0.

4.3. IRB Vice Chairs

4.3.1. The IRB Vice-Chair(s) is appointed by the IO, in consultation with the IRB Executive Chair, for a renewable 3 year term. The Vice-Chair must:

   4.3.1.1. Have at least two years of IRB experience.
4.3.1.2. Be knowledgeable about regulatory and institutional requirements for protection of human subjects.

4.3.1.3. Be committed to serving in a leadership role.

4.3.2. The IRB Vice-Chair(s) work closely with the IRB Chair and Executive Chair and serve in the absence of the IRB Chair and Executive Chair.

4.3.3. The IRB Vice-Chair(s) are also involved in the activities described in Section 4.5.4 of this policy.

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

4.3.5. The IRB Vice-Chair(s) must satisfy continuing education requirements per HRPP policy 1.24 (HRPP Training Requirements for IRB Members), section 5.0.

4.3.6. 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.

4.3.7. The performance of the Vice-Chair(s) will be reviewed in accordance with HRPP policy 1.22 (Assessment of Effectiveness and Efficiency of the HRPP).

4.4. IRB Executive Committee

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

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

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

4.4.4. The purpose of the IRB Executive Committee is to:

4.4.4.1. Perform ongoing assessment of the IRBs.

4.4.4.2. Assist in the development of HRPP policies and procedures.

4.4.4.3. Assist in the development of IRB forms.

4.4.4.4. Address concerns of any nature which impact the effectiveness of the HRPP in assuring the protection of the rights and welfare of research subjects.

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

4.5. IRB Members

4.5.1. IRB members will normally be identified and recruited by the IRB Executive Chair, IRB Chair(s) and the IRB Vice-Chairs. However, unsolicited nominations may be submitted to the IRB Executive Chair or the ORA at any time.

4.5.2. Prior to appointment to the board, the prospective member will be interviewed by the IRB Executive Chair or designee, to determine the relevant experience of the prospective member that will describe his/her chief anticipated contribution to IRB deliberations (AAHRPP element II.1.A).

4.5.3. IRB members are appointed by the IO, in consultation with the IRB Executive Chair, for a renewable 3 year term.
4.5.4. Each IRB member is expected to be fully engaged in the HRPP and will be involved in carrying out the following responsibilities as assigned:

4.5.4.1. Participate in all assigned IRB meetings and subcommittees with full voting privileges.

4.5.4.2. Serve as a primary or secondary reviewer for new protocols.

4.5.4.3. Serve as a primary reviewer for applications for continuing review.

4.5.4.4. Serve as an expedited reviewer once they are sufficiently experienced.

4.5.4.5. Serve as a primary reviewer for internal unanticipated problems involving risk to the subject or others.

4.5.4.6. Serve as a primary reviewer for changes in protocol and/or consent documents.

4.5.4.7. Serve as a primary reviewer for incidents of noncompliance.

4.5.4.8. Serve on IRB ad hoc subcommittees as needed.

4.5.4.9. Serve on the IRB Compliance Subcommittee as needed.

4.5.4.10. Serve on a quality improvement assessment team as needed.

4.5.5. IRB members are expected to attend the majority of scheduled meetings, and are required to attend all meetings for which they have been assigned reviews, unless prior arrangements have been made (e.g., written comments sent). IRB member attendance records will be maintained by the ORA in accordance with HRPP policy #1.22 (Assessment of the Effectiveness and Efficiency of the HRPP).

4.5.6. IRB members must satisfy initial and on-going education requirements as per HRPP policy 1.24 (HRPP Training Requirements for IRB Members), section 5.0.

4.5.7. The performance of all IRB members will be reviewed in accordance with HRPP policy 1.22 (Assessment of Effectiveness and Efficiency of the HRPP).

4.5.8. Upon completion of a member's term, the IRB Executive Chair, Chairs and Vice-Chairs, in consultation with the IRB Administrators, and based in part upon the performance evaluation (per HRPP policy 1.22: Assessment of the Effectiveness and Efficiency of the HRPP), will determine whether an additional term is offered.

4.5.9. Members accepting an additional term will be polled to evaluate changes in their roster information (per section 3.20 above).

4.5.10. An IRB Administrator may serve as a voting, or alternate voting, member of the IRB.

4.5.10.1. IRB administrators serving as voting or alternate members will be classified as scientist or non-scientist based on specific degree or education. Alternately, administrators with greater than 3 years prior work experience in a scientific field, or with greater than 3 years experience with review of biomedical protocols in current administrator position, may qualify as a scientist with approval of the IRB Executive Chair or Assistant VC for Regulatory Affairs.

4.5.10.2. An IRB administrator serving as a voting or alternate member of the IRB will have the same responsibilities and requirements as noted in section 5 above, except (1) term of appointment will be indefinite (section 5.3), and (2) an IRB administrator may not serve as reviewer for a new protocol, continuing review, adverse event or UP, or non-compliance incident, for a protocol which they are the primary administrator (section 5.4).
4.6. IRB Alternate Members

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

4.6.2. The alternate member must qualify in terms of expertise and role in order to serve in place of the regular member.

4.6.3. 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.

4.6.4. 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.

4.6.5. IRB Alternate members must satisfy initial and on-going education requirements as per HRPP policy 1.24 (HRPP Training Requirements for IRB Members), section 5.0.

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

4.6.7. The alternate member will not be counted as a voting member unless the regular member is absent.

4.6.8. The IRB minutes will document when an alternate member replaces a regular member.

4.7. Attendance Requirements

4.7.1. 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.

4.7.2. 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 and an appropriate replacement obtained. If the IRB member has a designated alternate, the alternate can serve during the regular member’s absence.

4.8. Training/Ongoing Education of IRB Members

Training of new and established IRB members and alternates is described in HRPP policy 1.24 (HRPP Training Requirements for IRB Members).

4.9. 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.
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: Financial and non-financial conflicts of interest that may 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.

3.2.1. The covered person currently serves as an investigator, participating personnel, or coordinator for the protocol as listed on the IRB application or is serving as a scientific/medical advisor to the PI.

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

3.2.3. 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.

3.2.4. 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.

3.2.5. 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.

3.2.6. 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 the covered
person knows or would be reasonably expected to know, is, or will be, in direct market competition with the product in the protocol under IRB review.

3.2.7. 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.

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 by members and consultants

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. Except as described below, an IRB member with a conflict of interest 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.

4.4.1. If the conflicted member is attending the meeting by conference call, videoconference, or web meeting, “absent from the meeting room” shall mean that the connection is terminated for the duration of the discussion and voting phases.

4.5. When an IRB member is listed on the IRB application as a participating personnel or other study personnel and will be involved in both obtaining and documenting informed, that individual may serve as a primary or secondary IRB reviewer and participate in the discussion, but are required to abstain from voting.

4.6. If an IRB member has a conflict of interest, but in his/her 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.
4.6.1. After disclosure of the specifics of the conflict to the Executive Chair, he/she will have the authority to grant exception.

4.6.2. The full IRB will be notified that an exception prior to the review of the protocol, and has the authority to overturn approval of an exception

4.6.3. Minutes will reflect that an exception was granted, but not specifics of the conflict.

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.

4.8. An IRB member with a conflict of interest may not serve as an expedited reviewer for a protocol for which he/she has a conflict.

5.0 Procedures for identification and management of conflict of interest by IRB staff

5.1. IRB staff must notify the IRB Executive Chair/designee if a conflict exists with any proposed or active research study under the jurisdiction of the IRB.

5.2. IRB staff who have any of the conflicts listed in section 3.2 above are excluded from serving as the key IRB administrator assigned to process the study in question.

5.2.1. IRB staff who have previously served as study personnel for an active protocol may serve as the key IRB administrator assigned to process the study; however, he/she may not be the sole expedited reviewer for any non-compliance, AEs or UPs in which he/she was directly involved during his/her tenure as study personnel.
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s policy and procedure for determining the investigational activities that require IRB approval.

2.0 Policy
2.1. It is the policy of the Organization that UNMC IRB review and approval is required for research involving human subjects (as defined in Section 3.0 below) which falls in the following categories regardless of the funding source:

2.1.1. Research conducted on the premises of any of the components of the Organization (defined in HRPP policy 1.1: Human Research Protection Program) by faculty, students, staff or other representatives of the Organization, or by any non-affiliated investigator.

2.1.2. Research performed elsewhere by faculty, students, staff or other representatives of the Organization, 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 policy 1.4: UNMC Ceding Review to an External IRB).

2.1.3. Research performed elsewhere by faculty, students, staff or other representatives of the Organization 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 policy 1.4: UNMC Ceding Review to an External IRB).

2.2. It is the policy of the Organization that 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

2.3. It is the policy of the Organization that IRB review will be performed in accordance with the authorities granted by institutions within the Organization in (accordance with HRPP policy 1.2: Authority Granted to the IRB by the Organization).

3.0 Definitions
3.1. HHS Regulations

3.1.1. Research is defined in the Federal Policy 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.

3.1.1.1. The definition of “research” in the HIPAA Privacy Rule (45 CFR 164.501) is identical to that in the Federal Policy; that is “a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge.”

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.

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).”

**Generalizable knowledge** means conclusions, facts or principles derived from the research which can be applied outside the specific study population and which enhance scientific or academic understanding. Generalizable knowledge usually includes one or more of the following concepts: Knowledge that contributes to a theoretical framework of an established body of knowledge; the primary beneficiaries of the research are other researchers, scholars, and practitioners in the field of study; dissemination of the results is intended to inform the field of study (though this alone does not make an activity constitute research “designed to contribute to generalizable knowledge”); the results are expected to be generalized to a larger population beyond the site of data collection; the results are intended to be replicated in other settings (after Emory University [http://irb.emory.edu/forms/review/index.html] and UC Berkeley HRPP [https://cphs.berkeley.edu/review.html])

3.1.2. After the effective date of the Revised Federal Policy, the following activities are deemed not to be research, as per 45 CFR 46.102(l):

3.1.2.1. Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected.

*Note: Studies using methods such as participant observation and ethnographic studies, in which investigators gather information from individuals in order to understand their beliefs, customs, and practices, and the findings apply to the studied community or group, and not just the individuals from whom the information was obtained, fall within the scope of the definition of research*

3.1.2.2. Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. Such activities are limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products).

3.1.2.3. Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.

3.1.2.4. Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions.

3.1.3. **Human Subject** is defined as follows:

3.1.3.1. Prior to the effective date for the Revised Rule:

3.1.3.1.1. “Human subject means 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" (per 45 CFR 46.102(f)).
3.1.3.1.2. Intervention includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject’s environment that are performed for research purposes.

3.1.3.1.3. Interaction includes communication or interpersonal contact between investigator and subject.

3.1.3.1.4. 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).

3.1.3.2. After the effective date of the Revised Rule:

3.1.3.2.1. “A living individual about whom an investigator (whether professional or student) conducting research: 1) obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens, or 2) obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens” (per rev 45 CFR 46.102(e))

3.1.3.2.1.1. Intervention means both physical procedures by which information or biospecimens 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.

3.1.3.2.1.2. 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.

3.1.3.2.1.3. 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).

3.1.3.2.1.4. Identifiable private information means private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information.

3.1.3.2.1.5. Identifiable biospecimen means a biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen.

3.1.3.3. Human subject research mean research activities which involve human subjects.

3.1.3.4. Engagement in Human Subject Research. The UNMC HRPP follows the OHRP guidance (October 16, 2008) in determining whether an institution is engaged in human subject research. In general, the Organization will be considered engaged in research when its employees or agents (that is, individuals who act on behalf of the institution; exercise institutional authority or responsibility; or perform institutionally designated activities) for the purposes of research obtain:

3.1.3.4.1. Data about the subjects of the research through intervention or interaction with them; or
3.1.3.4.2. Identifiable private information about the subjects of the research; or
3.1.3.4.3. Informed consent of the human subjects of the research.

3.2. FDA Regulations

3.2.1. **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.”

3.2.1.1. 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.

3.2.2. **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.”

3.2.2.1. 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)].

3.2.2.2. 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)].

3.2.3. **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.”

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

3.2.4.1. A drug is defined as a substance recognized by an official pharmacopoeia or formulary:
3.2.4.2. A substance intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease.

3.2.4.3. A substance (other than food) intended to affect the structure or any function of the body.

3.2.4.4. 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 for further information.

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

3.2.6. **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.”

3.2.7. **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.

3.2.8. **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.

3.2.9. **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).

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

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

3.2.12. **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 Classifications of Human Subject Research

4.1. **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. Biomedical research usually falls into one of two categories:

4.1.1. Clinical trial using a drug, medical device, technique or other intervention or strategy (including non-physical means, like diet, cognitive therapy, etc.) to diagnose, treat or otherwise study a particular condition or disease

4.1.2. Non-clinical biomedical research to study normal or abnormal physical or physiologic processes (for example, gait and balance testing, biomechanical assessments).

4.2. Human Biological Material Research: Human Biological Material (HBM) research includes the collection and/or use of 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; gametes (e.g., sperm and ova); and waste (e.g., hair, nail clippings, urine, feces, saliva, and sweat).

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

4.4. Behavioral and Social Science Research: Behavioral and social science research includes all research performed with intent to study behaviors, attitudes and interactions and social processes 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.

5.0 Activities Which Are Not Human Subject Research

5.1. 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 (1) there are no identifiers which would allow any of the investigators to readily identify the individual, and (2) where the specimen or data was not collected specifically for the purposes of the research does not constitute human subject research under 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.

5.2. 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.

5.3. Quality Improvement Activities: QI activities take place in a particular localized health care setting, their design is expected to incorporate the specific features of the setting, they are led by people who work in that setting, and they incorporate rapid feedback of results to bring about positive change for the patients in that setting. Instead of a fixed protocol implemented for a time period that may last for years, QI methods often require repeated modifications in the initial protocol as experience accumulates over time and as the desired changes engage the local structures, processes, patterns, habits, and traditions.
It is often difficult to determine whether a particular activity constitutes QI or research; therefore, a conversation between the person designing the activity, and the IRB, is useful and encouraged.

In general Quality Improvement activities have the following characteristics:

5.3.1. The activity is intended to improve the process/delivery of care while decreasing inefficiencies within a specific health care setting
5.3.2. The activity is intended to evaluate current practice and/or attempt to improve it based upon existing knowledge
5.3.3. There is sufficient existing evidence to support implementing this activity to create practice change
5.3.4. The activity is conducted by clinicians and staff who provide care or are responsible for the practice change in the institutions where the activity will take place
5.3.5. The methods for the activity are flexible and include approaches to evaluate rapid and incremental changes
5.3.6. The activity will involve a sample of the population (patients/participants) ordinarily seen in the institution where the activity will take place
5.3.7. The planned activity will only require consent that is already obtained in clinical practice, and could the activity be considered part of the usual care
5.3.8. Future patients/participants at the institution where the planned activity will be implemented will potentially benefit from the project
5.3.9. The risk to patients/participants is no greater than what is involved in the care they are already receiving OR participating in the activity can be considered acceptable or ordinarily expected when practice changes are implemented within a health care environment.

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.

5.4. Program Assessment: Program assessment (or program evaluation) is a systematic collection of information about the activities, characteristics and outcomes of a specific program or model, to contribute to continuous program improvement, and/or to inform decisions about future program development (https://www.cdc.gov/eval/index.htm). Program assessments do not constitute human subject research under this policy.

In general, Program Assessments have the following characteristics:

5.4.1. Intent of project is to evaluate a specific program, only to provide information for and about that program.
5.4.2. Activities are not designed to develop or contribute to generalizable knowledge; does not involve randomization of individuals, but may involve comparison of variations in programs.
5.4.3. Activities are mandated by the program, usually its funder, as part of its operations.
5.4.4. Findings of the evaluation are expected to directly affect the conduct of the program and identify improvements
5.4.5. No benefit to participants expected; evaluation concentrates on program improvements or whether the program should continue. (Source: Oregon State University
5.5. **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.

5.6. **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:** A systematic investigation conducted by a student with intent to present the results of the investigation outside of the confines of the institution 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-analyzes the data derived from the project in order to prove or disprove a hypothesis this does constitute human subjects research. Depending upon whether the subject identifiers are stripped from the data at the time of re-analysis, the project may be exempt.

5.7. **Secondary research involving non-identifiable newborn screening blood spots.**

6.0 **Other Activities Deemed Not Research:** After the effective date of the Revised Rule other activities specifically defined in rev 45 CFR 46.102(l) (and listed in section 3.1A above) are deemed “not research.” Specifically, this includes:

6.1. Scholarly and journalistic activities

   6.1.1. This includes, but is not limited to, oral history, journalism, biography, literary criticism, legal research, and historical scholarship, including the collection and use of information that focuses directly on the specific individuals about whom the information is collected. There is 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.

   6.1.2. Studies using methods such as participant observation and ethnographic studies, in which investigators gather information from individuals in order to understand their beliefs, customs, and practices, and the findings apply to the studied community or group, and not just the individuals from whom the information was obtained fall with the scope of the definition of research.

6.2. Public health surveillance activities
6.2.1. The collection and testing of information or biospecimens conducted, supported, requested, ordered, required, or authorized by a public health authority.

6.2.2. Such activities are limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products).

6.3. Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.

6.4. Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions.

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 human subjects 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 the OHRP Human Subject Decision Charts (http://www.hhs.gov/ohrp/regulations-and-policy/decision-trees/), and the criteria in Section 3.0 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 does not constitute human subject research, 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:

8.1.1. Full Board (FB) research will be reviewed by the IRB in accordance with HRPP policy 2.2.

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

8.1.3. 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:**
BRUCE G. GORDON, MD  IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS
CHRISTOPHER KRATOVIL, MD  INSTITUTIONAL OFFICIAL

**Policy Amended:**
- REVISED FEBRUARY 18, 2019
- REVISED MARCH 3, 2018
- REVISED SEPTEMBER 27, 2017
- INITIAL MAY 6, 2016
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
2.1. It is the policy of the Organization that during the conduct of research there must be adequate resources to protect human subjects
2.2. It is the policy of the Organization that the Principal Investigator is responsible for ensuring the necessary resources are available to protect the rights and welfare of human subjects.
2.3. It is the policy of the Organization that Departmental Chairperson/authorized delegate or appointed review committee of the Principal Investigator’s school, department or division must certify 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

3.0 PI and Certifier Obligation
3.1. The PI is required to sign an assurance (that is part of the IRB application) stating that there are adequate resources to protect the rights and welfare of subjects. These resources include (but are not limited to):

3.1.1. The PI has the necessary qualifications, experience and credentials to conduct the research.
3.1.2. There is an adequate number of qualified, licensed and credentialed research personnel and facilities/equipment to complete the research.
3.1.3. The PI has adequate time (in consideration of other academic or employment obligations, and other open research protocols in which he/she is participating) to conduct and complete the research.
3.1.4. The investigator has, or will have, necessary the financial resources to conduct the research.
3.1.5. There is adequate physical space, laboratory equipment, clerical support, data storage capability, and other resources necessary to complete the research.
3.1.6. There is appropriate emergency equipment, personnel, or services necessary to respond promptly to adverse events or unanticipated problems involving risk to the subject or other
3.1.7. Investigators have ethical access to a sufficient number of potential subjects for the purposes of the research.
3.1.8. There are adequate available medical or psychosocial resources in consideration of the nature of the research (for example, medical services, counseling, social support services), and resources necessary to facilitate communication with individuals who do not speak English or who have other impairments.
3.2. The Departmental Chairperson/authorized delegate or appointed review committee of the PI’s school, department or division must also certify (as part of the IRB application) that the resources described above, and any others necessary to fully protect the rights and welfare of research subjects, are available to the PI and research staff.

3.3. The PI is required to notify the IRB if, during the course of the research, the necessary resources become unavailable. If the necessary resources cannot be obtained and adequate protection of human subjects cannot be assured, the IRB may suspend or terminate the research, in accordance with HRPP policy 8.6 (Study Hold, Suspension, and Termination).

4.0 IRB Review of Resources

4.1. The IRB will review resources available as part of its review of the research at initial submission and at continuing review.

Administrative Approval:

Bruce G. Gordon, MD  IRB Executive Chair & Assistant Vice Chancellor for Regulatory Affairs
Christopher Kratochvil, MD  Institutional Official

Policy Amended:
- Revised March 3, 2018
- Revised September 27, 2017
- Initial May 6, 2016
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for scientific and scholarly merit review, and review by other component committees of the HRPP, of all human subject research protocols (see HRPP policy 1.9: Review of Resources Necessary to Protect Subjects).

2.0 Policy
2.1. It is the policy of the Organization that all human subject research must undergo a substantive scientific and scholarly merit review prior to initiating research.

2.2. It is the policy of the Organization that human subject research be reviewed by other component committees of the HRPP as appropriate.

3.0 College, Department or Division Review of Scientific Merit
3.1. The Department Chairperson/designee or appointed review committee in the PI’s college, department or division is responsible for review of the research proposal prior submission to the IRB. In addition to the review of resources described in HRPP policy 1.9 (Resources Necessary to Protect Subjects), the College, Department or Division review must determine the following:

3.1.1. The research has a sound scientific design:
   3.1.1.1. The methods are valid and practically feasible
   3.1.1.2. The research has a clear scientific objective
   3.1.1.3. The research is designed using accepted principles, methods, and reliable practices
   3.1.1.4. The research has sufficient power to definitively test the objective
   3.1.1.5. The research offers a plausible data analysis plan

3.1.2. The research has an acceptable level of scientific/scholarly merit; that is the knowledge to be gained from the research is sufficiently important.

3.1.3. The College, Department or Division reviewer must sign the attestation (certification) statement in the IRB application.

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

3.1.5. The IRB will also evaluate the scientific and scholarly merit of all proposed studies. If the IRB does not have the appropriate disciplinary expertise for review of the protocol, the Board will utilize a consultant.

4.0 Reviews by Other Components of the HRPP
Depending upon the nature of the research, proposals may be subject to additional review and approval by one or more of the following groups:
4.1. **Fred & Pamela Buffett Cancer Center Scientific Review Committee (SRC):**

4.1.1. 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).

4.1.2. The SRC reviews the scientific aspects of industry sponsored and investigator initiated cancer-related research involving human subjects conducted by members of the UNMC faculty and students and members of the Fred & Pamela Buffett Cancer Center.

4.1.3. The SRC is responsible for:

- **4.1.3.1.** 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.

- **4.1.3.2.** 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.

- **4.1.3.3.** Ensuring that there are no competing studies with overlapping eligibility criteria for a specific disease indication.

- **4.1.3.4.** Establishing each protocol’s priority based on NCI guidelines and institutional priorities.

- **4.1.3.5.** Performing annual scientific review of open cancer center protocols.

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

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

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

4.1.7. If SRC review follows IRB review, the designated IRB Administrator in consultation with the IRB Executive Chair, or one of the Chairs or Vice-Chairs will be responsible for assuring that no substantive changes have been made to the protocol or the consent forms by the SRC. If substantive changes have been made, re-review by the convened IRB will be required.

4.1.8. 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.

4.1.9. 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.

4.1.10. 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.

4.1.11. The SRC may not approve human subject research to commence that has not yet been approved or has been disapproved by the IRB.
4.2. **Pharmacy and Therapeutics Committee (P&T Committee):**

4.2.1. The purpose of the Nebraska Medicine P&T Committee review is to ensure safe use, adequate monitoring, 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:* The Nebraska Medicine P&T Committee does not review research conducted at CHMC. Review of research involving investigational and marketed drugs conducted at CHMC is accomplished by a designated CHMC pharmacist who is a member of IRB-04.

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

4.2.3. 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.

4.2.4. If the P&T Committee review follows IRB review, the ORA staff, in consultation with the designated IRB Administrator and the IRB Executive Chair, or one of the Chairs or Vice-Chairs will be responsible for assuring that no substantive changes have been requested by the P&T Committee. If substantive changes have been requested, re-review by the convened IRB will be required.

4.2.5. 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.

4.2.6. 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.

4.2.7. 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.

4.2.8. If a Request for Change involves a modification in dosing or route of administration of a study drug, P&T Committee must review, and any issues identified prior to full approval by the IRB, as above.

4.2.9. 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.

4.3. **Nebraska Medicine Investigational Device Committee**

4.3.1. 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:

4.3.1.1. General study overview

4.3.1.2. Specific services requested

4.3.1.3. Cost, if any, to the ancillary department, along with the availability of grant funding to cover those costs

4.3.1.4. Logistical considerations, including inventory of device(s), confirmation of billing account number(s),
4.3.1.5. Services that are considered investigational, impact on workload when adding research patients to conventional care patient workload.

4.3.2. 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.

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

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

4.4. Clinical Trial Master Matrix and Coverage Analysis

4.4.1. 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.

Note: Nebraska Medicine is utilizing the OnCore Clinical Trial Management System (CTMS) for management of clinical research. The clinical study calendar created through CTMS may be used in place of the matrix.

4.4.2. The Coverage Analysis (CA), using the CTMM, is conducted by the UNMC Center for Clinical and Translational Research (CCTR). The Coverage Analysis 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).

4.4.2.1. 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.

4.4.3. A CTMM and CA is required of any study that includes clinical care activities conducted at Nebraska Medicine/UNMC regardless of the funding source.

4.4.4. 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.

4.4.5. 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.

4.4.6. The IRB will not review a study that includes clinical care activities conducted at Nebraska Medicine/UNMC if the matrix has not been provided.

4.4.7. 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.
4.5. **UNMC Institutional Biosafety Committee (IBC):**

4.5.1. 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.)

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

4.5.3. 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.

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

4.5.5. 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.

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

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

4.5.8. A copy of the IBC review letters will be uploaded to RSS in the appropriate study file.

4.6. **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.

4.7. **Conflict of Interest Committee (COIC):** Refer to *HRPP policy 1.25 (Financial Conflicts of Interest).*

5.0 **Sponsored Programs Administration (SPA):** Refer to *HRPP policy 1.12 (Sponsored Research).*

**Administrative Approval:**

BRUCE G. GORDON, MD  IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS
CHRISTOPHER KRATOCHVIL, MD  INSTITUTIONAL OFFICIAL

**Policy Amended:**
- Revised February 12, 2018
- Initial May 6, 2016
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:

   3.1.1. UNMC Chief Compliance Officer
   3.1.2. UNMC Associate General Counsel
   3.1.3. UN Senior Associate General Counsel
   3.1.4. UN Associate General Counsel
   3.1.5. CHMC General Counsel and Assistant General Counsel
   3.1.6. CHMC Compliance Officer / Privacy Officer

3.2. The UNMC Chief Compliance Officer regularly attends meetings of IRB-01 and IRB-02 and is, therefore, available to address legal issues which arise during the meeting.

3.3. The CHMC Assistant General Counsel attends meetings of IRB-04 as often as possible, and is available by telephone to address legal issues which arise during the meeting.

3.4. The Assistant Vice-Chancellor for Regulatory Affairs and the UNMC Chief Compliance Officer are responsible for advising the IO, 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:

BRUCE G. GORDON, MD  IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS
CHRISTOPHER KRATOCHVIL, MD  INSTITUTIONAL OFFICIAL

Policy Amended:

- REVISED FEBRUARY 2, 2018
- INITIAL MAY 6, 2016
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, and in full compliance with all applicable HRPP policies, federal regulations for protection of human subjects, state and local laws and regulations, and University of Nebraska Board of Regents By-Laws.

3.0 Definitions

3.1. Sponsor is defined as the company (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 (for example, 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 reviewed by UNeHealth, UNMC Sponsored Programs Administration (SPA) or UNO SPA.

4.2. SPA and/or UNeHealth provides appropriate excerpts from the Contract to ORA. The IRB Administrator, in collaboration with SPA or UNeHealth Contract Specialists will 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:

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

   4.3.2. 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.

   4.3.3. 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.
4.3.4. Indemnification language must not compromise the rights and welfare of research subjects.

4.3.5. Contracts cannot include a financial bonus or financial penalty specifically linked to subject recruitment efforts (HRPP policy 3.7; Finders Fees and Recruitment Bonuses).

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

4.3.7. 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.

4.3.8. 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) (or rev 45 CFR 46.104(a)(4)), and HRPP policies.

4.3.9. 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.

4.3.10. 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.

4.3.11. 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) (or rev 45 CFR 46.104(a)(4)), and HRPP policies.

4.3.12. 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.

4.3.13. There are no requirements which would cause the Organization to violate the HIPAA Privacy Rule. When PHI is provided to the Sponsor the Sponsor must:

   4.3.13.1. Refrain from using PHI to recruit subjects or advertise additional studies to subjects.
   4.3.13.2. Refrain from using the PHI for marketing or market research.
   4.3.13.3. Place the same restrictions on any third party to whom the Sponsor discloses PHI.

4.3.14. 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.

4.3.15. There are no restrictions on publication of the results of the research which violate the University of Nebraska Board of Regents Policy.

4.3.16. All commercially sponsored research is assessed an ORA/IRB review fee.
4.3.16.1. The PI must complete the Charge for IRB Review of Commercially Sponsored Projects (Full Board and Expedited Review) forms.

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

4.4. 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.

4.5. 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. “Major modification” is defined as per HRPP policy 2.4 (Review of Changes in Approved Research).

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

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

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

4.9. 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.

   4.9.1. 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.

   4.9.2. 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:
BRUCE G. GORDON, MD IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS
CHRISTOPHER KRATOVIL, MD INSTITUTIONAL OFFICIAL

POLICY AMENDED:
- REVISED FEBRUARY 8, 2018
- INITIAL MAY 6, 2016
1.0 Purpose

The purpose of this policy and procedure is to describe the Organization’s requirements for compliance with the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) E6 Guidelines.

2.0 Policy

2.1. It is the policy of the Organization that, in addition to all applicable HRPP policies, the Organization will apply ICH-GCP E6 guidelines to IRB review and the conduct of clinical research when the sponsored agreement specifies adherence to ICH GCP.

2.2. It is the policy of the Organization that clinical trials subject to ICH-GCP will be conducted in accordance with the ethical principles that have the origin in the Declaration of Helsinki and that are consistent with good clinical practice and the applicable regulatory requirements.

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. When the protocol requires ICH GCP compliance, the IRB Administrator will ensure that the submission includes all necessary information in section 4.0.

3.3. When the full IRB reviews research that requires ICH GCP compliance, the IRB will ensure that all requirements are met prior to final approval.

4.0 ICH GCP Requirements

4.1. New research and substantive scientific modifications to approved research shall undergo scientific review (including review by outside experts as needed) and that the review is considered by the IRB in accordance with HRPP policy 1.10 (Scientific and Other Committee Review of Research).

4.2. In order to satisfy the ICH-GCP requirements, the IRB must be assured of the following:

4.2.1. The PI is 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)

Note: 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.

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

4.2.3. 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

4.2.4. The clinical trials is scientifically sound; adequately designed to answer the research question, and described in a clear, detailed protocol (ICH GCP 2.5).

4.2.5. In addition to the elements described in HRPP policy 5.1 (Obtaining Informed Consent from Research Subjects), consent form disclosures provide the following additional elements of information to potential subjects:

   4.2.5.1. The approval by the IRB.
   4.2.5.2. The probability for random assignment to each treatment.
   4.2.5.3. The participant’s responsibilities.
   4.2.5.4. When applicable, the reasonably foreseeable risks or inconveniences to an embryo, fetus, or nursing infant.
   4.2.5.5. 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)).
   4.2.5.6. The subject should be made aware if there is no intended clinical benefit to the subject.
   4.2.5.7. 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))
   4.2.5.8. The subject’s identity will remain confidential if the trial results are published.

4.2.6. Except as described in section 4.1.7 below, non-therapeutic clinical trials (trials in which there is no anticipated direct benefit to the subject), should be conducted in subjects who personally give consent and who sign and date the written informed consent form (ICH-GCP 4.8.13).

4.2.7. Non-therapeutic clinical trials conducted in subjects with consent of a legally authorized representative (LAR) fulfill the following additional requirements (ICH-GCP 4.8.14):

   4.2.7.1. The objectives of the clinical trial cannot be met by means of a trial in subjects who can give consent personally.
   4.2.7.2. The foreseeable risks to the subjects are low.
   4.2.7.3. The negative impact on the subject’s well-being is minimized and low.
   4.2.7.4. The clinical trial is not prohibited by law.
   4.2.7.5. The opinion of the IRBs is expressly sought on the inclusion of such subjects and the written opinion covers this aspect.
   4.2.7.6. 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.
4.2.8. In those situations where there is an exception for the requirements for informed consent for planned emergency research, the subject, or LAR, will 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.*

4.3. In order to satisfy the ICH-GCP requirements, the PI must assure the following:

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

4.3.2. 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)

4.3.3. During and following a subject’s participation in a trial, the PI must 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)

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

4.3.5. The PI must follow the trial’s randomization procedures, if any, and ensure 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)

4.3.6. When appropriate, the PI must 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)

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

4.3.8. 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)

4.3.9. 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. (ICG-GCP 4.6.3)

4.3.10. 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
4.3.11. The PI will permit monitoring and auditing by the sponsor, and inspection by the appropriate regulatory authority. (ICH-GCP 4.1.4)

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

4.3.13. 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)

4.3.14. The PI will report to the sponsor, IRB, and, as applicable, the Organization (ICH GCP 4.10.2):

   4.3.14.1. Any new information that may adversely affect the safety of the subject or the conduct of a clinical trial.
   
   4.3.14.2. Any changes significantly affecting the conduct of the clinical trial, or increasing risk to subjects.

4.3.15. 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). 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)

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

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

4.3.18. 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)

4.3.19. 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)

4.3.20. 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)

ADMINISTRATIVE APPROVAL:
BRUCE G. GORDON, MD  IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS
CHRISTOPHER KRATOCHVIL, MD  INSTITUTIONAL OFFICIAL

POLICY AMENDED:
- REVISED FEBRUARY 2, 2018
- INITIAL JANUARY 25, 2016
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. It is the policy of the Organization that the research specified in Section 2.1 above will comply with the following codes, regulations and guidance:

- 2.2.1. The Belmont Report
- 2.2.2. Title 32 Code of Federal Regulations Part 219 (32 CFR 219), Department of Defense Regulations, “Protection of Human Subjects” (DoD adoption of the “Common Rule”)
- 2.2.4. Title 21 Code of Federal Regulations 50, 56, 312, and 812, Food and Drug Administration (FDA) Regulations
- 2.2.5. DoDD 3216.02, “Protection of Human Subjects and Adherence to Ethical Standards in DoD-supported Research”
- 2.2.6. Title 10 United States Code Section 980 (10 USC 980), “Limitation on Use of Humans as Experimental Subjects”
- 2.2.7. DoDD 3210.7, “Research Integrity and Misconduct”
- 2.2.8. DoDD 6200.2, “Use of Investigational New Drugs in Force Health Protection”
- 2.2.9. Department of the Navy
  - 2.2.9.1. SECNAVINST 3900.39D of 6 November 2006
  - 2.2.9.2. SECNAVINST 5720.44B of 1 November 2005
  - 2.2.9.3. SECNAV M-5210.1 of 1 December 2005
  - 2.2.9.4. OPNAVINST 5300.8B of 23 April 1997

2.3. It is the policy of the Organization that research specified in Section 2.1 above will comply with the following requirements, as applicable:

- 2.3.1. Education and Training [DoDD 3216.02, para.4.5]
  - 2.3.1.1. 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 #1.23 (HRPP Training Requirements and Opportunities for Research Personnel). In addition, any other specific training will be determined by the ORA.

2.3.1.2. 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.

2.3.2. 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.

2.3.2.1. Subpart B

2.3.2.1.1. 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.

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

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

2.3.2.2. Subpart C

2.3.2.2.1. Research involving prisoners cannot be reviewed by the expedited review procedure.

2.3.2.2.2. During IRB review, at least one prisoner representative must be present for quorum. The prisoner representative may be a prisoner, an employee of the prison, or an individual not affiliated with the prison.

2.3.2.2.3. Epidemiological research is also allowable when:

2.3.2.2.3.1. The research describes the prevalence or incidence of a disease by identifying all cases or studies potential risk factor association for a disease.

2.3.2.2.3.2. The research presents no more than minimal risk.

2.3.2.2.3.3. The research presents no more than an inconvenience to the participant.

2.3.2.2.4. When a previously enrolled human participant becomes a prisoner, if the researcher asserts to the IRB that it is in the best interest of the prisoner-participant to continue to participate in the research while a prisoner:

2.3.2.2.4.1. The IRB chair may determine that the prisoner-participant may continue to participate until the convened IRB can review this request to approve a change in the research protocol and until the organizational official and DoD Component office review the IRB’s approval to change the research protocol. OR

2.3.2.2.4.2. The IRB chair must require that all research interactions and interventions with the prisoner-subject (including obtaining identifiable private
information) cease until the convened IRB can review this request to approve a change in the research protocol.

2.3.2.2.4.3. The convened IRB, upon receipt of notification that a previously enrolled human participant has become a prisoner, must promptly re-review the research protocol to ensure that the rights and wellbeing of the human subject, now a prisoner, are not in jeopardy.

2.3.2.2.4.4. The IRB should consult with a subject matter expert having the expertise of a prisoner representative if the IRB reviewing the research protocol does not have a prisoner representative.

2.3.2.2.4.5. If the prisoner-participant can continue to consent to participate and is capable of meeting the research protocol requirements, the terms of the prisoner-participant’s confinement does not inhibit the ethical conduct of the research, and there are no other significant issues preventing the research involving human participants from continuing as approved, the convened IRB may approve a change in the study to allow this prisoner-participant to continue to participate in the research. This approval is limited to the individual prisoner-participant and does not allow recruitment of prisoners as participants.

2.3.2.3. 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.

2.3.2.4. Other Vulnerable Subjects

Refer to DoDD 3216.02 for specific requirements.

If consent is to be obtained from the legal representative of the experimental subjects as defined in DODI 3216.02, the research must intend to benefit each participant enrolled in the study.

2.3.3. 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.

2.3.4. 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:

- The research is necessary to advance the development of a medical product for the Military Services,
- The research may directly benefit the individual subject,
- 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.

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

2.3.5.1. 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.

2.3.5.2. 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.

2.3.5.3. 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.

2.3.6. 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.

2.3.7. 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.

2.3.8. Classified research [SECNAVINST 3900.39D, para 6]

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, or for a waiver of consent.
2.3.9. 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.

2.3.10. 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 means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. This definition of the minimal risk 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 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. When reviewing research subject to DoD regulatory requirements, IRB members will be provided with a copy of this policy (HRPP policy 1.14) along with the IRB application, consent form, protocol, and all other related documents.

4.2. The IRB will review the application and complete the *Research Subject to Department of Defense Research Regulatory Requirements Checklist* and ensure compliance with all applicable DoD requirements, DoN requirements, and HRPP policies.

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

   4.3.1. 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.*

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

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

   4.3.4. 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:

      4.3.4.1. Discuss the research study with researchers.

      4.3.4.2. Observe subject recruitment and enrollment procedures.
4.3.4.3. Oversee study interventions and interactions.
4.3.4.4. Oversee data collection and analysis.
4.3.4.5. Interview human subjects.
4.3.4.6. Stop a research study in progress.
4.3.4.7. Remove subjects from a study.
4.3.4.8. Take any necessary steps to protect the safety and well-being of subjects until the IRB can assess the monitor’s report.
4.3.4.9. Consult with others outside of the research study.

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

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

4.5. Waivers of consent
4.5.1. Waivers of consent are prohibited for classified research.
4.5.2. Waivers of consent must meet the requirements of the Common Rule (HRPP policy 5.2; Waiver or Alteration of Informed Consent and HIPAA Authorization) and DoD approval requirements.

4.6. 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.

4.7. 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 days the following:

4.7.1. All suspensions or terminations of previously approved DoD and DoN supported research protocols.
4.7.2. The initiation and results of investigations of alleged non-compliance with human subject protections.
4.7.3. Unanticipated problems involving risks to subjects or others, or serious adverse events in DoD and DoN supported research.
4.7.4. All audits, investigations, or inspections of DoD and DoN supported research protocols.
4.7.5. All audits, investigations, or inspections of the institution’s HRPP conducted by outside entities (for example, the FDA or OHRP).
4.7.6. Significant communication between institutions conducting research and other federal departments and agencies regarding compliance and oversight.

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

4.8. Recordkeeping Requirements [DoDD 3216.02, para. 5.3.2; SECNAVINST 3900.39D, para. 8c(18)]

4.8.1. 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.

4.8.2. Representatives of the DoD/DoN may inspect and copy records at reasonable times and in a reasonable manner.

4.9. 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 days to the DoD human protection officer, the Navy Secretary General, and appropriate sponsors.

4.10. 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.

4.11. Additional Requirements for DoD and DoN Sponsored Research

4.11.1. The DoD Component must conduct an administrative review of the research involving human subjects. The DoD Component administrative review must be conducted before the research involving human subjects can begin, to ensure compliance with all applicable regulations and policies, including any applicable laws and requirements and cultural sensitivities of a foreign country when the research is conducted in a foreign country.”

4.11.2. New research and substantive scientific amendments to approved research shall undergo scientific review (including review by outside experts as needed) and that the review is considered by the IRB in accordance with HRPP policy 1.10 (Scientific and Other Committee Review of Research).

4.11.3. For DoD-supported non-exempt research involving human participants involving classified information reviewed by a non-DoD IRB, the involvement of classified information may be limited to information needed for IRB approval and oversight of the research; information needed to inform the human participants during the consent process; and information provided by human participants during the course of the research.

4.11.4. Disclosure regarding the provisions for research-related injury follows the requirements of the DoD/DoN component.

4.11.5. The DoD/DoN Protection Officer will be promptly notified (within 30 days) 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.

4.11.6. The DoD/DoN Protection Officer will be notified promptly (within 30 days) any change of reviewing IRB.
4.11.7. 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.

4.11.8. DoD institutions collaborating with non-DoD institutions may rely on a collaborating non-DoD institution’s IRB if the following conditions are met:

4.11.8.1. Each institution engaged in non-exempt human participant research must have a current federal assurance of compliance.

4.11.8.2. The involvement of DoD personnel in the conduct of the research is secondary to that of the non-DoD institution.

4.11.8.3. The DoD institution, non-DoD institution, and the non-DoD institution’s IRB have a written agreement defining the responsibilities and authorities of each organization in complying with all legal requirements. This agreement must be approved by the DoD component prior to the DoD institution’s engagement in the research.

4.11.9. For DoD sponsored research, the following are required elements that must appear on the informed consent document:

4.11.9.1. A statement that the DoD or a DoD organization is funding the study.

4.11.9.2. A statement that representatives of the DoD are authorized to review research records.

4.11.10. For DoD sponsored research, the following are the required elements that must be found in the consent form:

4.11.10.1. A statement that the DoD or a DoD organization is funding the study.

4.11.10.2. A statement that representatives of the DoD are authorized to review research records.

4.11.11. Civilian researchers attempting to access military volunteers should seek collaboration with a military researcher familiar with service-specific requirements.

Administrative Approval:
BRUCE G. GORDON, MD  IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS
CHRISTOPHER KRATOCHVIL, MD  INSTITUTIONAL OFFICIAL

Policy Amended:
- Revised March 3, 2018
- Initial April 13, 2016
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:

2.2.1. The Belmont Report.
2.2.2. Title 28 Code of Federal Regulations Part 46 (28 CFR 46), Department of Justice Regulations, “Protection of Human Subjects” (DoJ adoption of the “Common Rule”).
2.2.3. Title 28 Code of Federal Regulations Part 512 (28 CFR 512), Bureau of Prisons Regulations, “Research”.
2.2.4. Title 28 Code of Federal Regulations Part 22 (28 CFR 22), Confidentiality of Identifiable Research and Statistical Information.

2.3. Education and Training

2.3.1. All research personnel must complete training in accordance with HRPP policy #1.23 (HRPP Training Requirements and Opportunities for Research Personnel).
2.3.2. Any other specific training related to DOJ requirements will be provided as necessary by the ORA.

2.4. Responsibilities

2.4.1. Research Funded by the Department of Justice [28 CFR 46]
   2.4.1.1. It is the responsibility of the PI to ensure compliance with all additional DoJ requirements for human subject protection.
   2.4.1.2. 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.

2.4.2. Research Conducted Within the Bureau of Prisons
   2.4.2.1. Regulatory Compliance [28 CFR 512]
       2.4.2.1.1. It is the responsibility of the PI to ensure compliance with all additional BoP requirements for human subject protection.
       2.4.2.1.2. All research proposals must be reviewed and approved by the Bureau Research Review Board (BRRB).
       2.4.2.1.3. 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.

2.4.2.1.4. 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.

2.4.2.2. 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.

2.4.2.3. 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.

2.4.2.4. 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).

2.4.2.5. Limitations on Incentives for Inmate Subjects [28 CFR 512.11(a)(5)]

2.4.2.5.1. 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.

2.4.2.5.2. 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.

2.4.2.6. For research conducted within the Bureau of Prisons, implementation of Bureau programmatic or operational initiatives made through pilot projects is not considered research.

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:

3.1.1. Data through intervention or interaction with the individual and/or

3.1.2. 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

4.1.1. 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.

4.1.2. Requirement for Privacy and Confidentiality [28 CFR 22]: All research funded by the DoJ must maintain the following documents:

   4.1.2.1. 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.

   4.1.2.2. 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.

4.1.3. Requirement for Informed Consent [28 CFR 46.116; 28 CFR 22]: Research involving human subjects funded by the DoJ must include the following information in the ICF:

   4.1.3.1. The name(s) of the funding agency(ies)

   4.1.3.2. 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.

   4.1.3.3. 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.

4.1.4. 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

4.2.1. 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.

4.2.2. 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.

4.2.3. The research must have an adequate research design and contribute to the advancement of knowledge about corrections.

4.2.4. The selection of subjects within in one organization must be equitable.
4.2.5. 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.

4.2.6. 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.

4.2.7. For all research conducted within the Bureau of Prison, the PI must provide the following information:

4.2.7.1. A summary statement, which includes:

4.2.7.1.1. Names and current affiliations of the Researchers
4.2.7.1.2. Title of the study
4.2.7.1.3. Purpose of the study
4.2.7.1.4. Location of the study
4.2.7.1.5. Methods to be employed
4.2.7.1.6. Anticipated results
4.2.7.1.7. Duration of the study
4.2.7.1.8. Number of participants (staff or inmates) required and amount of time required from each
4.2.7.1.9. Indication of risk or discomfort involved as a result of participation

4.2.7.2. A comprehensive statement, which includes:

4.2.7.2.1. Review of related literature.
4.2.7.2.2. Detailed description of the research method.
4.2.7.2.3. Significance of anticipated results and their contribution to the advancement of knowledge.
4.2.7.2.4. Specific resources required from the BoP.
4.2.7.2.5. 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.
4.2.7.2.6. Description of steps taken to minimize any risks.
4.2.7.2.7. Description of physical or administrative procedures to be followed to:

4.2.7.2.7.1. Ensure the security of any individually identifiable data that are being collected for the study.
4.2.7.2.7.2. Destroy research records or remove individual identifiers from those records when the research has been completed.

4.2.7.2.8. Description of any anticipated effect of the research study in organizational programs and operations.
4.2.7.2.9. Relevant research materials such as vitae, endorsements, sample consent statements, questionnaires, and interview schedules.
4.2.7.2.10. A statement regarding assurance and certification required by 28 CFR 46, if applicable.
4.2.7.3. The researcher must demonstrate academic preparation of experience in the area of study of the proposed research.

4.2.8. Requirement for Confidentiality [28 CFR 512.11, 12, 13, 15]: For all research conducted with the BoP:

4.2.8.1. 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.

4.2.8.2. 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.

4.2.8.3. 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.

4.2.8.4. 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.

4.2.9. 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:

4.2.9.1. Identification of the PI and research personnel listed in Section I of the IRB application.

4.2.9.2. Anticipated uses of the results of the research.

4.2.9.3. 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).

4.2.9.4. 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.

4.2.9.5. A statement that participation in the study will have no effect on the inmate subject’s release date or parole eligibility.

4.2.10. Documentation and Waiver of Signed Informed Consent [28 CFR 512.16(a)(12)]

4.2.10.1. 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.

The PI may not be required to obtain the signature if the PI can demonstrate that:
4.2.10.1.1. The only link to the subject’s identity is the signed statement of informed consent, or
4.2.10.1.2. That there is significantly more risk to the subject if the statement is signed.

4.2.10.2. The signed statement shall be submitted to the chairperson of the IRB of record.

4.2.11. 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.

4.2.12. 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:

4.2.12.1. A progress report of the research at least once a year to the Chief and ORE.
4.2.12.2. 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.

4.2.13. Requirement for Publication of Results [28 CFR 512.20]

4.2.13.1. 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:

4.2.13.1.1. An acknowledgment of the BoP’s participation in the research study.
4.2.13.1.2. Expressly disclaiming approval or endorsement of the published material as an expression of the policies or views of the Bureau.

4.2.13.2. 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

4.3.1. New research and substantive scientific amendments to approved research shall undergo scientific review (including review by outside experts as needed) and that the review is considered by the IRB in accordance with HRPP policy #1.10 (Scientific and Other Committee Review of Research).

4.3.2. Disclosure regarding the provisions for research-related injury follows the requirements of the DoJ component.

ADMINISTRATIVE APPROVAL:
BRUCE G. GORDON, MD  IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS
CHRISTOPHER KRATOCHVIL, MD  INSTITUTIONAL OFFICIAL

POLICY AMENDED:
➤ Initial April 20, 2016
1.0 Purpose

The purpose of this policy and procedure is to describe the Organization’s requirements for maintenance of documentation of IRB and ORA activities.

2.0 Policy

It is the policy of the Organization that the ORA will maintain documentation of all IRB activities in accordance with 45 CFR 46.115 and 21 CFR 56.115 as applicable. 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 review, the type of review, and the current status of the study.

3.1.1. In general, research initially reviewed by the full IRB after January 16, 2012 is in electronic format accessed through RSS (https://net.unmc.edu/rss), and research initially reviewed by the full IRB prior and closed prior to January 16, 2012 is in paper files. Research initially reviewed by the full IRB prior to January 16, 2012 and either still active, or closed after that date may be partially in paper format and partially in electronic format.

3.2. Requirements for maintenance of protocol files: Each protocol file will include:

3.2.1. 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.

3.2.2. Detailed protocol (if required)

3.2.3. Investigators Brochure (if required)

3.2.4. Federal grant applications (if required)

3.2.5. ICF/information sheets (if required). HIPAA authorization are included in this document as per HRPP policy 5.1 (Obtaining Informed Consent from Research Subjects).

3.2.6. 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.

3.2.7. Documentation of review and approval of proposals by the Pharmacy and Therapeutics Committee (P&T Committee) (if required).

3.2.8. Documentation of review and approval by the Institutional Biosafety Committee (IBC) (if required).

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

3.2.10. Copies of any written reviews from consultants.
3.2.11. Review letters to the PI. Review letters include determinations in accordance with HRPP policy that the research satisfies, as applicable, all requirements of the following:

3.2.11.1. Subparts of 45 CFR 46 (Subparts B, C, and D)
3.2.11.2. 21 CFR 50 (Subpart D)
3.2.11.3. Categories under which research is approved under expedited review
3.2.11.4. Waiver or alteration of informed consent under applicable HHS regulations
3.2.11.5. Waiver or alteration of HIPAA authorization under 45 CFR 164.512
3.2.11.6. Waiver of documentation of consent under applicable HHS and FDA regulations.
3.2.11.7. The category of research approved as exempt in accordance with HHS and FDA regulations.

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.

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

3.2.13. Documentation of approval of recruitment materials and copies of the approval materials.

3.2.14. Requests for Change and correspondence pertaining to the request, including copies of the modified IRB approved and stamped ICF(s)/information sheets and/or protocols associated with the request.

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

3.2.16. Applications for Continuing Review and correspondence pertaining to the request, including copies of the ICF(s)/information sheets approved in conjunction with continuing review.

3.2.17. Interim progress reports and Data Safety Monitoring Board (DSMB) reports.

3.2.18. Reports of Internal adverse events and adverse device effects.

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

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

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

3.2.22. Requests for Single subject protocol deviations and violations.

3.2.23. Reports of Protocol Violations

3.2.24. Reports of Subject complaints

3.2.25. Reports of incidents of noncompliance, including documentation of investigation, correspondence, and reports to institutional officials, OHRP, and FDA where appropriate.

3.2.26. Results from Post Approval Monitoring reviews and correspondence regarding the findings.

3.2.27. IRB Review Checklists documenting:

3.2.27.1. The justification for using the expedited review procedure.
3.2.27.2. The rational for conducting continuing review of research that otherwise would not require continuing review.

3.2.27.3. The rational for a determination that research appearing on the list of eligible expedited review categories is greater than minimal risk.

3.2.27.4. Actions taken by the reviewer.

3.2.27.5. Any documentation for determinations and justifications required by laws, regulations, codes, and guidance

3.2.27.6. Exempt determinations

3.3. **Long-Term Record Storage**

   3.3.1. Paper copies of protocol records of non-exempt research are maintained in UNMC storage in either CD-ROM (prior to 2012) or paper format (after 2012). CD-ROM discs or hard copy will be stored indefinitely for future reference or inspection by HHS, FDA or other sponsor representatives.

   3.3.2. 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.

3.4. **UNMC Research Administration Database:**

   3.4.1. The ORA 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 other information necessary to allow the IRB staff to track and monitor the status of protocols, (for example, IRB approval periods), and perform searches in order to produce reports.

   3.4.2. The database is available in “view” mode to selected groups outside of the ORA (for example, Sponsored Programs Administration and the P&T Committee) to assist those groups in their roles in the HRPP.

3.5. **IRB Agendas, Meeting Minutes, and Membership Rosters:**

   Copies of all IRB agendas, minutes, IRB member Curriculum Vitae, and 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 ORA Staff are maintained in the ORA, either in paper or electronic format.

3.7. **HRPP Policies and Procedures:**

   Copies of HRPP policies and procedures as required by 45 CFR 46.115 and 21 CFR 56.115 are maintained on the IRB website, in RSS 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 and 21 CFR 56.115.

**Administrative Approval:**

BRUCE G. GORDON, MD                  IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS
POLICY AMENDED:
- REVISED FEBRUARY 2, 2018
- INITIAL APRIL 7, 2016
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for retention of research records by the investigator.

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 years beyond the termination of the study or longer as required by sponsors.

3.0 Required Records
3.1. The research records retained by the investigator should include the initial version as well as all amendments of the:
   3.1.1. IRB application
   3.1.2. Detailed protocol
   3.1.3. Grant (if applicable)
   3.1.4. Investigator brochure (if applicable)
   3.1.5. ICF(s)/Information sheet(s) (unsigned)
   3.1.6. Case report forms (blank)
   3.1.7. Applications for continuing review
   3.1.8. DSMB reports (if applicable)
   3.1.9. IND/IDE correspondence and annual reports (if applicable)
   3.1.10. Requests for change
   3.1.11. Adverse event reports (internal, internal fatal and external) with corresponding documentation (e.g., safety reports) and applicable consent documents
   3.1.12. Reports of unanticipated problems involving risk to the subject or others
   3.1.13. Reports of protocol deviations
   3.1.15. Reports of Audits and Post-Approval Monitoring
   3.1.16. Correspondence between the IRB and the PI (or research staff)
   3.1.17. Correspondence from the Sponsor, including contracts, MTAs, and DUAs.
   3.1.18. For research conducted outside the Organization where the UNMC IRB is the IRB of record, documentation of training in the protection of human subjects by external investigators or staff, external investigator agreements, and other contractual agreements
   3.1.19. Any other protocol-related documentation
3.1.20. Subject files including original signed consent documents, case report forms (CRFs), laboratory results and other applicable information.

3.2. For applications and reports generated within RSS (for example, the IRB Application, Request for Change, Continuing Review, Report of Protocol Deviation), a paper copy may be printed and retained as above, or the presence of the information within RSS constitutes “retention” of the record for the purpose of this policy.

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:**

BRUCE G. GORDON, MD  IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS
CHRISTOPHER KRATOCHVIL, MD  INSTITUTIONAL OFFICIAL

**Policy Amended:**

- **February 18, 2019**
- **Revised February 2, 2018**
- **Initial December 28, 2015 (Original Policy #3.5)**
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, as well as emerging ethical and scientific issues.

3.0 Review of HRPP Policies and Procedures
3.1. The IRB Administrators, the Assistant Vice-Chancellor for Regulatory Affairs, the IRB Executive Chair, and IO will review, at least annually, all HRPP policies and procedures. However, anytime a policy requires revision due to new or revised federal, state or local laws, federal regulations or guidance, changes in Organizational requirements, or identification of deficiencies, the policy will be revised accordingly.

3.2. New and revised (draft) HRPP policies and procedures which are regulatory in nature (that is, which are dictated by federal, state, and local laws, regulations, and guidance), or which solely describe ORA procedures, will be provided to the IRBs for their information, but do not require approval by the IRBs.

3.3. New and revised (draft) HRPP policies and procedures which are extra-regulatory in nature will be reviewed and approved by the full IRB, the IO, and in select cases, other Organizational officials.

3.4. All new and revised HRPP policies and procedures must be reviewed and approved by the IO and the Assistant Vice-Chancellor for Regulatory Affairs. The Assistant Vice-Chancellor for Regulatory Affairs, in consultation with the IO, will determine when policies also should be reviewed by other Organizational Officials (for example, Compliance Officer, Privacy Officer, General Counsel, and/or Vice Chancellor for Research).

4.0 Full IRB Review of Draft HRPP Policies and Procedures
4.1. New and revised (draft) HRPP policies and procedures requiring review by the full IRB (per section 3.3 above) will either be (1) discussed at all three regularly scheduled IRB meetings as described in section 4.2 below, or (2) subject to an email vote as described in section 4.3 below

4.2. Review at convened IRB meetings

   4.2.1. IRB members will receive a copy of the policy to be reviewed with the detailed meeting agenda in advance of the scheduled IRB meeting.

   4.2.2. All IRB members may 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.
4.2.3. For the vote to be valid, a majority of the entire IRB membership must cast a vote, either in person or by e-mail. For the policy to be approved, a majority of those voting must be attained.

4.2.4. 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 reconsideration.

4.3. Review by email

4.3.1. At the discretion of the IO, the Assistant Vice-Chancellor for Regulatory Affairs, or the IRB Executive Chair, voting procedure by e-mail alone will be allowed for consideration of a policy. In general this procedure should be limited to new policies that represent existing IRB practices, non-major revision of existing policies, or instances where approval of a policy is necessary before the next regularly scheduled meeting.

4.3.2. IRB members will receive by email a copy of the policy to be reviewed, as well as a summary of key points in the new policy, or relevant changes to the existing policy. The email will also describe the deadline for response, and the interpretation of non-response (that is, non-response is considered a vote in favor).

4.3.3. The email will include a “read receipt.”

4.3.4. IRB members may provide written statements in support of their vote or request that the policy be brought to a convened meeting for discussion. The IO has the authority to decide on such requests, based on the nature of the members’ concerns, and the urgency of the policy review.

4.3.5. For the vote to be valid, a majority of the entire IRB membership must cast a vote (or must have opened the email as documented by the “read receipt”). For the policy to be approved, a majority of those voting must be attained.

4.3.6. 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 reconsideration.

5.0 Organizational Notification of Changes to HRPP Policies and Procedures

5.1. Changes to HRPP policies and procedures will be communicated to the Organization’s research community by email, notification on the IRB website at http://unmc.edu/irb, and/or other media as appropriate.

5.2. IRB Administrators and staff will be notified by email and in person at the next staff meeting.

POLICY AMENDED:
- Revised June 28, 2018
- Initial January 25, 2016
1.0 Purpose
The purpose of this policy and procedure is to describe Organization’s requirements for granting signature authority for ORA correspondence.

2.0 Policy
It is the Organization’s policy that the IRB Executive Chair, the IRB Chairs and Vice-Chairs and qualified IRB staff will have appropriate signature authority on behalf of the ORA and the IRB.

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

3.1. 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.

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

3.3. IRB Expedited Reviewers (including IRB Administrators who are also voting IRB members) have the authority to sign: 1) IRB expedited review letters, and 2) other related IRB correspondence as necessary.

3.4. 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, chairs and vice-chairs or other IRB members as necessary and may refer IRB review letters or other correspondence to the IRB Executive Chair for signature.

3.5. Office Assistants have the authority to sign routine ORA correspondence, but not correspondence on behalf of the IRB (such as IRB review letters).
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 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 member of those communities.

3.0 Procedures
3.1. Involvement in Research Design, Implementation and Analysis of Research Results

3.1.1. 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.

3.1.2. 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 provide advice regarding 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:

3.2.1. Omaha Science Café: [http://www.unmc.edu/sciencecafe/](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 didactic presentation, followed by a question and answer period. The science cafes are available via Podcast.

3.2.2. Nebraska Science Festival: [http://www.nescifest.com/](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.

3.2.3. **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.

3.2.4. **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.

3.2.5. **Social Media**

3.2.5.1. University of Nebraska Medical Center: [http://www.facebook.com/unmcedu](http://www.facebook.com/unmcedu)
3.2.5.2. Nebraska Medicine: [http://www.facebook.com/NebraskaMed](http://www.facebook.com/NebraskaMed)
3.2.5.3. Children’s Hospital & Medical Center: [https://www.facebook.com/ChildrensOmaha/](https://www.facebook.com/ChildrensOmaha/)
3.2.5.5. University of Nebraska Omaha: [http://www.facebook.com/unomaha](http://www.facebook.com/unomaha)

3.2.6. **Websites**

The following websites within the Organization are available to the public and contain information about the Organization, including material pertinent to research.

3.2.6.1. University of Nebraska Medical Center:
3.2.6.1.2. [http://www.unmc.edu/cctr/community/cer/index.html](http://www.unmc.edu/cctr/community/cer/index.html)
3.2.6.1.3. [https://www.unmc.edu/newsfeed](https://www.unmc.edu/newsfeed)
3.2.6.2. Nebraska Medicine: [www.nebraskamed.com](http://www.nebraskamed.com)
3.2.6.3. Children’s Hospital & Medical Center: [http://www.childrensomaha.org](http://www.childrensomaha.org)
3.2.6.4. Bellevue Medical Center: [http://www.bellevuemed.com/](http://www.bellevuemed.com/)
3.2.6.5. University of Nebraska Omaha: [http://www.unomaha.edu/spr](http://www.unomaha.edu/spr)

3.3. **UNMC/Nebraska Medicine utilizes the following educational outreach activities:**

3.3.1. **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.

3.3.2. **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.

3.3.3. **Research Subject Advocate Office:** [http://unmc.edu/vcr/policies/regulation/rsa0.html](http://unmc.edu/vcr/policies/regulation/rsa0.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.

3.3.4. "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.

3.3.5. “Ask UNMC” on KETV Channel 7

3.3.6. “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.

3.3.7. “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.

3.3.8. 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. CHMC utilizes the following educational outreach activities:

3.4.1. IRB Brochure: A brochure titled “Participating in Clinical Trials” is provided to CHMC 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.

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

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

3.5. Evaluation of Outreach Activities

The ORA, 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:
BRUCE G. GORDON, MD  IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS
CHRISTOPHER KRATOCHVIL, MD  INSTITUTIONAL OFFICIAL

POLICY AMENDED:
• REVISED FEBRUARY 12, 2018
• INITIAL APRIL 14, 2016
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for post approval monitoring of research.

2.0 Policy
2.1. It is the policy of the Organization that a Post Approval Monitoring Program will be conducted in order to measure, maintain, and improve human subject research protection effectiveness, quality and compliance with all applicable regulations and HRPP policies.

2.2. It is the policy of the Organization that the Post Approval Monitoring 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 Post Approval Monitoring 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:
   3.4.1. Individualized training to meet the specialized needs of specific PIs and their research personnel.
   3.4.2. 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 Post Approval Monitoring.

4.0 Procedures
4.1. Study Selection Criteria
   4.1.1. Not-For-Cause Monitoring of Non-Exempt Research
      4.1.1.1. Categories of non-exempt research that will be considered for Post Approval Monitoring will be randomly selected, in order of priority listed below:
         4.1.1.1.1. Investigator-initiated research
         4.1.1.1.2. Research which would meet the criteria for increased monitoring and/or interim continuing review per HRPP policy 3.1 (Assessing the Need for Increased
Monitoring, Interim Continuing Review, and Verification from Sources Other than the PI).

4.1.1.1.3. Research involving vulnerable populations
4.1.1.1.4. Greater than minimal risk research
4.1.1.1.5. Research conducted under emergency waiver of informed consent (FDA regulations at 21 CFR 50.24)
4.1.1.1.6. Minimal risk research

4.1.1.2. Selected research must be currently IRB-approved and normally have been actively accruing subjects for at least one year.

4.1.2. For-Cause Post Approval Audit

4.1.2.1. “For-Cause” audit will generally be scheduled based upon recommendation by the IO, IRB Executive Chair, or the IRB. Indications for audit include, but are not limited to:

4.1.2.1.1. Noncompliance (as per HRPP policy 8.4: Review of Noncompliance Involving the PI and Study Personnel).
4.1.2.1.2. Errors, inconsistencies, omissions in continuing review (HRPP policy 2.7: Continuing Review of Research) or AE/UP reporting (HRPP policies 8.1: IRB Review of Adverse Events and Adverse Device Effects and 8.3: IRB Review of Unanticipated Programs Involving Risk to the Subject or Others).
4.1.2.1.3. Complaints (as per HRPP policy 8.2: IRB Review of Study Related Complaints).

4.1.3. Monitoring reports issued by outside agencies (pharmaceutical sponsors, FDA, OHRP or others) that revealed or suggested problems areas.

4.2. Post Approval Monitoring Process

4.2.1. Post Approval Monitoring will generally be performed by a designated IRB Administrator. Other IRB representatives may be included as necessary.

4.2.2. “Not-For-Cause” Audits

4.2.2.1. It is expected that at least twelve non-exempt studies will be selected for “Not-For-Cause” audit per year, however the actual number of audits will be contingent on available manpower

4.2.2.2. The Post Approval Monitoring visit will be scheduled at a time mutually acceptable to the PI and the designated IRB Administrator. Unannounced visits will not occur.

4.2.2.3. Prior to the Post Approval Monitoring visit, the PI will be informed, in writing, that a Post Approval Monitoring 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 Post Approval Monitoring of On-Going Research to be completed by the designated IRB Administrator during the visit.

4.2.2.4. 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 Post Approval Monitoring visit.
4.2.2.5. Visits must occur within 30 days of notification, unless delay is approved by the IRB Executive Chair.

4.2.2.6. Failure to comply with the Post Approval Monitoring Request constitutes non-compliance subject to HRPP policy 8.4 (Review of Noncompliance Involving the PI and Study Personnel).

4.2.2.7. The designated IRB Administrator will utilize the Checklist for Post Approval Monitoring of On-Going Research during review of investigator records.

4.2.2.8. 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. All subjects who have agreed must give written informed consent in advance by signing the Consent for IRB Observation of the Informed Consent Process. The designated IRB Administrator will utilize the IRB Observation of Consent Process Form to evaluate the process of consent.

4.2.2.9. Failure of the investigator or the research staff to cooperate with PAM, or interference with PAM by the investigator or the research staff, constitutes serious noncompliance subject to HRPP policy 8.4 (Review of Noncompliance Involving the PI and Study Personnel).

4.2.2.10. Following completion of the Post Approval Monitoring visit, the designated IRB Administrator will present preliminary findings to the investigator and/or staff, obtain additional clarifications and corrections, and provide education concerning IRB requirements as needed.

4.2.2.11. The designated IRB Administrator will prepare a written report of the PAM visit, including, as needed, a request for a corrective action plan. The written report will be given to the investigator, the IRB Executive Chair, and the IO.

4.2.2.12. The designated IRB Administrator, in consultation with the IO and the IRB Executive Chair, will evaluate the PAM report and the investigator’s corrective action plan, if provided.

4.2.2.12.1. Reports which suggest serious noncompliance or other concerns will be referred to the IRB for review in accordance with HRPP policy 8.4 (Review of Noncompliance Involving the PI and Study Personnel).

4.2.2.12.2. Reports which demonstrate few or no deficiencies, and/or the use of “best practices” will be reported to the IRB as a notification item, and will be communicated to the investigator.

4.2.2.13. The Post Approval Monitoring 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.

4.2.3. “For-Cause” Audit

“For-Cause” audits will follow the same procedure as above, except that unannounced visits may occur if authorized by the IO, and all PAM reports will be reviewed by the convened IRB.
ADMINISTRATIVE APPROVAL:
BRUCE G. GORDON, MD  IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS
CHRISTOPHER KRATOCHVIL, MD  INSTITUTIONAL OFFICIAL

POLICY AMENDED:
- Revised February 28, 2018
- Initial December 14, 2015 (Original title “Quality Improvement Assessment for the Conduct of Research”)
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

3.1.1. HRPP policies and procedures will be assessed on an ongoing basis by the IO, IRB Executive Chair and IRB staff.

3.1.2. Organizational officials may bring problems, or suggestions for improvement, to the attention of the IO and IRB Executive Chair for appropriate action.

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

3.1.4. Metric data on HRPP efficiency will be discussed in the ORA as well as at IRB staff meetings. These data will be provided to the IO, IRB Executive Committee and other Organizational officials as requested.

3.1.5. 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 (Full IRB Review) and OHRP Draft Guidance “Minutes of Institutional Review Board (IRB) Meetings: Guidance for Institutions and IRBs” (dated November, 2015)

3.1.6. 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.

3.1.6.1. The IRB Executive Chair and IRB Administrators will schedule focus group discussions with Investigators from UNMC, UNO, and CHMC to discuss the effectiveness of the HRPP, including policies, quality of IRB review, and efficiency of the IRB and other components of the HRPP.

3.1.6.2. 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.
3.1.6.3. PIs and other study personnel may utilize the “Report a Problem or Complaint” tab on the UNMC IRB website that provides access University of Nebraska EthicsPoint, which allows anonymous comments to the IRB.

3.1.7. 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

3.2.1. 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.

3.2.2. The IO will obtain feedback submitted from the IRB Members and IRB administrators via focus group discussion held annually (during or following a scheduled IRB-01, IRB-02, and IRB-04 meeting). This focus group may be mediated by the IO or one or more IRB Administrators, without the Executive Chair present.

3.2.3. If the IRB Executive Chair’s performance is judged to be deficient, the IO will discuss his/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.

3.3. Evaluation of the Chairs and Vice-Chairs

3.3.1. The IRB Executive Chair will review the performance of the IRB Chairs and Vice-Chairs on an annual basis utilizing the following criteria:

3.3.1.1. Attendance at meetings
3.3.1.2. Chairing IRB meetings
3.3.1.3. Completeness of reviews
3.3.1.4. Service on IRB subcommittees
3.3.1.5. Feedback submitted from the IRB Members and IRB administrators via focus group discussion held annually (during or following a scheduled IRB-01, IRB-02, and IRB-04 meeting). This focus group may be mediated by the IO, the Executive Chair, or one or more IRB Administrators, without the Chairs or Vice-Chairs present.
3.3.1.6. Creative recommendations which help improve the HRPP.

3.3.2. If an IRB Chair or Vice-Chair’s performance is judged to be deficient, the IRB Executive Chair will discuss his/her concerns with the Chair or 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 Chair or Vice-Chair.

3.4. Evaluation of IRB Members

3.4.1. The IRB Executive Chair will convene a meeting with the IRB Administrators and staff to evaluate the IRB Members using the following:

3.4.1.1. Metric data for individual IRB members based on the following criteria:
3.4.1.1.1. Attendance at meetings for which they have been assigned review items
3.4.1.1.2. Timeliness and completeness of IRB reviews
3.4.1.1.3. Participation in IRB discussions
3.4.1.1.4. Service on IRB subcommittees
3.4.1.1.5. Completion of required Continuing Education.

3.4.1.2. Individual Feedback to IRB Members
   
3.4.1.2.1. IRB members will be provided feedback regarding their service.
   
3.4.1.2.2. 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.
   
3.4.1.2.3. If an IRB member’s service is judged to be satisfactory or exceptional, the IRB Executive Chair will so inform the member.

3.4.2. 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.

3.4.3. 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.

3.5. Evaluation of IRB Administrators and Staff

3.5.1. The Assistant Vice-Chancellor for Regulatory Affairs will evaluate the performance of the IRB Administrators utilizing the UNMC Employee Evaluation Form and feedback submitted from the IRB Members via focus group discussion held annually (during or following a scheduled IRB-01, IRB-02, and IRB-04 meeting). This focus group may be mediated by the IO, or the Executive Chair, without the IRB Administrators present.

3.5.1.1. The Assistant Vice-Chancellor for Regulatory Affairs will provide feedback verbally to each IRB Administrator during the annual review process, as well as written comments on the UNMC Performance Evaluation Form.

3.5.1.2. The Assistant Vice-Chancellor for Regulatory Affairs will also provide ongoing feedback about the performance of the IRB Administrators throughout the year.

3.5.2. The supervising IRB Administrator will evaluate the performance of the IRB staff utilizing the UNMC Employee Evaluation.

3.5.2.1. 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.

3.5.2.2. The supervising IRB Administrator will also provide on-going feedback about the performance of the IRB staff throughout the year.

3.6. Annual Evaluation of the HRPP

Each component of the HRPP will conduct a self-assessment utilizing the Annual HRPP Assessment Form. The IO in conjunction with the Assistant Vice-Chancellor for Regulatory Affairs and any other personnel deemed appropriate will review each component’s Annual HRPP Assessment Form with the objective to:

3.6.1. Determine which items on the Annual HRPP Assessment Form are judged to be:

3.6.1.1. Excellent (E) or Satisfactory (S).

3.6.1.2. Unsatisfactory (US). The item requires a corrective action plan with set goal(s) in a time frame based upon the seriousness of the deficiency.
3.6.2. Determine which items rated Excellent or Satisfactory are to be targeted for further improvement before the next evaluation, and to set specific goals dependent upon available staff and resources.

3.6.3. Accomplishment of the goals arising out of the HRPP Evaluation will be evaluated by the IO in conjunction with the appropriate personnel in accordance with the corrective action and specified time frame.

ADMINISTRATIVE APPROVAL:
BRUCE G. GORDON, MD  IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS
CHRISTOPHER KRATOCHVIL, MD  INSTITUTIONAL OFFICIAL

POLICY AMENDED:
- REVISED FEBRUARY 2, 2018
- INITIAL APRIL 14, 2016
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements and opportunities for training for all personnel involved in conducting human subject research.

2.0 Policy
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.

3.0 Definitions
3.1. **Biomedical Research** is defined (as per HRPP policy 1.8: Investigational Activities Requiring IRB Review & Approval, section 4.1) as 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. Biomedical research includes:

3.1.1. Clinical trial using a drug, medical device, technique or other intervention or strategy (including non-physical means, like diet, cognitive therapy, etc.) to diagnose, treat or otherwise study a particular condition or disease

3.1.2. Non-clinical biomedical research to study normal or abnormal physical or physiologic processes (for example, gait and balance testing, biomechanical assessments). For the purpose of this policy “Biomedical Research” includes Human Biological Material Research and Medical Records Research (per HRPP policy 1.8: Investigational Activities Requiring IRB Review & Approval, sections 4.2 and 4.3 respectively)

3.2. **Social Science and Behavioral Research** is defined (as per HRPP policy 1.8: Investigational Activities Requiring IRB Review & Approval, section 4.4) as research performed with intent to study behaviors, attitudes and interactions and social processes 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.

4.0 Procedures
The Organization utilizes the following education and training methods for research personnel:

4.1. **Collaborative Institutional Training Initiative (CITI)**

4.1.1. Training in the protection of human subjects is primarily accomplished through completion of this web-based training program. CITI training is required for all investigators and research staff conducting non-exempt research who (a) participate in the process of consent, (b) have contact with subjects, or (c) have access to identifiable private information or identifiable biospecimens. In addition, Faculty Advisors of student investigators are required to be CITI trained.
4.1.2. The CITI Training Program is accessible via [http://www.citiprogram.org](http://www.citiprogram.org), or through a link on the UNMC IRB website ([http://www.unmc.edu/irb](http://www.unmc.edu/irb)).

4.1.3. CITI training course requirements

4.1.3.1. The Biomedical course must be completed by:

4.1.3.1.1. UNMC, CHMC, Nebraska Medicine, BMC and UNO personnel listed in section 3.1.1 who conduct non-exempt biomedical research within the Organization or at external sites where the UNMC IRB serves as the IRB of record.

4.1.3.1.2. Research personnel not associated with the Organization listed in section 3.1.1 who conduct non-exempt biomedical research within the Organization at external sites where the UNMC IRB is the IRB of record.

4.1.3.2. The Behavioral and Social Science course must be completed by:

4.1.3.2.1. UNMC, CHMC, Nebraska Medicine, BMC and UNO personnel listed in section 3.2 who conduct non-exempt Behavioral and Social Science research within the Organization or at external sites where the UNMC IRB serves as the IRB of record.

4.1.3.2.2. Research personnel not associated with the Organization listed in section 3.2 who conduct non-exempt Behavioral and Social Science research within the Organization at external sites where the UNMC IRB is the IRB of record.

4.1.3.3. The GCP (Good Clinical Practice) course must be completed by:

4.1.3.3.1. UNMC, CHMC, Nebraska Medicine, BMC and UNO personnel listed in section 3.1.1 who conduct a clinical trial funded by NIH. For the purpose of this policy, “clinical trial” is defined as “a research study in which one or more human participants are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes” (per NIH Policy NOT-OD-15-015)

4.1.3.3.2. UNMC, CHMC, Nebraska Medicine, BMC and UNO personnel listed in section 3.1.1 who conduct research utilizing an FDA regulated drug, device or biologic.

4.1.4. All research personnel must be CITI trained prior to IRB approval of initial research applications.

4.1.5. New research personnel listed in Section 3.0 added to IRB-approved research via a Request for Change or Application for Continuing Review must complete CITI training prior involvement in the research

4.1.6. The Organization will accept CITI Training records from other institutions if the other institution utilized the CITI training courses specified in Section 4.1.3 above. A copy of any training record must be provided to the ORA.

4.1.7. On a case by case basis, the Organization may accept other forms of Human Subject protection, or GCP training, instead of CITI, provided such training is substantively similar, was completed at a site that did not participate in the CITI Program, and had been completed in the previous three years. The Executive Chair, in consultation with the IO as needed, will have the sole authority to accept such training.

4.1.8. The Organization will accept other certificates of training from external organizations for external research personnel conducting non-exempt biomedical research at external sites
where the UNMC IRB is the IRB of record. The PI must certify that all external research personnel have completed appropriate training.

4.1.9. The Organization requires a passing score of 75% to receive credit for CITI training.

4.1.10. CITI training (including GCP Training) must be renewed every three years from the original date of completion. Training must be up to date for the individual to be listed on new IRB applications or added to existing IRB-approved applications, in the roles defined in Section 4.1.3.

4.2. **UNMC IRB Website**

4.2.1. Research personnel can access the IRB website at [http://www.unmc.edu/irb](http://www.unmc.edu/irb).

4.2.2. The HRPP Policy Manual is posted on the IRB website. When policies are updated, a Summary of Changes will be included with the HRPP Policy Manual.

4.2.3. 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.

4.2.4. IRB Staff will periodically post access to relevant presentations and other educational materials on the IRB website.

4.3. **IRB Education Series**

The IRB Education Series is scheduled on a regular basis, and research personnel within the Organization are notified in advance. The series consists of didactic presentations relevant to the protection of human subjects of research. Some presentations will subsequently be made available on the IRB or other Organization websites.

4.4. **“HRPP: Working Together” Bulletins**

The bulletins are issued electronically on regular intervals and contain practical information from HRPP policies, often in a question and answer format.

4.5. **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. Research personnel within the Organization are notified in advance.

4.6. **Student Education**

Didactic classroom presentations are offered to UNMC and UNO students on topics pertaining to human subject protection by request.

4.7. **Webinars**

The ORA facilitates access to webinars sponsored by external organizations on topics relevant to Human Subject Research.

4.8. **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.

4.9. **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 within the Organization.
4.10. **Conflict of Interest Training**

Conflict of Interest Training is required in accordance with UNMC Conflict of Interest policy #8010 and HRPP policy 1.25 (Financial Conflicts of Interest).

4.11. **Annual Regional Conference (“Hot Topics in the Protection of Human Subjects”)**

The Regional Conference, produced in collaboration with the Great Plains Health Research Consortium, and partially funded by the Great Plains IDeA-CTR Network, brings together national and local speakers for a day-long conference exploring cutting edge topics in human research subject protection. The conference has been occurred annually since 2010. The target audience is IRB administrators and staff, IRB members, investigators and research coordinators.

5.0 **Procedures for Assessing Training Requirements and Opportunities**

5.1. At regular intervals, the Assistant Vice-Chancellor for Regulatory Affairs, the Executive Chair, the IO and the ORA will re-evaluate the specific training and requirements for research personnel associated with the Organization. This assessment will include and consider:

5.1.1. Review of the current literature and evolving federal guidance regarding various aspects of research ethics and human subject protection.

5.1.2. Feedback from research personnel regarding their training needs.

5.1.3. Assessment of the quality and completeness of IRB submissions by IRB members and the IRB Administrators

5.1.4. Implementation of new IRB requirements, which require training.

6.0 **Procedures for Maintaining Training Records**

The ORA maintains all training records for CITI Training and didactic activities described above, and maintains copies of materials sent by mail or email or posted on the website.
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for training for IRB members and alternates.

2.0 Policy
It is the policy of the Organization that IRB members and alternates will be qualified through initial and continuing education in order to fulfill their responsibility to protect the rights and welfare of human subjects.

3.0 Definitions
3.1. CITI (Collaborative Institutional Training Initiative) available through www.citiprogram.org or through the IRB website (http://unmc.edu/irb).

4.0 Initial Training and Orientation
4.1. New IRB members, including alternate members, will meet with the IRB Executive Chair or designee, and appropriate IRB Administrators for orientation to cover the following items:
   4.1.1. Overview of HHS and FDA regulations
   4.1.2. HRPP overview
   4.1.3. Structure of IRB meetings
   4.1.4. Responsibilities of IRB members
   4.1.5. Overview of the Research Support System (RSS).
4.2. New IRB members are provided with the following documents, or a link to those documents on-line, for example, via the UNMC IRB website (http://www.unmc.edu/irb/research-education/regulatory-sites.html).
   4.2.1. Belmont Report
   4.2.2. Declaration of Helsinki
   4.2.3. HHS Regulations at 45 CFR 46
   4.2.4. FDA Regulations at 21 CFR 50, 56, 312, 812, 814
   4.2.5. Categories of Expedited Review
   4.2.6. HRPP policies and procedures
4.3. New IRB members and alternates who also act as investigators or research personnel will be required to complete CITI training (including GCP as appropriate) as per HRPP policy 1.23 (HRPP Training Requirements and Opportunities for Research Personnel). For new IRB members and alternates who do not act as investigators or research personnel, orientation (as described above) will be considered the equivalent of initial CITI training.
4.4. New IRB members are invited to attend an IRB meeting as a guest during the orientation period.

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

4.6. New IRB members are assigned an experienced IRB member as a mentor, to provide assistance as necessary.

5.0 Continuing Education

5.1. 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.

5.2. IRB members are expected to participate in continuing education which may be obtained through any or all of the following mechanisms:

   5.2.1. In-service training at IRB meetings.
   5.2.2. Training workshops/webinars.
   5.2.3. Regional IRB conferences.
   5.2.4. Review of publications distributed by the ORA at IRB meetings or via email.
   5.2.5. Review of new information affecting the HRPP such as new laws and regulations, new OHRP/FDA guidance documents, and new or revised HRPP policies distributed by the ORA via email or at IRB meetings.

5.3. Completion of required continuing education will be reviewed with IRB members at the time of their annual evaluation (see HRPP policy 1.22: Assessment of the Effectiveness and Efficiency of the IRB). Members who remain deficient after this review may have their appointment terminated.

6.0 Training Records

The ORA will maintain initial and continuing education training records, and copies of materials distributed to members or presented at IRB meetings. The ORA will maintain all training records for CITI Training by IRB members.

Administrative Approval:

Bruce G. Gordon, MD  IRB Executive Chair & Assistant Vice Chancellor for Regulatory Affairs
Christopher Kratochvil, MD  Institutional Official

Policy Amended:

- Revised February 1, 2018
- Initial December 28, 2015
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 of interest (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 (1) within the premises of the Organization, or (2) by any faculty, students, staff or other representatives of the Organization, or by 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; d) University of Nebraska Board of Regents Policies #3.2.8.10 and #4.4.2, e) 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. It is the policy of the Organization that the IRB will interact with the COI Officers, Conflict of Interest Committees (COICs), and/or senior administrators of the applicable components of the Organization who are responsible for compliance and/or COI, 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. It is the policy of the Organization that any changes in financial interest must be promptly disclosed and managed in accordance with Section 2.1 above.

2.4. It is the policy of the Organization that 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 any faculty, students, staff or other representatives of the Organization 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: Principal Investigator, 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.

3.4.1. Financial interests not considered in the determination of “significant financial interest include (1) salary or other remuneration from the Organization, (2) income from seminars, lectures, or teaching engagements sponsored by governmental entities, and (3) income from service on advisory committees or review panels for governmental entities.

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. **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.

3.7. **COI Committee (COIC)**: the Committee 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. If a component of the organization does not have a committee per se, COIC hereinafter will mean the Conflict of Interest Officer, or the senior administrator of the applicable components of the Organization who are responsible for compliance and/or COI.

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, at a minimum, an appropriate disclosure of the presence of a financial COI of the Responsible Person(s) in the consent form, as well as in any presentations, publications, or news articles regarding the research.

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:

5.2.1. More frequent monitoring of the research.

5.2.2. Independent monitoring of the research.
5.2.3. 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.

5.2.4. Designation of a peer or supervising co-investigator with no COI in the project to assume the lead investigative role.

5.2.5. Monitoring of the consent process.

5.2.6. 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.

5.2.7. Severing relationships existing between the Covered Person and the company or other entity that is the source of the COI.

5.2.8. Removing contract terms which create the COI.

5.2.9. Disqualification of the Covered Person from participation in all or a portion of the research (e.g., may not obtain informed consent or analyze data).

5.2.10. Any additional management strategies as determined by the appropriate COIC and/or the IRB.

5.3. The following are prohibited:

5.3.1. Any arrangement where the value of ownership interests will be affected by the outcome of the research.

5.3.2. 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 full IRB will be provided with the COI management plan approved by the COIC.

6.2. The COI Officer, the IRB Executive Chair, the IRB chair or designee will verbally describe the nature of the financial interest, and the specifics of the management plan proposed by the COIC. 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 proposed by the COIC before the protocol is approved and released, or may require a more stringent COI management plan. The IRB may not adopt a less stringent plan than that approved by the COIC.

6.4. The IRB’s COI Management plan may be reviewed by Organizational officials, who may require a more stringent COI management plan. The Organization may not adopt a less stringent plan than that approved by the IRB.

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 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, or any of its component parts, 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.

9.4. Organizational COI may be identified through the required disclosure of financial interest of the Responsible Personnel at the time the IRB application is submitted.

9.5. Organizational COI may be identified through the required annual disclosure of financial interest of senior administrators when it relates to human subject research.

9.6. Organization COI may be identified by technology transfer officials or other officials at UNMC, UNO, and CHMC.

9.7. If an Organizational COI is identified the COI Officer of the involved component shall convene a group of senior Organizational officials and unaffiliated individuals, appointed by the appropriate Chancellor, CEO or designee, to review the potential Organizational COI and propose any required management plans for approval.

9.8. The COI Officer will provide the full IRB with the COI committee’s approved COI Management Plan.

9.9. The COI Officer or the IRB Executive Chair/designee will describe the nature of the financial interest, and the specifics of the management plan proposed by the COIC.

9.10. 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.

9.11. The IRB must be assured that any Organizational COI is appropriately managed in the interest of the safety and welfare of human subjects.

9.12. Organizational COI management plans approved by the IRB will be maintained in the ORA for no less than seven years following cessation of the activity.
POLICY AMENDED:
- Revised June 13, 2018
- Initial April 14, 2016 (Previous Policy #3.12)
1.0 Purpose

The purpose of this policy and procedure is to describe 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 (Human Research Protection Program).

3.0 Definitions

3.1. Investigator is defined broadly by the Organization as an individual who actually conducts human subject research as either a Principal Investigator (PI) or a Secondary Investigator (SI).

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:

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

3.1.2. Obtaining identifiable private information about living individuals for research purposes.

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

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

3.2. Principal Investigator (PI) is 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.

3.3. Secondary Investigator (SI) is an individual who shares responsibility with the PI for the safe and proper conduct of the research in full compliance with all applicable regulations and UNMC HRPP policies.

3.4. External Investigator (XI) is an investigator who is not employed by or otherwise representing the Organization who is engaged in research for which the UNMC IRB is the IRB of record.

3.4.1. A researcher employed or otherwise representing another institution who is under the jurisdiction of another IRB which has a reliance agreement with UNMC and for which the UNMC is acting as a central or single IRB is NOT considered an XI (per HRPP policy 1.28; External Investigator Assurance).
3.5. **Investigational New Drug** is a new drug or biologic that is used in a clinical investigation (21 CFR 312.3(b))

3.6. **Investigation New Drug Application (IND)** is an application submitted to FDA to conduct a clinical investigation with an investigational new drug.

3.7. **Investigational Device** is a device, including a transitional device, which is the object of the investigation.

3.8. **Investigational Device Exemption (IDE)** is an application submitted to FDA to conduct a clinical investigation with an investigational device that is classified as a significant risk device (SRD).

3.9. **Sponsor-Investigator** is the individual, who initiates the research, assumes overall responsibility for the research as indicated in section 3.2 above and also fulfills the FDA-required responsibilities of a sponsor.

3.10. **External Investigator Assurance (XIA)** is 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 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.

4.2.1. When a student or trainee is the PI, a researcher sufficiently experienced in the area of the trainee’s research interest must serve as a co-investigator for research and be jointly responsible for oversight of the research.

4.2.2. A student may not serve as the PI of a study which involves the administration or use of an FDA regulated drug, device or biologic.

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 detailed protocol, the IRB application, 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 (Human Research Protection Program)*.

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 1.23 (HRPP Training Requirements and Opportunities for Research Personnel)*.
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 disclose, and assure that responsible personnel and other covered persons disclose potential financial COI, in accordance with HRPP policy 1.25 (Financial Conflicts of Interest) and Organizational policies.

5.11. The PI will ensure risks to subjects and others have been minimized to the greatest extent possible, as per HRPP policy 3.2 (Data and Safety Monitoring).

5.12. The PI will ensure the protocol contains a plan for just, fair, and equitable recruitment and selection of subjects.

5.13. The PI will ensure the protocol contains adequate provisions for monitoring the data collected to ensure the safety of subjects.

5.14. The PI will ensure there are adequate provisions to protect the privacy of subjects and the confidentiality of data, as per HRPP policy 3.3 (Privacy Interests and Confidentiality of Research Data).

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 46.108(a)(3)(iii) 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 (IRB Review of Changes in Previously Approved Research).

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 (IRB Review of Changes in Previously Approved Research).

5.18. The PI is responsible for informing all study personnel and participating sites (as applicable) of IRB approved modifications in the protocol, IRB application, and/or consent form.

5.19. The PI will ensure that when some or all of the subjects are likely to be vulnerable to coercion or undue influence, additional safeguards have been included in the study to protect the rights and welfare of these subjects in accordance with HRPP policy 4.1 (Additional Protections for Vulnerable Populations).

5.20. 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 (Obtaining Informed Consent From Research Subjects).

5.21. 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.

5.22. The PI will ensure that all secondary investigator(s) and other study personnel promptly report to the PI the following as applicable:

   5.22.1. Internal Adverse Events which are unexpected and related, or possibly related, to the study interventions, and Unanticipated Adverse Device Effects, per HRPP policy 8.1 (IRB Review of Adverse Events and Adverse Device Effects).

   5.22.2. Unanticipated problems involving risk to the subject or others, per HRPP policy 8.3 (IRB Review of Unanticipated Problems Involving Risk).

   5.22.3. Noncompliance, per HRPP policy 8.4 (Review of Noncompliance)

   5.22.4. Complaints, per HRPP policy 8.2 (IRB Review of Study Related Complaints)

5.23. The PI will ensure that all of the incidents listed under Section 5.20 above are reported to the IRB in accordance with the applicable HRPP policies.

5.24. 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.

5.25. The PI, or a qualified person(s) designated by the PI, shall conduct periodic audits of research records.

5.26. The PI is responsible for the accuracy, completeness, legibility, and timeliness of the data recorded and reported in presentations and publications about the research.

5.27. The PI will fulfill registration and reporting requirements of ClinicalTrials.gov in compliance with HHS regulations at 42 CFR 11 (Final Rule for Clinical Trials Registration and Results Information Submission), and the NIH Policy on the Dissemination of NIH-Funded Clinical Trial Information.

5.28. 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.

5.29. 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.

5.30. Upon completion of the research (or premature closure of the study), the PI will provide the IRB with the Study Completion Report and will provide the funding and regulatory agencies with any required reports.

5.31. 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.

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:

6.3.1. IRB initial review
6.3.2. IRB continuing review
6.3.3. IRB review of amendments
6.3.4. Consent requirements
6.3.5. HIPAA requirements
6.3.6. Information security including the confidential collection and transmission of data
6.3.7. Reporting requirements for:
   6.3.7.1. Unanticipated problems involving risks to the subject or others
   6.3.7.2. Adverse events
   6.3.7.3. Noncompliance
   6.3.7.4. Complaints

6.4. The PI will ensure that all external investigators promptly report to the PI the following (as applicable):

6.4.1. Adverse Events which are unexpected, related or possibly related to the research.
6.4.2. Unanticipated Adverse Device Effects
6.4.3. Unanticipated problems involving risk to the subject or others
6.4.4. Noncompliance
6.4.5. Complaints
6.4.6. Audits by sponsors, CRO's, FDA, OHRP, or other federal authorities,
6.4.7. Study reports as required by the protocol,
6.4.8. Continuing review reports
6.4.9. Interim results
6.4.10. DSMB results

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:

6.7.1. The IRB application identifies the external sites.
6.7.2. A copy of all of the following documents from the external sites are maintained in the research records:
6.7.2.1. A copy of the external IRB approval letter(s) and approved ICF(s)/information sheet(s).

6.7.2.2. The external site’s FWA number (required for HHS funded research)

6.7.2.3. The external site’s IRB Registration number (required for FDA registered research)

6.7.2.4. 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:

6.8.1. Compliance with HRPP policy 1.3 (UNMC IRB Serving as Central IRB).

6.8.2. The IRB application identifies the external site(s).

6.8.3. An ICF is developed for each site deferring to UNMC IRB review.

6.8.4. The research records contains:

6.8.4.1. Signed copies of each signed External Investigator Assurance (XIA).

6.8.4.2. A copy of each external investigator’s Curriculum Vitae (CV).

6.8.4.3. 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 requirements of the external IRB.

7.2. The PI will fulfill all applicable requirements specified in HRPP policy 1.4 (UNMC IRB Ceding Review to an External IRB), and as described in the Reliance Agreement.

8.0 Additional Responsibilities of the PI During Conduct of FDA Regulated Research

Note: FDA guidance regarding investigator responsibilities can be found in “Investigator Responsibilities - Protecting the Rights, Safety, and Welfare of Study Subjects” (October 2009)

8.1. For clinical investigations involving an investigational drug, the PI is responsible for ensuring that the conditions of 21 CFR 312.60, 61, 62, 64, 66, 68, and 69, are met:

8.1.1. Ensure that an investigation is conducted according to the signed investigator statement, the investigational plan, and applicable regulations; for protecting the rights, safety, and welfare of subjects under the investigator’s care; and for the control of drugs under investigation (21 CFR 312.60).

8.1.2. Ensure that informed consent is obtained in accordance with the provisions of 21 CFR 50. (21 CFR 312.60)

8.1.3. Ensure control of the investigational drug in accordance with 21 CFR 312.61.

8.1.4. Prepare, maintain and retain records in accordance with 21 CFR 312.62 and Nebraska State Law per HRPP policy 1.17 (Retention of Research Records).

8.1.5. Report to sponsor in accordance with 21 CFR 312.64.

8.1.6. Assure that the IRB complies with 21 CFR 56 (21 CFR 312.66)
8.1.7. Report to the IRB all changes in the research activity and all unanticipated problems involving risk to human subjects or others; and not make any changes in the research without IRB approval, except where necessary to eliminate apparent immediate hazards to human subjects (21 CFR 312.66)

8.1.8. Allow inspection of investigator's records and reports by FDA, in accordance with 21 CFR 312.68.

8.1.9. Handle controlled substances in accordance with 21 CFR 312.69.

8.2. For clinical investigations involving an investigational device the PI is responsible for ensuring that the conditions of CFR 812.100 and 110 are met:

8.2.1. Ensure that an investigation is conducted according to the signed agreement, the investigational plan and applicable FDA regulations, for protecting the rights, safety, and welfare of subjects under the investigator’s care, and for the control of devices under investigation (21 CFR 812.100)

8.2.2. Ensure that informed consent is obtained in accordance with the provisions of 21 CFR 50 (21 CFR 812.100).

8.2.3. Not request the written informed consent of any subject to participate, and not allow any subject to participate before obtaining IRB and FDA approval (21 CFR 812.110(a)).

8.2.4. Conduct the investigation in accordance with the signed agreement with the sponsor, the investigational plan, applicable FDA regulations, and any conditions of approval imposed by an IRB or FDA (21 CFR 812.110(b))

8.2.5. Permit use of the investigational device only with subjects under the investigator’s supervision (21 CFR 812.110(c)).

8.2.6. Disclose financial information to sponsor, as required per 21 CFR 54 (21 CFR 812.110(d)).

8.2.7. Dispose of remaining devices per 21 CFR 812.110(e).

8.3. For clinical investigations subject to ICH GCP the investigator is responsible for requirements of ICH E6 (Guideline for Good Clinical Practice) section 4.

8.4. The PI is responsible for ensuring all study personnel:

8.4.1. Read and understand the information in the Investigator's Brochure, including the potential risks and side effects of the drug or device.

8.4.2. Ensure 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.

8.4.3. Control drugs, biological products, and devices according to FDA regulations.

8.5. 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.

9.0 Additional Responsibilities of a Sponsor-Investigator under an Investigator-Initiated IND

9.1. When the investigator also acts as a sponsor for a clinical investigation involving an investigational drug he/she must submit a signed assurance that he/she understands and accepts his/her obligations per FDA regulations (21 CFR 312) (see Addendum O).

9.2. When the investigator also acts as a sponsor for a clinical investigation involving an investigational device, in addition to all responsibilities as investigator as above, he/she is also responsible for ensuring that the following regulatory obligations are met:

9.2.1. General responsibilities, including select qualified investigators, provide them with the information they need to conduct an investigation properly, ensure proper monitoring of the investigation(s), ensure that the investigation(s) is conducted in accordance with the general investigational plan and protocols contained in the IND, maintain an effective IND with respect to the investigations, and ensure that FDA and all participating investigators are promptly informed of significant new adverse effects or risks with respect to the drug (21 CFR 312.50).

9.2.2. Select qualified investigators and monitors, who make the required assurances and commitments as per 21 CFR 312.53.

9.2.3. Keep each participating investigator informed of new observations discovered by or reported to the sponsor on the drug, particularly with respect to adverse effects and safe use, as per 21 CFR 312.55.

9.2.4. Monitor the progress of the clinical investigation (21 CFR 312.56)

9.2.5. Monitor the compliance of investigators and respond accordingly, including ending the investigator’s participation in the clinical investigation, in accordance with 21 CFR 312.56.

9.2.6. Review and evaluate the evidence relating to the safety and effectiveness of the drug, and make reports to the FDA regarding the safety of the drug and the progress of the investigation (21 CFR 312.56)

9.2.7. Discontinue the investigation if he/she determines that the investigational drug presents an unreasonable and significant risk to subjects, and notify FDA, all institutional review boards, and all investigators, and assure the disposition of all stocks of the drug outstanding (21 CFR 312.56)

9.2.8. Maintain and retain adequate records as described in 21 CFR 312.57, and allow FDA access to such records, as per 21 CFR 312.58.

9.2.9. Handle controlled substances in accordance with 21 CFR 312.59.

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 such evaluation 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.
10.0 Additional Responsibilities of a Sponsor-Investigator under an Investigator-Initiated IDE

10.1. When the investigator also acts as a sponsor for a clinical investigator involving an investigational device he/she must submit a signed assurance that he/she understands and accepts his/her obligations per FDA regulations (21 CFR 812) (see Addendum P).

10.2. When the investigator also acts as a sponsor for a clinical investigator involving an investigational device, in addition to all responsibilities as investigator as above, he/she is also responsible for ensuring that the following regulatory obligations are met:

10.2.1. General Duties (21 CFR 812.40), including submitting an IDE to the FDA in accordance with the requirements of 21 CFR 812.20.

10.2.2. Selection of Investigators (21 CFR 812.43)

10.2.3. Monitoring (21 CFR 812.46)

10.2.4. Controlling Distribution and Disposition of Devices. The sponsor-investigator must take proper measures to ensure that devices are not diverted outside of legally authorized channels, may ship investigational devices only to qualified investigators participating in the clinical investigation (21 CFR 812.43(b)), must maintain complete, current, and accurate records pertaining to the shipment and disposition of the investigational device (21 CFR 812.140(b)), take appropriate measures to instruct investigators regarding their responsibilities with respect to recordkeeping and device disposition per 21 CFR 812.140(a).

10.2.5. Prohibition of Promotion and Other Practices (21 CFR 812.7)

10.2.6. Supplemental Applications [21 CFR 812.35(a) and (b)]

10.2.7. Maintaining Records [21 CFR 812.140(b)]

10.2.8. Submitting Reports [21 CFR 812.150(b)]

10.2.9. Inspections [21 CFR 812.145]

10.3. The PI shall ensure there is on-going review and evaluation of evidence relating to the safety and effectiveness of the device and report such evaluation to (a) FDA, and (b) the UNMC IRB when there is a safety concern.

10.4. 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, in accordance with 21 CFR 812.45.

Administrative Approval:
Bruce G. Gordon, MD                IRB Executive Chair & Assistant Vice Chancellor for Regulatory Affairs
Christopher Kratochvil, MD        Institutional Official

Policy Amended:
- Revised September 5, 2018
- Revised March 3, 2018
- Revised September 27, 2017
- Initial May 6, 2016
1.0 Purpose

The purpose of this policy and procedure is to describe the qualifications and responsibilities of personnel conducting research within the Organization and at external sites under the jurisdiction of the UNMC IRB.

2.0 Policy

It is the policy of the Organization that personnel involved in the conduct of research must possess the required experience, skill, education and (as appropriate) licensure to safely conduct the research in full compliance with all applicable regulatory and Organizational requirements specified in HRPP policy 1.1 (Human Research Protection Program).

3.0 General Requirements

3.1. Research personnel who are Responsible Personnel per HRPP policy 1.25 (Financial Conflicts of Interest) must comply with the Organizational Conflict of Interest Policy as described in that policy.

3.2. Research personnel who (a) participate in the process of consent, (b) have contact with subjects, or (c) have access to identifiable private information or identifiable biospecimens, and Faculty Advisors of student investigators, are required to comply with HSP subject protection training as described in HRPP policy 1.23 (HRPP Training Requirements and Opportunities for Research Personnel)

3.3. For FDA regulated research, research personnel must comply with applicable FDA requirements, including completion and submission of FDA Form 1572 to the sponsor if applicable.

4.0 Definitions of Research Personnel and Specific Requirements

4.1. Principal Investigator (PI):

4.1.1. The PI assumes overall responsibility for the conduct of the research. Specific responsibilities are described in HRPP policy 1.26 (PI Qualifications & Responsibilities).

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

4.1.3. The PI must be an employee, faculty, or student associated with the Organization.

4.1.4. The PI must be qualified by education, training, experience and 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.

4.1.5. If the PI is a student, resident, or house officer, a faculty advisor or program director must be identified on the IRB application. The faculty advisor/program director assumes responsibility for overall supervision of the student’s research and must sign off on the IRB application before submission to the IRB.
4.2. **Secondary Investigator(s) (SI):**

4.2.1. Secondary Investigator(s) responsibilities may include (but are not limited to):

4.2.1.1. Development of the research plan (in conjunction with the PI and other investigators)

4.2.1.2. Obtainment of legally effective informed consent/assent from prospective subjects.

4.2.1.3. Performance of research interventions or tests, or analysis of data or biospecimens

4.2.1.4. Presentation or publication of the data (in conjunction with the PI and other investigators).

4.2.2. The SI shares responsibility with the PI for assure safe conduct of the research in full compliance with the protocol, HRPP policies, IRB requirements, HHS or other Federal regulations, applicable FDA regulations and state law.

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

4.2.4. The SI is not required to be associated with the Organization; however an unaffiliated investigator must sign an external investigator agreement unless he/she does not have access to subjects or identifiable private information or identifiable biospecimens

4.2.5. The SI must be qualified by education, training, experience and licensure (as applicable) to perform the specific responsibilities described above.

4.3. **Participating Personnel:**

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

4.3.2. Participating Personnel responsibilities may include (but are not limited to):

4.3.2.1. Obtainment of legally effective informed consent/assent from prospective subjects, if authorized by the PI in accordance with HRPP policy 5.1 (Obtaining Informed Consent from Research Subjects).

4.3.2.2. Performance of research interventions or tests in the course of providing clinical care or routine services to the patient/subject, or analysis of data or biospecimens

4.3.2.3. Presentation or publication of the data (in conjunction with the PI and other investigators).

4.3.3. More than one PP may be named on the IRB application.

4.3.4. Participating personnel are not required to be associated with the Organization; however unaffiliated personnel must sign an External Investigator Agreement unless they do not have access to subjects or identifiable private information or identifiable biospecimens

4.3.5. Participating personnel must be qualified by education, training, experience and licensure (as applicable) to perform the specific responsibilities described above.

4.4. **Lead Coordinator:**

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

4.4.2. The Lead Coordinator serves as the primary regulatory contact point for the ORA. All correspondence from the IRB will be directed to both the PI and Lead Coordinator.
4.4.3. The Lead Coordinator may be authorized by the IRB to obtain informed consent/assent in accordance with HRPP policy 5.1 (Obtaining Informed Consent from Research Subjects).

4.4.4. Performance of research interventions or tests in the course of providing clinical care or routine services to the patient/subject, or analysis of data or biospecimens.

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

4.4.6. 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. Coordinator

4.5.1. Coordinators may be authorized to obtain informed consent/assent in accordance with HRPP policy 5.1 (Obtaining Informed Consent from Research Subjects).

4.5.2. Coordinators may be involved with performance of research interventions or tests in the course of providing clinical care or routine services to the patient/subject, or analysis of data or biospecimens.

4.5.3. More than one coordinator may be named on the IRB application.

4.5.4. Coordinators must be qualified by education, training, experience and licensure (as applicable) to perform the specific responsibilities described above.

4.6. Administrative and Data Management Personnel:

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

4.6.2. 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.

4.6.3. Administrative and Data Management Personnel do not have direct subject contact, but may have access to subject's identifiable private information, or protected health information (PHI).

Administrative Approval:

BRUCE G. GORDON, MD IRB Executive Chair & Assistant Vice Chancellor for Regulatory Affairs
CHRISTOPHER KRATOCHVIL, MD Institutional Official

Policy Amended:

- Revised February 18, 2019
- Initial January 12, 2018
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 (XI) who are not employed by or otherwise representing the Organization.

3.0 Definitions
3.1. An External Investigator (XI) is an investigator who is not employed by or otherwise representing the Organization who is engaged in research for which the UNMC IRB is the IRB of record.

3.1.1. A researcher employed by or otherwise representing another institution who is under the jurisdiction of another IRB which has an IRB Reliance Agreement with UNMC and for which the UNMC is acting as a central or single IRB is NOT considered an XI for the purpose of this policy. The reliance agreement which exists between UNMC and the relying institution obligates that institution to hold investigators at that institution to the same standards as the XIA.

3.1.2. An Individual Engaged in Research means a person who obtains (1) data about the subjects of the research through intervention or interaction with them; (2) identifiable private information about the subjects of the research; or (3) the informed consent of human subjects for the research.

3.1.3. In general, the Organization considers the criteria for “engagement” of an individual in the same manner as for an institution, as described in “OHRP Guidance: Engagement of Institutions in Human Subjects Research (2008).”

Examples of individuals “not engaged” include (but are not limited to) a clinician who provides standard of care treatment according to the protocol, or who performs routine clinical follow-up tests which would be performed outside of the research context, or who administers the study interventions being evaluated under the protocol on a one-time or short-term basis.

4.0 Procedures for External Investigator Agreement (XIA)
4.1. An XIA is required when an XI is engaged in research under a UNMC IRB approved research protocol at an external site for which there is not an IRB Reliance Agreement in place between UNMC and the site.

4.2. The XIA must be in effect before any research activities may be performed at that site.

4.3. An XIA must be in effect for each XI at that site and a copy maintained on file with the UNMC PI.
4.4. The XIA describes responsibilities of the XI including, but not limited to, assuring compliance with 45 CFR 46 including subparts as applicable, 21 CFR 50, 56, 312, 812, and HIPAA Privacy Rule), state laws, HRPP policies, and the protocol.

4.5. An XIA is effective for all studies that the XI conducts under the oversight of the UNMC IRB; therefore only one XIA is required.

4.6. The Organization, ORA, the UNMC IRB or the UNMC investigator may revoke the XIA at any time, if there is reason to believe that the XI is not satisfying responsibilities as described in the XIA.

Administrative Approval:
Bruce G. Gordon, MD IRB Executive Chair & Assistant Vice Chancellor for Regulatory Affairs
Christopher Kratochvil, MD Institutional Official

Policy Amended:
- Revised February 6, 2018
- Initial January 12, 2018 (Previous Policy #3.14)
1.0 Purpose
The purpose of this policy and procedure is to describe the requirements and procedures for submission of clinical trials to ClinicalTrials.gov.

2.0 Policy
2.1. It is the Policy of the Organization that all applicable drug, biologic, and device clinical trials will be registered and updated as required on ClinicalTrials.gov in compliance with HHS regulations at 42 CFR 11 (Final Rule for Clinical Trials Registration and Results Information Submission).

2.2. It is the Policy of the Organization that all NIH funded clinical trials will be registered and updated as required on ClinicalTrials.gov in compliance with the NIH Policy on the Dissemination of NIH-Funded Clinical Trial Information.

2.3. The Organization requires that investigators adhere to the statutory provisions of 42 CFR 11 (rather than the abbreviated provisions described in this policy when there are discrepancies), as well as clarifications and definitions found at www.clinicaltrials.gov.

3.0 Definitions
3.1. Clinical Trial:
3.1.1. Per 42 CFR 11.10(a) a clinical trial is a “clinical investigation (or clinical study) in which human subject(s) are prospectively assigned, according to a protocol, to one or more interventions (or no intervention) to evaluate the effect(s) of the intervention(s) on biomedical or health-related outcomes”

3.1.2. Per NIH Policy NOT-OD-16-149 a clinical trial is a "research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes."

3.1.2.1. For the purposes of this Policy, the regulatory definition at 42 CFR 11.10(a) and the definition in NIH policy are treated as synonymous.

3.1.2.2. The NIH definition of "clinical trial" is, however, broader than the term "applicable clinical trial" as defined in 42 CFR 11 (below).

3.2. Applicable Clinical Trials (ACTs)
3.2.1. ACT generally include interventional studies (with one or more arms) of FDA-regulated drugs, biological products, or devices that meet one of the following conditions:

3.2.1.1. The trial has one or more sites in the United States.

3.2.1.2. The trial is conducted under an FDA investigational new drug application or investigational device exemption.

3.2.1.3. The trial involves a drug, biologic, or device that is manufactured in the United States or its territories and is exported for research.
3.2.2. Applicable Clinical Trials include the following:

3.2.2.1. Trials of drugs and biologics: Controlled clinical investigations, other than phase 1 clinical investigations, of drugs or biological products subject to Food and Drug Administration (FDA) regulation

3.2.2.2. Trials of devices: 1) Controlled trials with health outcomes of devices subject to FDA regulation, other than small feasibility studies, and 2) pediatric postmarket surveillance required by FDA

3.3. Responsible Party:

3.3.1. The sponsor of the trial will be considered the responsible party unless and until a principal investigator has been designated the responsible party in accordance with 42 CFR 11.4(c)(2).

3.3.2. If an ACT or clinical trial is being conducted under an IND or IDE, then the holder of the IND or IDE is the responsible party regardless of how the clinical trial is being funded.

3.3.3. For clinical trials not conducted under an IND or IDE:

3.3.3.1. If the clinical trial is being conducted under a grant or sponsored research agreement, the funding recipient is generally considered to be responsible party.

3.3.3.2. If the clinical trial is being conducted under a contract, the funder is generally considered to be the responsible party

3.3.3.3. If there is no funding agreement supporting the clinical trial, the person or entity who initiated the clinical trial by preparing and/or planning the clinical trial is considered to be the responsible party.

3.3.4. The sponsor of the clinical trial may designate the principal investigator to be the responsible party, if the PI satisfies the requirements of 42 CFR 11.4(c)(2).

3.3.5. For NIH funded clinical trials, the awardee is usually the responsible party. If he/she is not the responsible party, then he/she is still obligated to coordinate with the responsible party to ensure that all regulatory requirements are met.

4.0 Investigator Responsibilities

Per 42 CFR 11 and the NIH Policy the Responsible Party is responsible to register the ACT and/or the NIH-funded clinical trial, and fulfill reporting responsibilities as described in those regulations and NIH Policy. The following describes the responsibilities of the PI if he/she is the Responsible Party. If he/she is not the Responsible Party, then the UNMC HRPP Policies do not apply

4.1. The PI must register the ACT and/or NIH-funded clinical trial and submit results as required by 42 CFR 11 and the NIH Policy.

4.2. Registration and Reporting Requirements for Applicable Clinical Trials

4.2.1. Registration is required for trials that meet the definition of an "applicable clinical trial" (ACT)

4.2.2. The following types of studies are generally excluded from the registration and results submission requirements of 42 CFR 11. This is not a complete list.

4.2.2.1. Phase 1 drug trials, including studies in which investigational drugs are used as research tools to explore biological phenomena or disease processes
4.2.2.2. Small clinical trials to determine the feasibility of a device or a clinical trial to test prototype devices, where the primary outcome measure relates to feasibility and not to health outcomes

4.2.2.3. Trials that do not include drugs, biologics, or devices (such as behavioral interventions)

4.2.2.4. Non-interventional (observational) clinical research (such as cohort or case-control studies)

4.2.3. The IRB will not issue full approval of any protocol where the Responsible Person is part of the Organization until the ACT is registered.

Note: Per the requirements of 42 CFR 11 the Responsible Party for an ACT must submit the required clinical trial information no later than 21 days after enrollment of the first participant; however, the Organization requires registration prior to full IRB approval.

4.2.4. If the ACT is amended in such a manner that changes are communicated to human subjects in the clinical trial, the PI must update any relevant clinical trial registration information data elements not later than 30 days after the protocol amendment is approved by the IRB (42 CFR 11.64(a)(1)(ii)(O)).

4.2.4.1. The IRB will not issue full approval of protocol amendment until the ClinicalTrials.gov PRS database has been updated, unless such change is necessary to reduce immediate risk to subjects.

4.2.4.2. The PI must review and update ClinicalTrials.gov PRS database at the time of each annual Continuing Review.

4.2.4.2.1. The IRB will not issue full re-approval of the protocol until the ClinicalTrials.gov PRS database has been updated

4.2.4.3. For ACTs with a Primary Completion Date on or after January 18, 2017, the PI is required to submit the results information specified in 42 CFR 11.48

4.2.4.3.1. The results must be submitted no later than 1 year after the study’s Primary Completion Date, unless the ACT satisfies the conditions for delayed submission of results information under 42 CFR 11.44(b).

4.2.4.3.2. If the ACT includes a device not previously approved or cleared by FDA for any use, full posting of the trial information on ClinicalTrials.gov will be delayed until after the device has been approved or cleared.

4.3. Registration and Reporting Requirements for NIH funded clinical trials

4.3.1. All NIH-funded awardees and investigators conducting clinical trials will register and report the results of their trial in ClinicalTrials.gov regardless of study phase, type of intervention, or whether they are subject to 42 CFR 11.

Note: For example, NIH-funded phase 1 clinical trials of an FDA-regulated product are covered by this policy as are clinical trials studying interventions not regulated by the FDA, such as behavioral interventions.

4.3.2. The IRB will not issue full approval of any protocol where the Responsible Person is part of the Organization until the NIH-funded clinical trial is registered.

4.3.3. If the NIH-funded clinical trial is amended, the PI must update any relevant clinical trial registration information data elements as required by the NIH Policy.
4.3.3.1. The IRB will not issue full approval of protocol amendment until the ClinicalTrials.gov PRS database has been updated, unless such change is necessary to reduce immediate risk to subjects.

4.3.4. The PI must review and update ClinicalTrials.gov PRS database at the time of each annual Continuing Review.

4.3.4.1. The IRB will not issue full re-approval of the protocol until the ClinicalTrials.gov PRS database has been updated.

4.3.5. The PI is required to submit the results information specified in the NIH Policy.

4.4. The PI is responsible for assuring that the IRB Application correctly reflects that a clinical trial is registered with clinicaltrials.gov and that the NCT number is accurate, and for uploading a copy of the ClinicalTrials.gov front sheet into RSS.

4.5. If the clinical trial is not registered with ClinicalTrials.gov the PI must provide justification why the trial is not registered.

5.0 ORA Procedures

5.1. At the time of the initial IRB review and approval of all clinical trials, the IRB administrator responsible for the trial will confirm that the application states the trial is registered (and that the front sheet from ClinicalTrials.gov is uploaded into RSS), or presents adequate justification for absence of registration.

5.2. Full approval of an ACT or of an NIH-funded clinical trial will not be granted until the trial is registered.

5.3. If the responsible party is not part of the Organization (that is, if it is an external investigator or sponsor) no further action regarding Clinicaltrial.gov reporting will be taken. If the responsible party is part of the Organization, the following additional procedures will be followed:

5.3.1. At time of each annual Continuing Review, the administrator will be responsible for assuring that the PI has updated the ClinicalTrials.gov PRS database. This assurance can take the form of an assertion from the PI that such an update has been made.

5.3.2. At the time of any protocol change for which changes are communicated to human subjects in the clinical trial, the administrator is responsible for assuring that the PI has updated the ClinicalTrials.gov PRS database. This assurance can take the form of an assertion from the PI that such an update has been made.

5.3.3. When an ACT or an NIH-funded clinical trial is completed (that is, when the investigator files a completion report, or when the trial is closed by the ORA for non-response to continuing review), the ORA will notify the responsible party that submission deadline for results information is no later than 1 year after the study’s Primary Completion Date, unless the ACT satisfies the conditions for delayed submission of results information under 42 CFR 11.44(b). The ORA will repeat the notification as per standard operating procedures.

5.3.4. The ORA will periodically (but not less often than monthly) review the Clinicaltrials.gov PRS database to determine any trials that non-compliant.

5.3.5. ORA will contact Responsible Party of non-compliant trials as per standard operating procedures. Investigators who remain non-compliant 30 days after the first notice will be subject to disciplinary actions as per HRPP policy 8.4 (Review of Noncompliance Involving the PI and Study Personnel), and per the Office of the Vice-Chancellor for Research.
1.0 Purpose

The purpose of this policy and procedure is to describe the criteria for use of, and the procedures for review by, the Rapid Response IRB (RR-IRB; IRB-03).

2.0 Policy

2.1. It is the policy of the Organization that the Rapid Response IRB (RR-IRB) will be utilized as appropriate to facilitate the review of human subject research that meets criteria listed below.

2.2. It is the policy of the Organization that the standard procedures for full IRB review (as per HRPP policy 2.2: Full IRB Review) may be modified as described below, to facilitate rapid and meaningful IRB review, in accordance with federal regulations at 45 CFR 46 and 21 CFR 56.

3.0 Constitution

3.1. The RR-IRB is a fully constituted and registered IRB (IRB00002686) operating under FWA 00002939.

3.2. The RR-IRB is composed of 8 members (at least one of whom is a non-scientist and one who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution), and a variable number of alternates.

3.3. The RR-IRB will include one Chair and at least one Vice-Chair.

3.4. Members will include representatives from UNMC, Nebraska Medicine and CHMC, representing a variety of colleges, departments and medical disciplines, including but not limited to College of Public Health, Infectious Disease, Pharmacy, and ethics.

3.5. The RR-IRB shall include a prisoner representative with appropriate background and experience to serve in that capacity, as per 45 CFR 46.304(b).

3.6. Membership will satisfy requirements of HRPP policy 1.6 (IRB Composition, Leadership, Qualifications, & Responsibilities).

4.0 Criteria for Use

4.1. The RR-IRB may be activated by the Executive Chair for rapid review of new protocols, previously tabled protocols, requests for change in approved research or continuing reviews of approved research.

   4.1.1. In order for the RR-IRB to review a previously tabled protocol, one member of the convened RR-IRB must also have been present at the IRB meeting during which the protocol was tabled, or a member of the board that tabled the protocol must be present at the RR-IRB meeting as a non-voting observer.

4.2. Activation is at the discretion of the Executive Chair, in consultation, if necessary, with the IO. In general, the RR-IRB will review research which fits the following criteria:
4.3. The research provides the potential for meaningful benefit to potential subjects that cannot be
obtained outside the context of the specific research protocol, or the research provides the
potential for significant benefit to the Organization.

4.3.1. Review is urgent; that is, there is insufficient time to wait for a scheduled meeting of
IRB-01, IRB-02 or IRB-04.

4.3.2. The research is not eligible for expedited review, per HRPP policy 2.3 (Expedited
Review).

4.4. In general, the RR-IRB will not review research where the urgency arises from delays on the
part of the investigator.

5.0 Procedures

5.1. Upon activation, one or more IRB Administrators will be responsible for contacting members
by phone, email and/or text message, in order to identify a quorum, and an appropriate meeting
day/time. Once a quorum and meeting time are identified, the investigator will be notified.

5.2. The investigator will begin the process of completing the IRB application online
(https://net.unmc.edu/rss)

5.3. The RR-IRB will review as per HRPP policy 2.2 (Full IRB Review), except as noted below.

5.4. Depending on the urgency of the review, any or all of the following modifications may be
utilized as deemed appropriate by the Executive Chair and/or the RR-IRB Chair

5.4.1. The investigator and the IRB Administrator, Executive Chair and/or the RR-IRB Chair
may discuss issues related to the protocol, IRB application and CF in an iterative fashion
during the completion of the online application, in order to proactively address potential
concerns.

5.4.2. The primary and secondary reviewers may begin review of the draft IRB application
and CFs as they become available prior to the meeting; they will be supplied with any
revisions of these documents as they are available. All RR-IRB members will be supplied with
the agenda, complete IRB application, full protocol, and CFs at the time of the meeting.

5.4.3. RR-IRB review will occur concurrent with review by other committees (for example,
Pharmacy and Therapeutics, IBC)

5.4.4. The investigator or his/her designee may be present in the room during the
presentation of the protocol, and discussion by the board, in order to interactively address
concerns or questions raised by the RR-IRB. The investigator will then leave the room
allowing the RR-IRB adequate time for more discussion, and then the vote.

5.4.5. The IRB administrator assigned to the RR-IRB will make modifications to the IRB
Application and the CF based on discussion with the investigator during the RR-IRB meeting,
and the investigator’s responses to IRB directed comments following the meeting.

5.4.6. The RR-IRB Administrator, in consultation with the Executive Chair and/or the RR-
IRB Chair as appropriate, will review the investigator’s written responses, and revised
application and CFs, and are authorized to grant final approval if the conditions placed by the
full RR-IRB have been satisfied
ADMINISTRATIVE APPROVAL:

BRUCE G. GORDON, MD  IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS
CHRISTOPHER KRATOCHVIL, MD  INSTITUTIONAL OFFICIAL

POLICY AMENDED:

- Initial February 5, 2018
1.0 Purpose

The purpose of this policy and procedure is to describe the Organization’s requirements for allowing observers at convened IRB meetings.

2.0 Policy

2.1. It is the policy of the Organization that non-members who have a legitimate reason, may be allowed to observe convened IRB meetings.

2.2. It is the policy of the Organization that an investigator whose protocol is being reviewed by the IRB at that convened meeting may attend that portion of the meeting for the purpose of providing information to, and answering questions of, the convened board.

3.0 Justification for Attendance

3.1. With appropriate justification, the full IRB, the IRB Executive Committee, or the IRB Executive Chair has authority to permit an observer at a convened meeting of any of the IRBs

   3.1.1. In general, adequate justification would include a legitimate job related interest in the process of IRB review, or an academic interest in research ethics and the functioning of IRBs in general.

   3.1.2. Persons who are being considered as potential IRB members may observe one or more convened IRB meetings.

3.2. In deciding whether to allow a particular observer, the full IRB, the IRB Executive Committee, or the IRB Executive Chair will consider whether the same or similar benefit could be obtained from alternate experience (for example, an IRB orientation or didactic presentation).

3.3. The full IRB may invite an investigator whose protocol is being reviewed by the IRB at that convened meeting to attend that portion of the meeting, for the purpose of providing information to, and answering questions of, the convened board.

4.0 Procedure

4.1. The IRB Administrator responsible for coordinating the meetings will arrange for the appropriate meeting for the observer to attend.

4.2. The observer will be required to sign a confidentiality agreement prior to the scheduled meeting.

4.3. The presence of an observer will be recorded in the IRB minutes, as per HRPP policy 2.2 (Full IRB Review).

4.4. For observers:

   4.4.1. In general, observers will not participate in the discussion of agenda items.

   4.4.2. The observer may be required to leave the room during any discussion or vote as determined by the Chair or Executive Chair, or at the request of any board member.
4.4.3. No observer will be permitted to attend a portion of the meeting where he/she has a COI, as per HRPP policy 1.7 (IRB Member, Consultant, Staff COI Identification and Management).

4.5. For invited investigators:

4.5.1. An invited investigator may only attend during the review of his/her protocol.

4.5.2. An invited investigator may provide information to, and answer questions of, the convened board. He/she may, at the request of the board, participate in the discussion regarding his/her protocol.

4.5.3. The invited investigator will leave the room after he/she has provided the requested information, before final discussion or vote.

ADMINISTRATIVE APPROVAL:

BRUCE G. GORDON, MD  IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS
CHRISTOPHER KRATOCHVIL, MD  INSTITUTIONAL OFFICIAL

POLICY AMENDED:

➢ Initial February 26, 2018
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements and practices for assuring confidentiality of the process of review of human subjects research.

2.0 Policy
2.1. It is the policy of the Organization that the deliberations of the IRB in a convened meeting or subcommittee meeting, or of an expedited reviewer, are confidential, and details of such discussions and deliberations may not be shared with the investigator or any other person outside the IRB or the ORA.

2.2. It is the policy of the Organization that findings and decisions of the IRB, or of a subcommittee of the IRB, or of an expedited reviewer, will be shared with the investigator or with the investigator’s staff verbally, by email or by letter, following that meeting or review. The details of the deliberations will not be shared as per section 2.1 above.

2.3. It is the policy of the Organization that violation of this policy, and especially the deliberate communication of the details of the deliberation of the IRB, the subcommittee or the expedited reviewer, is cause for action against that IRB member, ORA staff member or other responsible party as described below.

3.0 Process
3.1. IRB members will sign a Confidentiality Agreement at the time they are appointed to the board, and again at every re-appointment. The signed agreement will be retained by the ORA.

3.2. ORA Staff will sign a Confidentiality agreement at the time they are hired. The signed agreement will be retained by the ORA.

3.3. Guests to the IRB meeting will sign a Confidentiality agreement prior to attending the meeting in accordance with HRPP policy 1.31 (Observers at IRB Meetings). The signed agreement will be retained by the ORA.

3.4. Consultants to the IRB will sign a Confidentiality Agreement prior to attending the meeting. The signed agreement will be retained by the ORA.

3.5. Allegations of violation of this policy will be handled and investigated as described in HRPP policy 8.5 (Noncompliance by the IRB or Other Components of the HRPP).

3.5.1. The event, however, will not be considered “non-compliance” as per that policy, and is not reportable outside the Organization.

3.6. Violation of this policy may lead to actions against the IRB member, the ORA Staff, or other responsible party, as determined by the IO. These actions could include, but are not limited to, dismissal from the board, disciplinary actions, or termination of employment.

ADMINISTRATIVE APPROVAL:
BRUCE G. GORDON, MD  IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS
CHRISTOPHER KRATOCHVIL, MD  INSTITUTIONAL OFFICIAL

POLICY AMENDED:
➢ INITIAL JANUARY 12, 2018
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. All new IRB applications must be submitted using the online Research Support System (RSS) (https://net.unmc.edu/rss).
3.2. All CRs, RFCs, SSD, NCRs, and SCRs for research protocols approved after January 16, 2012, are submitted through RSS. UPs and Cs are submitted by a variety of mechanisms specified in HRPP policies 8.2 (IRB Review of Study Related Complaints) and 8.3 (IRB Review of Unanticipated Problems Involving Risk to the Subject or Others).
3.3. All CRs, RFCs, SSD, NCRs, and SCRs for research protocols approved prior to January 16, 2012 will continue to be submitted on paper. All necessary forms are available on the UNMC IRB website (http://www.unmc.edu/irb) and the IRB will maintain paper files for the duration of these studies.
3.4. All internal adverse events that meet the criteria specified in HRPP policy 8.1 (IRB Review of Adverse Events and Adverse Device Effects) will continue to be reported to the IRB through RSS system.

4.0 Deadlines for Submission
4.1. The deadline for submission of any materials requiring review by the full IRB is 2 weeks prior to each meeting. The deadlines are published on the IRB website at http://unmc.edu/irb.
   4.1.1. All new applications and re-submissions of tabled protocols will undergo pre-review to the greatest extent possible in consideration of the submission date, and ORA workload.
   4.1.2. Exceptions to the above deadline may be made on a case-by-case basis by the IRB Executive Chair or his/her designee.
   4.1.3. Since CRs are only reviewed by IRB-02 on the third Thursday of the month, CRs and SCRs must be submitted by the last day of the previous month (e.g., the last day of January to be reviewed by the third Thursday of February).
   4.1.4. Items that qualify for expedited review in accordance with HRPP policy 2.3 (Expedited Review) have no deadlines for submission.
4.1.5. Items that qualify as exempt in accordance with HRPP policy 2.6 (Exempt Research) have no deadlines for submission.

5.0 IRB Review Limits

5.1. The IRB will normally review no more than 15 protocols (new submissions and previously tabled protocols) at each full 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.

5.2. The IRB will review reports of internal AEs, potential UPs, NCRs, Cs, and RFCs at the earliest possible full IRB meeting without review limits.

6.0 Determination of Required IRB Review

6.1. Protocols and other action items submitted through RSS will be triaged to the appropriate IRB administrator and processed in accordance with ORA SOPs.

6.2. 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 (Full IRB Review) and 2.3 (Expedited Review).

ADMINISTRATIVE APPROVAL:
BRUCE G. GORDON, MD IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS
CHRISTOPHER KRATOVIL, MD INSTITUTIONAL OFFICIAL

POLICY AMENDED:
- REVISED FEBRUARY 5, 2018
- INITIAL APRIL 4, 2016
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 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.

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 1.13 (Compliance with ICH-GCP Guidelines).

2.4. The IRB will conduct continuing review of research at intervals appropriate to the degree of risk, in accordance with 45 CFR 46.109 and HRPP policy 2.7 (Continuing Review of Research).

2.5. The status of studies reviewed by the full IRB are maintained in the Research Administration (RA) database and Research Support Services (RSS) application system.

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 (Submission of Items for Review).

3.2. IRB Meeting Schedule

3.2.1. The schedule of IRB meeting dates is posted on the IRB website at http://unmc.edu/irb.

3.2.1.1. IRB-01 meets the first Thursday of every month (except January and July), and IRB-02 meets the third Thursday of every month.

3.2.1.2. IRB-04 meets the fourth Tuesday of every month, generally at Children’s Hospital & Medical Center.
3.2.1.3. IRB-03 (Rapid Response IRB) meetings are held on demand and convened as soon as possible, as per HRPP policy 1.30 (Use of the Rapid Response IRB).

3.3. Quorum

3.3.1. A full IRB meeting cannot be convened without the presence of a quorum. A quorum must represent a majority of the voting membership of the IRB, including at least one member whose primary concerns are in nonscientific areas.

3.3.2. Each IRB includes one member that is not affiliated with the Institution. It is expected that at least one unaffiliated member will be present at each meeting of each IRB as per HRPP policy 1.6 (IRB Composition, Leadership, Qualifications, & Responsibilities).

3.3.3. Some or all IRB members may participate in the meeting by conference call, videoconference or web meeting. Utilization of video conferencing or teleconferencing technology in the conduct of an IRB meeting will only be done at the discretion of the Chair, Executive Chair or IO. 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.

3.3.4. When the IRB reviews any research involving children, or cognitively impaired persons, an IRB member who is knowledgeable about and experienced in working with that specific population will be present in accordance with HRPP policy 1.6 (IRB Composition, Leadership, Qualifications, & Responsibilities).

3.3.5. When the IRB reviews any research involving other vulnerable populations, an IRB member who is knowledgeable about and experienced in working with vulnerable populations (preferably but not exclusively the particular population in question) will be present in accordance with HRPP policy 1.6 (IRB Composition, Leadership, Qualifications, & Responsibilities).

3.3.6. When the IRB reviews any research involving prisoners, a prisoner representative must be present in accordance with HRPP policy 4.3 (Research Involving Prisoners).

3.3.7. Any IRB member who abstains from voting (for reasons other than a COI as defined in HRPP policy 1.7: IRB Member, Consultant, Staff COI Identification and Management) is included in the quorum. This is recorded as an abstention in the minutes.

3.3.8. Any IRB member who has a COI will be recused in accordance with 45 CFR 45.107(e) [rev 45 CFR 46.107(d)], 21 CFR 56.107(e), and HRPP policy 1.7 (IRB Member, Consultant, Staff COI Identification & Management). 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.

3.3.9. 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.

3.3.10. If attendance at a convened full IRB meeting falls below quorum (including losing all non-scientist members, or another required member), the meeting will be immediately suspended and no official business will be conducted until a 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

3.4.1. Reviewers will be assigned by the IRB administrators with advice from the IRB Executive Chair/designee as necessary. At least one 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 1.6 (IRB Composition, Leadership, Qualifications, & Responsibilities).

3.4.2. For new IRB Applications, and tabled IRB Applications the following reviewers will be assigned:

3.4.2.1. For IRB-01 and IRB-02 a primary, secondary and non-scientist reviewer will be assigned

3.4.2.2. For IRB-04 a primary, secondary, and non-scientist reviewer will be assigned; for all research involving drugs a pharmacy reviewer will also be assigned.

3.4.2.3. For IRB-03 a primary and secondary reviewer will be assigned.

3.4.3. For all IRBs, only a primary reviewer will be assigned to applications for continuing review, internal 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.

3.4.4. Two agendas will be created:

3.4.4.1. An abbreviated agenda which lists the new items for review and assigned reviewers. This is attached to the review packet mailed to IRB members who will be attending the meeting.

3.4.4.2. A detailed agenda which is emailed to all IRB members prior to 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) notification of items approved by expedited review (in accordance with HRPP policy 2.3: Expedited Review) and per requirements of 45 CFR 46.110(c), 21 CFR 56.110(c), 5) IRB approval criteria, and 6) IRB actions.

3.5. Review Materials Distributed to IRB Members

3.5.1. All members and alternates scheduled to attend an IRB meeting (in person, or by teleconference or videoconference) will receive paper copies of the following (at least seven days prior to that meeting):

3.5.1.1. Abbreviated (Reviewer) Agenda (per section 3.4.4.1 above)

3.5.1.2. IRB applications for initial review including all consent forms, information sheets, and recruitment materials.

3.5.1.3. Modified IRB applications for tabled research, including the IRB review letter, and the PI response to the IRBs review.

3.5.1.4. Continuing review applications, including the consent form signed by the last subject enrolled in the research, any newly proposed consent form(s), status report on the progress of the research, and as applicable DSMB/DSMC reports, and study reports.
3.5.1.5. Requests for change application, including sponsor’s summary of changes if available
3.5.1.6. Single subject deviation
3.5.1.7. Reports of adverse events
3.5.1.8. Reports of potential unanticipated problems involving risk to the subject or others
3.5.1.9. Reports of noncompliance.
3.5.1.10. Reports of complaints.
3.5.1.11. COI management plans for all protocols where a COI has been identified (in accordance with HRPP policy 1.25: Financial Conflicts of Interest).

3.5.2. Documentation associated with items 3.5.1.2 thru 3.5.1.11 are available to all members through the RSS system at https://net.unmc.edu/rss.

3.5.3. Assigned reviewers for an IRB meeting (as per sections 3.4.2 and 3.4.3 above) will also receive the following:

3.5.3.1. Detailed research protocol, for protocols to which they have been assigned
3.5.3.2. Investigator’s Brochure, for protocols to which they have been assigned, if available

3.5.4. At least two days prior to each meeting, all members and alternates of all Boards receive PDF or DOC files of the following:

3.5.4.1. IRB minutes of the last meeting of that Board
3.5.4.2. Education, Policy and Information items
3.5.4.3. Full agenda for that meeting

3.6. IRB Member Review Procedures

3.6.1. 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, and HRPP policy 2.5 (Criteria for IRB Approval).

3.6.2. IRB members are expected to consult the IRB study files in RSS, applicable regulations, and HRPP policies, as necessary during their review of the protocol.

3.6.3. IRB members are expected to submit written reviews, as early as possible, to ORA.

3.6.4. Deficiencies and/or major points of clarification which require revision of the IRB application or other review item should be described fully, and referenced to sections of the submitted application, or to the Criteria for Approval at 45 CFR 46.111.

3.6.5. Deficiencies, errors, inadequate explanations, and excessively high readability level should be described sequentially according to the section of the ICF.

3.7. IRB Meeting Procedures

3.7.1. When a quorum of the Board is present, the IRB meeting is called to order by the IRB Executive Chair, Chair, Vice Chair or designee (subsequently referred to as “Chair” in this policy) and each item on the agenda is acted upon.
3.7.2. The Primary Reviewer will present the review followed by the other assigned reviewers (secondary reviewer, non-scientist reviewer, pharmacy 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.

3.7.3. 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.

3.7.4. Whenever a controverted issue arises during an IRB meeting, or when the vote is less than unanimous, members will be asked if they wish to submit written comments or minority opinion. These items will be appended to the minutes of the meeting.

3.7.5. IRB discussion of any one item on the agenda is generally limited to 20 minutes. If the discussion reaches the time limit, the Chair may call the question, or call for a motion to extend discussion. If a motion to extend debate fails to pass by my simple majority, the protocol or issue then under discussion will immediately come to a vote of the convened IRB.

3.8. Voting Requirements

3.8.1. The Primary Reviewer will recommend an action which must be seconded by another IRB member, normally the Secondary Reviewer.

3.8.2. 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.

3.8.3. Except as specified in other sections of this policy, no motion shall pass unless two-thirds of the IRB members which constitute the quorum are present during the discussion and vote in favor of the motion.

3.8.4. If a member must leave the meeting temporarily 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.

3.8.5. Only those members physically in the room, or attending by conference call, videoconference or web meeting may vote. Absentee voting is not permitted.

3.8.6. 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.

3.8.7. If a protocol or issue has been referred to an IRB subcommittee, the Chair or a member of the subcommittee will present the results of the subcommittee meeting at any subsequent full Board meeting.

3.8.8. The Chair will abstain from voting.
3.9. **Criteria for IRB Approval and Other Determinations**

3.9.1. Criteria for IRB approval of all human subject are described in [HRPP policy 2.5](#) (*Criteria for IRB Approval*).

3.9.2. During the review, the IRB must also determine:

3.9.2.1. Whether the research requires continuing review more often than annually, as required at 45 CFR 46.109E; 21 CFR 56.109(a)(2), as appropriate to the degree of risk. The IRB may consider other factors as well:

3.9.2.1.1. The nature of and any risks posed by the clinical investigation.
3.9.2.1.2. The degree of uncertainty regarding the risks involved.
3.9.2.1.3. The vulnerability of the participants.
3.9.2.1.4. The experience of the clinical investigator in conducting the clinical research.
3.9.2.1.5. The IRBs previous experience with that researcher or sponsor (e.g., compliance history, previous problems with the researcher obtaining informed consent, prior complaints from participants about the researcher).
3.9.2.1.6. The projected rate of enrollment
3.9.2.1.7. Whether the study involves novel therapies.

3.9.2.2. Whether the research 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). The IRB will consider:

3.9.2.2.1. Whether the research should have a third party observe the consent process in accordance with [HRPP policy 1.2, Section 2.7](#) (*Authority Granted to the IRB by the Organization*).
3.9.2.2.2. Whether the current consent form is still accurate and complete.
3.9.2.2.3. Whether the research requires an audit of research records in accordance with [HRPP policies 1.21](#) (*Post Approval Monitoring of Research*) and 8.4 (*Review of Noncompliance Involving Risk to the Subject or Others*).
3.9.2.2.4. Whether there are any significant new findings that arise from the review process that might relate to a subject’s willingness to continue participation in the study.

3.9.2.3. When the PI is the lead researcher of a multi-site trial, whether the management of information to the protection of human subjects is adequate, such as reporting of unanticipated problems, interim results, and protocol modifications.

3.9.3. If the research involves an FDA regulated investigational device, the IRB will also determine and document the basis for determination that the investigation involves a significant risk device or non-significant risk device (in accordance with 21 CFR 812.66 and [HRPP policy 6.2](#) (*Research involving Investigational and Marketed Devices*).

3.9.4. 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 3.10.1 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 3.10.2 below),
3.10. **IRB Actions**

3.10.1. Final Approval and full release; initiation of the research is authorized.

3.10.1.1. All of the criteria for IRB approval are satisfied and no changes are required.

3.10.2. 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

3.10.2.1. All of the criteria for IRB approval are satisfied provided the investigator makes the specified changes. The IRB requirements for final approval and release are considered minor and not substantive in nature.

3.10.3. Tabled, full IRB re-review required

3.10.3.1. The IRB requires additional information in order to determine whether the criteria for approval have been satisfied, and/or the IRB had concerns which warrant re-review by the full IRB.

3.10.4. Disapproved

3.10.4.1. Applications may be disapproved if, after thoughtful deliberation, including, as appropriate, discussions with the investigator, the IRB finds serious design flaws that either make obtainment of generalizable knowledge highly unlikely or places subjects at undue risk, or the risk/benefit relationship is unfavorable, or the protocol does not meet institutional policy or requirements, and the investigator is unwilling or unable to make modifications to remedy these situations.

3.10.4.2. The investigator has the right to appeal to the IRB in accordance with HRPP policy 8.6 (Study Hold, Suspension, and Termination).

3.10.5. Decline to complete the review

3.10.5.1. Adequate review of the protocol could not take place because the application is significantly deficient in information and content.

3.10.6. Suspension of IRB approval

3.10.6.1. The IRB requires all research activities be halted immediately in accordance with HRPP policy 8.6 (Study Hold, Suspension, and Termination). This action may be taken in relation to continuing review, complaints, noncompliance, adverse events, and unanticipated problems involving risk to the subject or others.

3.10.7. Termination of the research

3.10.7.1. The IRB requires the study be terminated in accordance with HRPP policy 8.6 (Study Hold, Suspension, and Termination). 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. **IRB Review Letters**

3.11.1. 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.

3.11.2. 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 IRB application, ICF(s)/information sheet(s) and/or other associated documents.

3.11.3. The IRB review letters will clearly document the determinations of the Board, as referenced above in Sections 3.9 and 3.10 of this policy, including:

   3.11.3.1. The decision to approve, disapprove, or require modifications.
   
   3.11.3.2. A list of any modifications/clarifications required by the Board.
   
   3.11.3.3. If the IRB disapproves the action, a statement providing the rationale for the disapproval, and an invitation for the investigator to appeal.

3.11.4. Review letters will include specific findings, comments, requests for clarification and questions related to the materials submitted by the investigator and the IRB’s review of the action.

3.11.5. Review letters will include the following additional documentation as applicable:

   3.11.5.1. 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).*

3.11.6. Documentation of the level of risk (i.e., minimal risk, greater than minimal risk), and the rationale supporting this classification.

3.11.7. 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.

3.11.8. 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.

3.11.9. 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.

3.11.10. Documentation that the IRB considered protocol specific findings for research involving decisionally impaired subjects.
3.11.11. Documentation of the IRB rationale for nonsignificant or significant risk device determinations.

3.11.12. 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.

3.11.13. Documentation that the IRB determined that the research satisfies the requirements for waiver of informed consent/ HIPAA authorization as per HRPP policy 5.2 (Waiver or Alteration of Informed Consent and 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.

3.11.14. Documentation that the IRB determined that the research satisfies the requirements for waiver of child assent as per HRPP policy 4.4 (Research Involving Children); 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).

3.11.15. Documentation that the IRB determined that the research satisfies the requirements for waiver of signed consent as per HRPP policy 5.4 (Waiver of the Requirement to Obtain Signed Consent Form); 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).

3.11.16. Signature authority is granted in accordance with HRPP policy 1.19 (IRB Signature Authority).

3.12. IRB Meeting Minutes

3.12.1. Basic Information

3.12.1.1. 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.

3.12.1.2. The IRB minutes consist of the core minutes and addenda (which contain the detailed review letters provided to PIs that reflect the IRBs requirements.

3.12.1.3. Copies of the core IRB minutes are provided via e-mail to: a) IRB members before the next IRB meeting, and b) the IO after the meeting.

3.12.1.4. 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 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.

3.12.1.5. IRB members for each board have the opportunity to review and correct minutes for the previous convened meeting of that board.

3.12.1.6. 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.
3.12.2. **Core IRB Minutes:**

3.12.2.1. Identification of the individuals present at the meeting: IRB members, non-voting IRB member alternates, consultants, IRB administrative staff, and guests.

*Note: If consultants are present, a brief description of the consultant expertise will be noted as well as documentation that the consult did not vote on any actions.*

3.12.2.2. Identification of IRB members classified as non-scientists, and as unaffiliated with the institution.

3.12.2.3. Identification of IRB members, non-voting IRB member alternates and consultants who attended the IRB meeting via videoconferencing or teleconferencing.

3.12.2.4. Identification of alternate IRB members and the IRB member for whom they are substituting.

3.12.2.5. The names of IRB members who have a COI and are recused at the time of the discussion and vote on each board action.

3.12.2.6. 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.

3.12.2.7. IRB special notification items (e.g., items approved by expedited review) per IRB minutes template.

3.12.2.8. Documentation of quorum for each separate vote count for all board actions (i.e., in favor, opposed, and abstentions) in the following categories per the IRB minutes template:

3.12.2.8.1. Previously reviewed (tabled) research proposals

3.12.2.8.2. Initial review of research proposals

3.12.2.8.3. 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).

3.12.2.8.4. Reports of noncompliance

3.12.2.8.5. Internal adverse event reports that may be unanticipated problems involving risk to the subject or others

3.12.2.8.6. Requests for change in approved research protocols

3.12.2.8.7. Continuing review applications

3.12.2.9. In the event a consultant provided an in-depth review of research the agenda will document the information provided by the consultant and verify that the consultant did not vote.

3.12.2.10. Verification that all IRB members who attended through videoconferencing or teleconferencing were able to actively participate in all discussions and votes.

3.12.2.11. 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.

3.12.2.12. 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.

3.12.2.13. The reason(s) for disapproval of research.

3.12.2.14. A determination of when continuing review is required more often than annually.

3.12.2.15. A determination of which projects need verification from sources other than the PI that no material changes have occurred since the previous IRB review.

3.12.2.16. A determination of which projects should have a third party observe the consent process.

3.12.2.17. A determination of which projects require an audit of research records.

3.12.2.18. Following the effective date of the Revised Rule, the following determinations must also be documented in the minutes, as applicable:

3.12.2.18.1. Rationale for conducting continuing review on research that otherwise would not require continuing review.

3.12.2.18.2. Rationale for an expedited reviewer’s determination that research appearing on the expedited reviewer list is more than minimal risk.

3.12.3. Addenda

3.12.3.1. The IRB minutes addendum consists of IRB review letters to PIs, for all protocol related activities (including, but not limited to, review of tabled and new research proposals, Change Requests in approved research protocols, Reports of Adverse Events and potential Unanticipated Problems, Reports of noncompliance or complaints).

4.0 Deadlines for PI Responses

4.1.1. The PI is given 60 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 60-day period, the PI and Lead Coordinator (if applicable) are contacted by either phone or email to determine the status of their response.

4.1.1.1. Extensions will be granted on a case-by-case basis, as determined by the IRB Administrator in consultation (if needed) with the IRB Executive Chair.

4.1.1.2. If there has been no response by 60 days (or by the expiration of the extension provided per section 4.1.1 above) the study will be withdrawn or closed.

5.0 Review of PI Responses

5.1.1. 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.
5.1.2. If, on consultation with the Executive Chair, the Administrator determines that the investigator’s response to the IRB review is inadequate, incomplete, or contains significant changes not initially reviewed by the IRB, he/she will refer the submission for review by the full convened IRB.

5.1.3. If the IRB required modifications/clarifications that are more than minor in nature (that is, if the submission was tabled), the investigator’s response will be returned to the full convened 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.

6.0 IRB Approval Periods

6.1. The approval period for protocols for which continuing review is required is based on the date that the convened IRB gave conditional approval of the research. Studies approved with annual continuing review are valid for 364 days from the date of conditional approval; the approval period expires on the 365th day.

6.2. The IRB database will include the following dates:

   6.2.1. Date of full Board review.
   6.2.2. Date all conditions set by the IRB were determined to be met and the study was granted final approval and release.
   6.2.3. Expiration Date (per section 6.1 above).

7.0 Final IRB Approval Letter

7.1. The IRB final approval letter will document the following determinations:

   7.1.1. Pertinent dates:
   7.1.1.1. Date of full Board review.
   7.1.1.2. Date all conditions set by the IRB were determined to be met and the study was granted final approval and release.
   7.1.1.3. Expiration Date (per section 6.1 above).
   7.1.2. Compliance with applicable HHS and FDA regulations.
   7.1.3. Risk determination for the research (with rationale if the IRB’s determination is different than that suggested by the investigator)
   7.1.4. Subpart B category for inclusion of pregnant women, neonates, and fetus: viable and non-viable (as applicable)
   7.1.5. Subpart C category for inclusion of prisoners (as applicable)
   7.1.6. Subpart D category for inclusion of children (as applicable), including the number of parents who must provide and document informed consent (permission).
   7.1.7. Waiver or alteration of the requirements for informed consent (as applicable)
   7.1.8. 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 ORA must receive verification of approval or completion of review by the following committees/offices as applicable:

8.1.1. Pharmacy & Therapeutics Committee
8.1.2. Fred & Pamela Buffett Cancer Center Scientific Review Committee
8.1.3. Institutional Biosafety Committee
8.1.4. Radioactive Drug Research Committee
8.1.5. Investigational Device Review Committee
8.1.6. Conflict of Interest Committee
8.1.7. IT Security and Compliance
8.1.8. Sponsored Programs Administration/ Contracts Office
8.1.9. Research Billing/Coverage Analysis Office

Administrative Approval:
BRUCE G. GORDON, MD  IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS
CHRISTOPHER KRATOCHVIL, MD  INSTITUTIONAL OFFICIAL

Policy Amended:
- REVISED MARCH 29, 2018
- INITIAL APRIL 4, 2016
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 (Criteria for Approval).

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 OHRP Expedited Review Categories (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. Following the effective date of the Revised Rule, protocols for which limited IRB review is a condition of exemption under (rev) 45 CFR 46.104(d)(2)(iii), or (d)(3)(i)(C) are eligible for expedited review.

Note: the Organization does not utilize exempt categories 7 and 8 (rev 45 CFR 46.104(d)(7) or (8)).

2.4. Expedited review will not be used for initial or continuing review of (1) classified research, or (2) research involving prisoners.

2.5. Minor changes in IRB-approved research qualify for expedited review in accordance with HRPP policy 2.4 (IRB Review of Changes in Previously Approved Research).

2.6. Continuing review of research previously approved by a convened IRB where no subjects have been enrolled and no additional risks have been identified may undergo expedited review.

2.7. Continuing review of research which satisfies the requirements of OHRP Expedited Review Categories (1998) category 9 (“research not conducted under an investigational new drug application or investigational device exemption where [expedited] categories 2 through 8 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”) may undergo expedited review.

2.8. Continuing review of research which has been previously approved by the full IRB prior to the effective date for the Revised Rule, when the research meets the requirements of OHRP Expedited Review Categories (1998) category 8, is eligible for expedited review.

2.9. Complaints which are considered minor, unexpected incidents involving no more than minimal risk to subjects or others, and noncompliance which is not serious is eligible for expedited review in accordance with HRPP policies 8.2 (IRB Review of Study Related Complaints) and 8.4 (IRB Review of Noncompliance Involving the PI and Study Personnel).

2.10. It is the policy of the Organization that expedited review be substantive and meaningful in accordance with OHRP guidance (November 10, 2010); and FDA guidance (1998 FDA Information
Sheets), and that the standard requirements for informed consent will be applied to all studies undergoing expedited review.

2.11. The status of studies reviewed by an Expedited Review process are maintained in the Research Administration (RA) database and Research Support Services (RSS) application system.

3.0 Definitions

3.1. **Expedited Review** is a method of review of research involving human subjects 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** means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests (per 45 CFR 46.102(i) (rev 45 CFR 46.102(j)), and 21 CFR 56.102(i)).

4.0 Expedited Review Categories

4.1. 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.

Following the effective date of the Revised Rule inclusion of research activities on the list is presumed to mean that the activity is minimal risk (FR 82 (12):7206, 2017) unless the reviewer determines and documents the rationale for considering the activity greater than minimal risk.

4.1.1. **Category 1**: Clinical studies of drugs and medical devices only when condition (a) or (b) is met:

*4.1.1.1. 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.*

*4.1.1.2. Research on medical devices for which:*

*4.1.1.2.1. An investigational device exemption application (21 CFR Part 812) is not required; or*

*4.1.1.2.2. The medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.*

4.1.2. **Category 2**: Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:

*4.1.2.1. From healthy, non-pregnant 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*

*4.1.2.2. From other adults and children, 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.*
4.1.3. **Category 3:** Prospective collection of biological specimens for research purposes by noninvasive means.

*Note:* Examples of such biological specimens include but are not limited to (a) Hair and nail clippings in a non-disfiguring 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 gumbase 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.

4.1.4. **Category 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.

*Note:* 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.

*Note:* Examples of such non-invasive procedures include but are not limited to (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.

4.1.5. **Category 5:** Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for non-research 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. This listing refers only to research that is not exempt.

4.1.6. **Category 6:** Collection of data from voice, video, digital, or image recordings made for research purposes.

4.1.7. **Category 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. This listing refers only to research that is not exempt.

4.1.8. **Category 8:** Continuing review of research previously approved by the convened IRB as follows:
4.1.8.1. 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

4.1.8.2. Where no subjects have been enrolled and no additional risks have been identified; or

4.1.8.3. Where the remaining research activities are limited to data analysis.

4.1.9. Category 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. All IRB applications are submitted to the ORA and processed in accordance with HRPP policy 2.1 (Submission of Items for Review by the IRB).

5.2. The designated Expedited Reviewer will have access to and review all documentation that the full IRB would normally receive for an initial review, Continuing Review, Change Requests, and other actions. Documentation will be available online through RSS (https://net.unmc.edu/rss).

5.3. Appointment of Designated Expedited Reviewers

5.3.1. An IRB member may serve as an expedited reviewer once he/she has been judged by the IRB Executive Chair to be sufficiently qualified and experienced. Specifically, the reviewer must have:

5.3.1.1. An acceptable level of knowledge about the area of research under review.

5.3.1.2. An understanding of the categories of research that qualify for expedited review.

5.3.1.3. The ability to apply the IRB approval criteria and determine conditions required for IRB approval.

5.3.1.4. An absence of a COI in accordance with HRPP policy 1.7 (IRB Member, Consultant, Staff COI Identification & Management) and verified on the IRB Review Checklist: Full and Conditional Approval.

5.3.2. An IRB administrator who is also a voting board member may serve as an expedited reviewer, provided he/she meets the requirements above.

5.3.3. Assignment of an expedited reviewer for a protocol will be made by the Executive Chair or his/her designee. In the absence of a specific designation to the contrary the expedited reviewer will be the IRB Administrator responsible for the protocol, provided he/she meets the requirements above.

5.4. Criteria for Expedited IRB Approval and Other Determinations

5.4.1. Criteria for IRB approval of all human subject are described in HRPP policy 2.5 (Criteria for IRB Approval).
5.4.2. During the review, the IRB reviewer must also determine, as appropriate:

5.4.2.1. The research is no more than minimal risk and represents one or more approvable expedited review categories of research.

5.4.2.2. The research does not include activities where identification of the subjects or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

5.4.2.3. The research does not involve classified research.

5.4.2.4. Whether the research requires continuing review more often than annually, as required at 45 CFR 46.109E; 21 CFR 56.108(a)(2), as appropriate to the degree of risk. The IRB may consider other factors as well:

5.4.2.4.1. The nature of and any risks posed by the clinical investigation.

5.4.2.4.2. The degree of uncertainty regarding the risks involved.

5.4.2.4.3. The vulnerability of the participants. When research involves vulnerable populations, additional safeguards have been included in the study to protect the rights and welfare of these participants.

5.4.2.4.4. The experience of the clinical investigator in conducting the clinical research.

5.4.2.4.5. The IRBs previous experience with that researcher or sponsor (e.g., compliance history, previous problems with the researcher obtaining informed consent, prior complaints from participants about the researcher).

5.4.2.4.6. The projected rate of enrollment.

5.4.2.4.7. Whether the study involves novel therapies.

5.4.2.5. Whether the research need verification from sources other than the PI that no material changes have occurred since the previous IRB review, as required at 45 CRF 46.102(a)(4) (or rev 45 CFR 46.108(a)(3)(ii)), or 21 CFR 56.108(a)(2). The IRB will consider:

5.4.2.5.1. Whether the research should have a third party observe the consent process in accordance with HRPP policy 1.2, Section 2.7 (Authority Granted to the IRB by the Organization).

5.4.2.5.2. Whether the current consent form is still accurate and complete.

5.4.2.5.3. Whether the research requires an audit of research records in accordance with HRPP policies 1.21 (Post Approval Monitoring of Research) and 8.4 (Review of Noncompliance Involving Risk to the Subject or Others).

5.4.2.6. Whether there are any significant new findings that arise from the review process that might relate to a subject’s willingness to continue participation in the study.

5.4.2.7. When the PI is the lead researcher of a multi-site trial, whether the management of information to the protection of human subjects is adequate, such as reporting of unanticipated problems, interim results, and protocol modifications.

5.4.3. The Expedited Reviewer cannot disapprove research. The reviewer retains the right to refer any protocol for review by the full convened IRB. Such protocols are then reviewed in
accordance with HRPP policy 2.2 (Full IRB Review). The reviewer must document the rationale for this determination and the rationale for review by the convened IRB.

6.0 Expedited Review Actions

6.1. Final approval and full release; initiation of the research is authorized.

6.1.1. 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 review and acceptance of specified modifications and/or submission of additional documents

6.2.1. All of the criteria for IRB approval are satisfied provided the investigator makes the specified changes. The IRB requirements for final approval and release are considered minor and not substantive in nature.

6.3. Refer to full IRB for review

6.3.1. The expedited reviewer is unable to make either of the above two findings.

7.0 Development of IRB Expedited Review and Final Approval Letters

7.1. Expedited review letters, which reflect the deliberations and decisions of the expedited reviewer(s), are developed by the IRB Administrators, in consultation with the IRB Executive Chair and reviewers as applicable.

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:

7.3.1. The decision to approve, or require modifications.

7.3.2. List any modifications/clarifications required by the Expedited Reviewer.

7.3.3. Signature authority is granted to the Expedited Reviewer in accordance with HRPP policy 1.19 (IRB Signature Authority).

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.

8.1.1. Extensions will be granted on a case-by-case basis, as determined by the IRB Administrator in consultation (if needed) with the IRB Executive Chair.

8.2. If there has been no response by 45 days (or by the expiration of the extension provided per section 8.1.1 above) the study will be withdrawn or closed.
9.0 Review of PI Responses

9.1. 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.

9.1.1. If, on consultation with the Executive Chair, the IRB Administrator determines that the investigator’s response to the IRB review is inadequate, incomplete, or contains significant changes not initially reviewed by the IRB, he/she will refer the submission for review by the full convened IRB.

Note: If the original submitted protocol required modification that were more than minor it would have been referred to the full IRB and reviewed in accordance with HRPP policy 2.2 (Full IRB Review).

10.0 Final IRB Approval Letter

10.1. The IRB final approval letter will document the following determinations:

10.1.1. Pertinent dates:

10.1.1.1. Date of full Board review.

10.1.1.2. Date all conditions set by the IRB were determined to be met and the study was granted final approval and release.

10.1.1.3. Expiration Date (per section 11.0)

10.1.2. Compliance with applicable HHS and FDA regulations

10.1.3. Verification that the research is classified as minimal risk

10.1.4. The applicable expedited review category

10.1.5. Subpart B category for inclusion of pregnant women (as applicable)

10.1.6. Subpart D category for inclusion of children (as applicable)

10.1.7. Waiver or alteration of the requirements for informed consent (as applicable)

10.1.8. Waiver of the requirement for documentation of informed consent. (as applicable)

11.0 IRB Approval Periods

11.1. The approval period for protocols for which continuing review is required is based on the date that the convened IRB gave conditional approval of the research. Studies approved with annual continuing review are valid for 364 days from the date of conditional approval; the approval period expires on the 365th day.

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. The full convened IRB retains the authority to require modification of the protocol and/or ICF(s) of research reviewed and approved under the expedited process, or to 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:

13.1.1. Fred & Pamela Buffett Cancer Center Scientific Review Committee
13.1.2. Conflict of Interest Committee
13.1.3. Sponsored Programs Administration/Contracts Office
13.1.4. Research Billing/Coverage Analysis Office

Administrative Approval:

Bruce G. Gordon, MD  IRB Executive Chair & Assistant Vice Chancellor for Regulatory Affairs
Christopher Kratochvil, MD  Institutional Official

Policy Amended:
- Revised June 13, 2018
- Initial April 11, 2016
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, including single subject protocol deviations.

2.0 Policy

2.1. It is the policy of the Organization that any proposed 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) (rev 45 CFR 46.108(3)(iii)); 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.

2.2. It is the policy of the Organization that protocol changes that are minor are eligible for expedited review under the provisions of HHS regulations at 45 CFR 46.110(b)(2) (rev 45 CFR 46.110(b)(1)(ii)) and FDA regulations at 21 CFR 56.110(b)(2), as applicable.

2.3. It is the policy of the Organization that single subject protocol deviations represent a change in protocol for a single subject and must be reviewed by the IRB prior to implementation; single subject protocol deviations that are minor may be eligible for expedited review by the Executive Chair, IRB Chairs, or designee under HHS or FDA regulations as above.

3.0 Definitions

3.1. **Major change in protocol** is a change that, in general, adversely affects the risk-benefit relationship by adding appreciably increasing risks, or appreciably decreasing potential benefits, or impacts the process of consent in a manner that might effect a reasonable person’s willingness to participate in the research. Specific activities which constitute major changes are listed in the appendix to this policy.

3.2. **Minor change in protocol** is a change that is not characterized as major per 3.1 above. Specific activities which constitute major changes are listed in the appendix to this policy.

3.3. **Single subject protocol deviation** is 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).

3.4. **Administrative change** is a change where 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 for Change Request in Protocol (other than Single Subject Protocol Deviation)

4.1. The PI must submit a Change Request in accordance with HRPP policy 2.1 (Submission of Items for Review by the IRB).

4.2. The Change Request will be processed for review in accordance with HRPP policy 2.1 (Submission of Items for Review by the IRB).

4.3. Administrative changes are reviewed and processed by an IRB Administrator or ORA staff.

4.4. The procedure for review via full IRB review or expedited review is in accordance with HRPP policies 2.2 (Full IRB Review) and 2.3 (Expedited Review), respectively.

4.5. The criteria for approval via full IRB review or expedited review is in accordance with HRPP policies 2.2, Section 3.9 (Full IRB Review) and 2.3, Section 5.4 (Expedited Review), respectively.

4.6. The date of continuing review is not changed based on the date of IRB approval of a Change Request.

4.7. Changes in protocol for research classified as exempt per HRPP policy 2.6 (Exempt Research) do not need to be submitted to the ORA provided the changes do not:

   4.7.1. Affect the risk-benefit relationship of the research

   4.7.2. Pose new risks which are greater than minimal

   4.7.3. Constitute a new risk to privacy or confidentiality

   4.7.4. Involve sensitive topics (including but not limited to personal aspects of the subject’s behavior, life experiences or attitudes)

   4.7.5. Involve deception

   4.7.6. Target a vulnerable population (as defined in HRPP Policy 4.1; Additional Protections for Vulnerable Populations)

   4.7.7. Include prisoners or children

   4.7.8. Otherwise suggest loss of the exempt status of the research.

   Note: Investigators are encouraged to contact the ORA to discuss whether changes to exempt research requires review by ORA.

5.0 Procedure for Single Subject Protocol Deviation

5.1. A Single Subject Protocol Deviation Request must be submitted to the ORA and be approved by either the IRB Executive Chair, IRB Chair or designee or the full IRB prior to the initiation of the deviation.

5.2. 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.

5.3. The IRB Executive Chair, IRB Chair or designee will obtain any additional information required for the review.

5.4. Single subject protocol deviation requests that are more than minor cannot be approved by the IRB Executive Chair, IRB Chair, or designee and will be referred to the full IRB by the designated IRB Administrator for review and approval.
5.5. Single subject protocol deviation requests that are minor will be reviewed and approved by the IRB Executive chair, IRB Chair, or designee.

5.6. All minor single subject protocol deviation requests approved by IRB Executive Chair, IRB Chair, or designee will be submitted to the IRB for their notification.

5.7. Initiation of a single subject protocol deviation without IRB approval represents noncompliance and addressed in accordance with HRPP policy 8.4 (Review of Noncompliance Involving the PI and Study Personnel).

6.0 Changes in a research activity requiring immediate implementation

6.1. If the change is required to eliminate an apparent, immediate hazard to the subject(s), the PI may implement the change without prior IRB approval in accordance with 45 CFR 46.103(b)(4) (rev 45 CFR 46.108(3)(iii)); 21 CFR 56.108(a)(4).

6.2. The ORA must be notified as soon as possible, but no later than two business days from the time the change was initiated.

   6.2.1. If the change was initiated for all subjects, a Change Request, the revised IRB application and other required documents must be submitted in accordance with this policy.

   6.2.2. If the change was initiated for a single subject, the Single Subject Protocol Deviation Request must be completed and submitted.

6.3. 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.

7.0 Provision of new information to subjects which requires immediate implementation

7.1. 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 46.103(b)(4) (rev 45 CFR 46.108(3)(iii)); 21 CFR 56.108(a)(4) and HRPP policy 5.1 (Obtaining Informed Consent from Research Subjects).

7.2. The ORA must be notified as soon as possible, but no later than two business days from the time the change was initiated. No new subjects can be accrued without IRB approval of a revised ICF that includes the relevant information.

7.3. If a Change Request 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.

7.4. 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.

ADMINISTRATIVE APPROVAL:
BRUCE G. GORDON, MD  IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS
CHRISTOPHER KRATOCHVIL, MD  INSTITUTIONAL OFFICIAL

POLICY AMENDED:
- AMENDED OCTOBER 4, 2018
- AMENDED JANUARY 24, 2018
- INITIAL JANUARY 5, 2016
Appendix to HRPP Policy 2.4 (Changes in Previously Approved Research)

Examples of Major and Minor Changes in Protocol or Single Subject Protocol Deviations (per Sections 3.1 and 3.2)

Examples of Major Changes:

- Changes in inclusion or exclusion criteria that broaden eligibility (i.e., broadening the range of the inclusion criteria or narrowing the range of the exclusion criteria) when risks to new subjects will be different than to previously eligible subjects.
- Addition of a vulnerable population (e.g., children, cognitively impaired, prisoners, socially or educationally disadvantaged, students).
- Increase in target accrual of subjects in studies where UNMC, CHMC and/or UNO are the only sites.
- Increase in study wide accrual of subjects in a multi-institution study.
- Increase in subject payment amount that exceeds criteria in HRPP Policy.
- Change in study design, where such change might affect risk, potential benefit to subject or scientific value or validity.
- Alterations in the dosage or route of administration of an administered drug.
- Addition of research activities that carry greater than minimal risk.
- Change in research activities where the change might negatively impact the potential benefit of the research (e.g., change from one questionnaire to another which is not substantively similar, or to a non-validated questionnaire; change from CT-based staging to clinically based staging of a tumor).
- Modification of research questionnaires or data collection instruments/processes to collect sensitive information (e.g., depression, sexuality, illegal activities).
- Addition of an element that may affect subject confidentiality (e.g., specimen banking or genetic testing; addition of focus groups or identifiable surveys).
- Extending substantially the duration of exposure to the test material or intervention.
- Deletion of laboratory tests, monitoring procedures, or study visits directed at the collection of information for safety evaluations.
- Addition of serious adverse events, serious UADEs or other significant risks to the Informed Consent process or form.
- Addition of a new (additional) consent form.
- Addition of a qualified investigator with a disclosable conflict of interest.
- Changes, which, in the opinion of the IRB chairperson or his/her designee, do not meet the criteria or intent of a minor modification.

Note: Multiple minor changes in the protocol, instruments, and/or consent may, together, be considered a major change subject to convened IRB review.
Examples of Minor Changes:

- Changes in inclusion or exclusion criteria that narrow eligibility (i.e., narrowing the range of the inclusion criteria or broadening the range of the exclusion criteria). Note: such changes should not appreciably reduce the likelihood that the research can be completed in a timely manner.
- Changes in inclusion or exclusion criteria that broaden eligibility (i.e., broadening the range of the inclusion criteria or narrowing the range of the exclusion criteria) when the investigator provides evidence that risks to the new subjects will not be different than to previously eligible subjects.
- Increase in local enrollment of subjects in a multi-institution study without a change in the overall study wide enrollment target.
- Addition of research activities that constitute no more than minimal risk. Note: addition of clinically indicated procedures where data will be used for research purposes (i.e., where the incremental risk is no more than minimal) are considered a minor change.
- Addition of research activities that would be eligible for expedited IRB review (per §3.110(b)(ii)) under categories 1-7 (unless specifically defined as “major” above).
- Alterations in the dosage form (e.g., tablet to capsule or oral liquid) of an administered drug, provided the dose and route of administration are unchanged.
- Decrease in the number or volume of biological samples collection, provided that such a change does not affect the collection of information related to safety evaluations.
- Decrease in the length of hospitalization or number of study visits, provided such a decrease does not affect the collection of information related to safety evaluations.
- Alternations subject payment schedule, provided such payments remain fairly pro-rated.
- Increase in subject payment amount provided such amounts are within criteria in HRPP Policy.
- Changes to improve the clarity of statements or to correct typographical errors in the protocol, CF or any questionnaire, provided that such a change does not alter the content or intent of the statement.
- Changes in recruitment materials and advertising, provided such items continue to satisfy criteria in HRPP Policy.
- Consent form modifications that add or remove information from the consent form so that it is consistent with an already approved IRB requirement.
- Updating a consent form using IRB approved boiler plate language.
- Addition or deletion of qualified investigators or personnel.
- Addition of study sites (that have a valid FWA and Reliance agreement as appropriate); or that serve as performance sites where informed consent will not be obtained; or that serve as performance sites where informed consent will be obtained by a UNMC, CHMC or UNO investigator.
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s criteria for IRB approval for human subject research, reviewed both by the full convened IRB or thorough an expedited review process.

2.0 Policy
It is the policy of the Organization human subject research must satisfy certain basic ethical and regulatory requirements, including those described in 45 CFR 46.111 and 21 CFR 56.111.

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 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.

3.1.1. The IRB will:

3.1.1.1. Ensure that the PI and other study personnel have the necessary qualifications, experience and medical licensure

3.1.1.1.1. The credentialing processes at Nebraska Medicine, BMC or CHMC in advance of IRB review will facilitate IRB assessment that investigators and study staff are qualified

3.1.1.2. Evaluate the research design in order to ensure that it is both sound and does not unnecessarily expose subjects to risk.

3.1.1.3. Ensuring that the research uses procedures already being performed on the subjects for diagnostic or treatment purposes

3.1.1.4. Assess whether risks are minimized by using alternative procedures that have less risk, precautions to decrease the likelihood that harms will occur, and contingencies to deal with harms if they occur.

3.1.1.5. Utilize reviewers (or other members or consultants) who have familiarity with the procedures being performed, and who therefore can more ably assess whether risks are minimized.

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.

3.2.1. 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.
3.2.2. The IRB will not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) in determining whether the risk-benefit relationship is acceptable.

3.2.3. 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.

3.2.4. 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.

3.2.5. 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 (for example, the detailed protocol or the published literature) which support the PI’s statement of anticipated benefits. The IRB does not classify financial compensation to the subject as a "benefit" in the context of the risk-benefit relationship.

3.2.6. 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.

3.2.7. The IRB will assess that the research has the necessary resources to protect subjects:

   3.2.7.1. Adequate time for the researchers to conduct and complete the research.
   3.2.7.2. Adequate number of qualified staff.
   3.2.7.3. Adequate facilities.
   3.2.7.4. Access to a population that will allow recruitment of the necessary number of participants.
   3.2.7.5. Availability of medical or psychosocial resources that participants may need as a consequence of the research.

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 that involves a category of subjects who are vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons.

3.3.1. The IRB will assess the IRB application and other related materials (for example, recruitment materials) 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.

3.3.2. In making this assessment the IRB will evaluate at least the following:

   3.3.2.1. Purpose of the research.
3.3.2.2. Setting in which the research occurs
3.3.2.3. Whether prospective subjects will be vulnerable to coercion or undue influence
3.3.2.4. The selection (inclusion/exclusion) criteria
3.3.2.5. Scientific and ethical justification for inclusion of vulnerable populations
3.3.2.6. Scientific and ethical justification for excluding classes of persons who might benefit from the research.
3.3.2.7. Subject recruitment and enrollment procedures
3.3.2.8. The influence of compensation to participants

3.3.3. 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.**

3.4.1. 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) under circumstances that provide sufficient opportunity to discuss and consider whether or not to participate and that minimize the possibility of coercion or undue influence, and which includes information that a reasonable person would want to have in order to make an informed decision about whether to participate. 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.

3.4.2. 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.**

3.5.1. 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.

3.5.2. 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.**

3.6.1. 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.

3.6.2. 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).
3.6.3. The IRB will also determine whether the research requires review more often than annually, as described in HRPP policy 3.1 (Assessing the Need for Increased Monitoring, Interim Continuing Review, and Verification from Sources Other than the PI).

3.6.4. The approval period will be documented in the IRB records and conveyed to the PI.

3.6.5. 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.

3.6.6. 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.

3.7.1. Privacy refers to persons and their interest in controlling access to themselves. In order to ensure protection of subject’s privacy, the IRB will apply the following criteria:

   3.7.1.1. The methods used to identify and contact prospective subjects is acceptable.
   3.7.1.2. The settings in which the individual will participate in the consent process as well as the research adequately protect privacy.
   3.7.1.3. The personnel involved in the research are appropriate in consideration of their responsibilities.
   3.7.1.4. All necessary procedures are in place during the research to protect privacy.

3.7.2. 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:

   3.7.2.1. The reason(s) for disclosing data to individuals, sponsors or other organizations is justified.
   3.7.2.2. The procedures for securing and transmitting data are acceptable.
   3.7.2.3. 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, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

3.8.1. The IRB will review the characteristics of the proposed subject population in consideration of:

   3.8.1.1. The nature and risks of the research.
   3.8.1.2. Whether the subjects are likely to be vulnerable to coercion, undue influence, or more susceptible to risk.

3.8.2. 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 4.1 (Additional Protections for Vulnerable Populations).
4.0 Additional Considerations
In addition to the specific criteria described in section 3.0, the IRB will consider other applicable federal, state and local law and regulations, Organization policies, and basic ethical principles (as described in the Belmont Report, or the World Medical Association Declaration of Helsinki) when deciding whether a research proposal is approvable.

ADMINISTRATIVE APPROVAL:
BRUCE G. GORDON, MD  IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS
CHRISTOPHER KRATOCHVL, MD  INSTITUTIONAL OFFICIAL

POLICY AMENDED:
- REVISED JANUARY 24, 2018
- INITIAL JANUARY 11, 2016
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 101.b (rev 45 CFR 46.104(d)) and 21 CFR 56.104, 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. Investigators or individuals with a conflict of interest in the research are not permitted to make a final determination of the exempt status of research.

2.2. It is the policy of the Organization that the ORA has the authority to refer to the full IRB for review and approval any exempt human subject research where such review and approval would meaningfully enhance protection of the rights and welfare of human subjects.

2.3. It is the policy of the Organization that exempt human subject 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. The status of Exempt research is maintained in the Research Administration (RA) database and Research Support Services (RSS) application system.

3.0 Categories of Exemption
3.1. Prior to the effective date of the Revised Rule, the following research is exempt from 45 CFR 46

3.1.1. Category 1: Research is that which is conducted in established or commonly accepted educational settings, involving normal educational practices, such as (i) research on regular and special education instructional strategies, or (ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods (45 CFR 46.101(b)(1)).

3.1.1.1. Category 1: Per HRPP policy to be eligible for exemption under category 1

3.1.1.1.1. Study procedures must not involve sensitive subjects (e.g., sex or substance abuse education)

3.1.1.1.2. The research is not regulated by the US FDA.

3.1.1.1.3. Provisions must be made to ensure the existence of a non-coercive environment for those students who choose not to participate

3.1.1.1.4. The school or other institution must grant written approval for the research to be conducted

3.1.1.1.5. Informed consent must be obtained from the prospective subject or their parent or LAR unless a waiver is granted by the IRB Executive Chair/designee

3.1.2. Category 2: Research that only involves educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public
behavior, unless: (i) information obtained is recorded in such 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.

3.1.2.1. Survey procedures involving children is not exempt under category 2

3.1.2.2. Observation of public behavior which involves children is only exempt when the investigator(s) do not participate in the activities being observed

3.1.2.3. The research is not regulated by the US FDA.

3.1.3. **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 category 2, 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.

3.1.3.1. The research is not regulated by the US FDA.

3.1.4. **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))

3.1.5. **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))

3.1.5.1. 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.

3.1.5.2. The research or demonstration project must be conducted pursuant to specific federal statutory authority.

3.1.5.3. There must be no statutory requirement that the project be reviewed by an Institutional Review Board (IRB).

3.1.5.4. The project must not involve significant physical invasions or intrusions upon the privacy of participants.

3.1.5.5. The research is not regulated by the US FDA.

3.1.6. **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))

3.2. Following the effective date of the Revised Rule, the preceding exemptions (section 3.1) are no longer valid, and are replaced by the following categories:

3.2.1. **Category 1:** Research which specifically involves normal educational practices that are not likely to adversely impact students’ opportunity to learn required educational content or the assessment of educators who provide instruction. This includes most research on regular and special education instructional strategies, and research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods (rev 45 CFR 46.104(d)(1))

3.2.1.1. Per HRPP Policy to be eligible for exemption under category 1

- 3.2.1.1.1. Study procedures must not involve sensitive subjects (e.g., sex or substance abuse education)
- 3.2.1.1.2. The research is not regulated by the US FDA.
- 3.2.1.1.3. Provisions must be made to ensure the existence of a non-coercive environment for those students who choose not to participate
- 3.2.1.1.4. The school or other institution must grant written approval for the research to be conducted
- 3.2.1.1.5. Informed consent must be obtained from the prospective subject or their

3.2.2. **Category 2:** Research which only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior (including visual or auditory recording) if at least one of the following criteria is met: (i) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects; or (ii) any disclosure of the human subjects’ responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects’ financial standing, employability, educational advancement, or reputation; or (iii) the information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review per HRPP policy 2.8 (Limited IRB Review) (rev 45 CFR 46.104(d)(2))

3.2.2.1. Under the Revised Rule research involving educational tests performed on minors, or the observation of public behavior of minors is not eligible for exemption under criteria (i) and (ii) above unless the investigator does not participate in the activities being observed.

3.2.2.2. Under the Revised Rule research involving minors is not eligible for exemption under criterion (iii) above.

3.2.2.3. The research is not regulated by the US FDA.

3.2.3. **Category 3:** Benign behavioral interventions in conjunction with the collection of information from an adult subject through verbal or written responses (including data entry) or audiovisual recording if the subject prospectively agrees to the intervention and information collection and at least one of the following criteria is met: (i) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot
readily be ascertained, directly or through identifiers linked to the subjects; or (ii) any disclosure of the human subjects’ responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects’ financial standing, employability, educational advancement, or reputation; or (iii) the information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review per \textit{HRPP policy 2.8 (Limited IRB Review)}.\end{itemize}

\textbf{3.2.3.1.} Benign behavioral interventions are brief in duration, harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact on the subjects, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing. Examples of such benign behavioral interventions would include having the subjects play an online game, having them solve puzzles under various noise conditions, or having them decide how to allocate a nominal amount of received cash between themselves and someone else.

\textbf{3.2.3.2.} Consent of the subject is required, as per section 6.7 below.

\textbf{3.2.3.3.} If the research involves deceiving the subjects regarding the nature or purposes of the research, this exemption is not applicable unless the subject authorizes the deception through a prospective agreement to participate in research in circumstances in which the subject is informed that he or she will be unaware of or misled regarding the nature or purposes of the research.

\textbf{3.2.3.4.} Research involving minors is not eligible for exemption under category 3.

\textbf{3.2.3.5.} The research is not regulated by the FDA.

\textbf{3.2.4. \textit{Category 4}:} Secondary research for which consent is not required: Secondary research uses of identifiable private information or identifiable biospecimens, if at least one of the following criteria is met: (i) The identifiable private information or identifiable biospecimens are publicly available; or (ii) information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects; or (iii) the research involves only information collection and analysis involving the investigator’s use of identifiable health information when that use is regulated under the HIPAA Privacy Rule (45 CFR 164 subpart E) (45 CFR 46.104(d)(4)).

\textbf{3.2.4.1.} It is expected that use of this exemption will include, where appropriate, individual’s authorization for future, secondary research use of PHI, or waiver of authorization per \textit{HRPP policy 5.2 (Waiver or Alteration of Informed Consent and HIPAA Authorization)}.

\textbf{3.2.4.2.} This exemption does not apply where the PHI originates at an entity subject to HIPAA but is disclosed to an investigator who is not subject to HIPAA.

\textbf{3.2.5. \textit{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 public benefit or service programs, including procedures for obtaining benefits or services under those programs, possible changes in or alternatives to those programs or procedures, or possible changes in methods or levels of payment for benefits or services under those programs (45 CFR 46.104(d)(5)).

\textbf{3.2.5.1.} The research or demonstration project must be listed on a Federal Web site maintained by the department or agency, as per requirements of 45 CFR 46.104(d)(5)(i).
3.2.5.2. 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.

3.2.5.3. There must be no statutory requirement that the project be reviewed by an Institutional Review Board (IRB).

3.2.5.4. The research is not regulated by the US FDA.

3.2.6. **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 46.104(d)(6))

3.2.7. **Categories 7 and 8**: Storage, maintenance and secondary research for which broad consent is required: Storage or maintenance of identifiable private information or identifiable biospecimens for potential secondary research use; and Research involving the use of identifiable private information or identifiable biospecimens for secondary research use (45 CFR 46.104(d)(7 and 8)).

3.2.7.1. UNMC does not currently allow investigators within the Organization to use broad consent for storage, maintenance or secondary use of identifiable private information or identifiable biospecimens.

3.2.7.2. Identifiable private information or identifiable biospecimens obtained under broad consent by investigators outside the Organization may be transferred to, and used by an investigator within the organization, provided appropriate Material Transfer Agreements and/or Data Use Agreements are in place, and the ORA has determined that:

3.2.7.2.1. The Broad Consent form obtained by the outside investigator included all the required elements of broad consent per 45 CFR 46.116(d); and

3.2.7.2.2. The research to be conducted within the Organization is within the scope of the general description of the types of research that might be conducted (per 45 CFR 46.116(d)(2)); that is, the broad consent form included sufficient information such that a reasonable person would expect that the broad consent would permit the types of research to be conducted within the Organization.

3.3. **FDA Category (c)**: Emergency use of a test article, provided that such emergency use is reported to the IRB within 5 working days (21 CFR 50.104(c))

3.3.1. This exemption applies only to the first use of the test article within the Organization. Any subsequent use of the test article at the Organization is subject to IRB review per **HRPP policy 6.4 (Emergency Use of a Test Article)**.

3.4. **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))
4.0 Limitations on Categories of Exemption

4.1. Research involving children where research involves survey or interview procedures or observation of public behavior that qualify under category 2 are not exempt if the investigator(s) will participate in the activities being observed (45 CFR 46.101, or rev 45 CFR 46.104(b)(3)).

4.2. Research involving prisoners is not exempt, except for research aimed at involving a broader subject population that only incidentally includes prisoners (45 CFR 46.101, or rev 45 CFR 46.104(b)(2)).

4.3. Research involving vulnerable populations, sensitive topics (including but not limited to personal aspects of the subject’s behavior, life experiences or attitudes), deception, or greater than minimal risk to subjects, even when allowable under sections 3.0 or 4.0 above, may be deemed not exempt, on a case by case basis. This decision is made by the IRB Administrator in consultation with the IRB Executive Chair or IO.

4.4. Any human subjects research where review by the full IRB would meaningfully enhance protection of the rights and welfare of human subjects may be deemed not exempt. This decision is made by the IRB Administrator in consultation with the IRB Executive Chair or IO review.

5.0 Procedures

5.1. Protocols which may be eligible for exemption are submitted to ORA using the following applications:

5.1.1. **Exempt Educational, Behavioral, and Social Science Research Application** will be used for the following:

5.1.1.1. Categories 1-3, 5-6, and FDA category (d)

5.1.1.2. Category 4 research which involves only identifiable private information not obtained from medical records.

5.1.2. **Human Biological Materials Research Application** will be used for the following:

5.1.2.1. Category 4 research which involves identifiable biospecimens, with or without associated medical records.

5.1.3. **Medical Records Research Application** will be used for the following:

5.1.3.1. Category 4 research which involves only identifiable private information from medical records.

*Note: The Organization does not utilize Exemption categories 7 and 8.*

5.2. Protocols which appear to be eligible for exemption 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 as per HRPP policy 1.7 (IRB Member, Consultant, Staff COI Identification & Management).

5.3. The IRB Administrator will:

5.3.1. In consultation, as necessary, with the IRB Executive Chair/designee, make the final determination of exempt status.

5.3.2. Determine whether criteria for approval described in section 6.0 are satisfied. If necessary, the IRB Administrator is authorized to require clarification or modification of the IRB Application to determine whether the criteria re satisfied.
5.3.3. Complete the *Exempt Research Checklist* which includes the category under which the research qualifies for exemption.

5.3.4. Communicate the determination with the PI and Coordinator(s) via letter, email and/or the electronic file.

5.4. 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 (per HRPP policy 2.3: Expedited Review of Research).

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.

5.5. If *Behavioral and Social Science Research Application* is submitted and subsequently determined to be exempt, the PI is notified accordingly.

6.0 Criteria for Approval of Exempt Research

6.1. The research must qualify for exemption under the categories specified above (section 4.0)

6.2. The research must represent no more than minimal risks to subjects.

6.3. Selection of subjects must be equitable.

6.4. If identifiable private information is recorded, there must be adequate provisions to maintain the confidentiality of the data.

6.5. There must be adequate provisions to maintain the privacy interest of subjects.

6.6. The rights and welfare of research subjects must be adequately protected.

6.7. If the investigator or his/her staff interacts with subjects, there must be a process of informed consent that will disclose at least (1) a statement that the activity involves research; (2) a statement that participation is voluntary; (3) a description of the procedures; (4) a description of risks if any; and (5) the name and contact information for the researcher.

6.8. Following the effective date of the Revised Rule, the following additional criteria apply:

   6.8.1. For exempt research under categories 2 or 3 where the information is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects (as per rev 45 CFR 46.104(d)(2)(iii) or rev 45 CFR 46.104(d)(3)(i)(C); sections 4.2B and 4.2C above), the IRB must conduct a limited review as described in HRPP policy 2.8 (Limited IRB Review).

   6.8.2. For exempt research under category 4 where the research involves only information collection and analysis involving the investigator’s use of identifiable health information (as per rev 45 CFR 46.104(d)(4)(iii); section 3.4 above), the ORA must determine that such use is regulated under the HIPAA Privacy Rule (45 CFR 164 subpart E).

7.0 Actions

7.1. **Approval and full release; initiation of the research is authorized:** Criteria in section 6.0 are satisfied. 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:** Criteria in section 6.0 will be satisfied if specified modifications are made by the investigator. Once the modifications are made, and are accepted by the IRB Administrator, the investigator will be notified of the approval in writing and is authorized to start the study.

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:** The protocol is referred for review by the full IRB in accordance with section 4.0 above.

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:

   - 8.1.1. Fred & Pamela Buffett Cancer Center Scientific Review Committee
   - 8.1.2. Conflict of Interest Committee
   - 8.1.3. Sponsored Programs Administration/executed contracts office

**Administrative Approval:**
Bruce G. Gordon, MD  IRB Executive Chair & Assistant Vice Chancellor for Regulatory Affairs
Christopher Kratochvil, MD  Institutional Official

**Policy Amended:**
- Revised February 5, 2018
- Initial January 5, 2016
1.0 Purpose

The purpose of this policy and procedure is to describe the Organization’s requirements for continuing review of approved research.

2.0 Policy

2.1. It is the policy of the Organization that non-exempt research which is subject to the Common Rule or FDA Regulations shall undergo continuing review at intervals appropriate to the degree of risk, but not less than once per year, except as allowed under 45 CFR 46.109(f) after the effective date of the Revised Rule.

2.2. It is the policy of the Organization that non-exempt research which is not subject to the Common Rule or FDA Regulations shall undergo continuing review at intervals appropriate to the degree of risk.

3.0 Continuing Review Frequency

3.1. Non-exempt research which is subject to the Common Rule or FDA Regulations shall undergo continuing review at intervals appropriate to the degree of risk, but not less than once per year, except as described in sections 3.3 or 3.4 below.

3.1.1. The IRB may determine that continuing review is required more often than annually, as described in HRPP policy 3.1 (Assessing the Need for Increased Monitoring, Interim Continuing Review, and Verification from Sources Other than the PI).

3.1.2. Non-exempt research which is not subject to the Common Rule or FDA Regulations shall undergo continuing review at intervals appropriate to the degree of risk.

3.1.3. Unless the IRB specifically determines at the time of initial review or continuing review that a protocol should be reviewed less often than annually, the research will be subject to review annually.

3.2. Unless an IRB determines otherwise, continuing review of research is not required in the following circumstances:

3.2.1. Research which underwent expedited review in accordance with 45 CFR 46.110 after the effective date of the Revised Rule.

3.2.2. Research approved after the effective date of the Revised Rule that has progressed to the point that it involves only data analysis, including analysis of identifiable private information or identifiable biospecimens.

3.2.3. Research approved after the effective date of the Revised Rule that has progressed to the point that it involves only accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care.

3.2.4. If the IRB determines that continuing review is required for research in any of the above categories, the rationale will be recorded in accordance with 45 CFR 46.115(a)(3).

Note: Non-exempt research approved prior to the effective date of the Revised Rule requires continuing review as per sections 3.1 and 3.2.
3.3. Unless the ORA determines otherwise, continuing review is not required for exempt research.

3.3.1. If the ORA determines that continuing review is required for a specific research protocol which was eligible for exemption under categories 2 and 3 (rev 45 CFR 46.104(d)(2) and (3)) and had initially undergone limited IRB review after the effective date of the Revised Rule, the rationale will be recorded in accordance with rev 45 CFR 46.115(a)(3).

Note: Following the effective date of the Revised Rule, the Organization will not utilize exempt categories 7 and 8 (rev 45 CFR 46.104(d)(7) or (8)).

4.0 Criteria for Review

4.1. The criteria for continuing approval of all human subject research (either by full board or by expedited review) are described in HRPP policy 2.5 (Criteria for IRB Approval).

4.1.1. During continuing review by the full IRB, the IRB must also determine:

4.1.1.1. Whether the research requires continuing review more often than annually [as required at 45 CFR 46.109(e); 21 CFR 56.108(a)(2)], as appropriate to the degree of risk. The IRB will consider:

4.1.1.1.1. The nature of and any risks posed by the clinical investigation.
4.1.1.1.2. The degree of uncertainty regarding the risks involved.
4.1.1.1.3. The vulnerability of the participants.
4.1.1.1.4. The experience of the clinical investigator in conducting the clinical research.
4.1.1.1.5. The IRBs previous experience with that researcher or sponsor (e.g., compliance history, previous problems with the researcher obtaining informed consent, prior complaints from participants about the researcher).
4.1.1.1.6. The projected rate of enrollment
4.1.1.1.7. Whether the study involves novel therapies.

4.1.1.2. Whether the research need verification from sources other than the PI that no material changes have occurred since the previous IRB review as required at 45 CFR 46.103(a)(4) (or rev 45 CFR 46.108(a)(2)(i)), or 21 CFR 56.108(a)(2).

4.1.1.2.1. Whether the current consent form is still accurate and complete.
4.1.1.2.2. Whether the research should have a third party observe the consent process in accordance with HRPP policy 1.2, Section 2.7 (Authority Granted to the IRB by the Organization).
4.1.1.2.3. Whether the research requires an audit of research records in accordance with HRPP policies 1.21 (Post Approval Monitoring of Research) and 8.4 (Review of Noncompliance Involving the PI and Study Personnel).

4.1.1.3. Whether there are any significant new findings that arise from the review process that might relate to a subject’s willingness to continue participation in the study.

4.1.1.4. When the PI is the lead researcher of a multi-site trial, whether the management of information to the protection of human subjects is adequate, such as reporting of unanticipated problems, interim results, and protocol modifications.
4.2. During continuing review by an expedited reviewer, the reviewer will consider the additional factors described in section 4.1.1 above. If the reviewer believes any of these situations apply, the protocol will be referred to the full IRB.

5.0 Procedures

5.1. Continuing review, when it is required, is conducted by the convened IRB, except under the following circumstances:

5.1.1. Research previously approved by a convened IRB where no subjects have been enrolled and no additional risks have been identified may undergo expedited review.

5.1.2. Research which satisfies the requirements of OHRP Expedited Review Categories (1998) and HRPP policy 2.3 ( Expedited Review), section 4.1.9, expedited category 9 (“research not conducted under an investigational new drug application or investigational device exemption where [expedited] categories 2 through 8 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”) may undergo expedited review.

5.2. Protocols that were initially approved by IRB-01 or IRB-02 will undergo continuing review at the IRB-02 meeting. If the Executive Chair determines that earlier review is necessary to minimize risk or inconvenience to subjects, protocols can be reviewed at the IRB-01 meeting as a “Special Review Item”.

5.3. Protocols that were initially approved by IRB-04 will undergo continuing review at the IRB-04 meeting. If the Executive Chair determines that review earlier review is necessary to minimize risk or inconvenience to subjects, protocols can be reviewed at the IRB-02 as a “Special Review Item”, provided at least one member of IRB-04 who was present at the time of the initial conditional approval is present at IRB-02 and can serve as primary reviewer.

5.4. Protocols that were initially approved by IRB-03 will undergo continuing review at the IRB-02 meeting or the IRB-04 meeting, depending on the nature of the research and the predominant subject population, at the discretion of the Executive Chair.

5.5. For continuing review by the full IRB, IRB members will be provided documents for review as defined in HRPP policy 2.2 (Full IRB Review).

5.6. The expiration date of protocols for which continuing review is required is based on the date that the convened IRB gave conditional approval of the research. Studies approved with annual continuing review are valid for 364 days from the date of conditional approval; the approval period expires on the 365th day.

5.7. The ORA will send emails to the PI and the lead coordinator at least 60 days and 45 days prior to the date of expiration.

5.8. If a protocol for which continuing review is required has not received full approval by the expiration date, the protocol is considered “expired”, and investigators are no longer authorized to conduct research activities or enroll subjects.

5.8.1. Approval expiration is not study suspension, and the protocol is not subject to reporting as per HRPP policy 8.6 (Study Hold, Suspension, and Termination).

5.8.2. The investigator and the lead coordinator will be notified by email that a study is expired and that investigators are no longer authorized to conduct research activities or enroll subjects. It is the responsibility of the PI to notify all investigators.
5.8.3. If the investigator believes that it would be in the best interests of a subject participating in an expired research study to continue research activities, a request may be made to the IRB.

5.8.3.1. The Executive Chair or his/her designee has the authority to grant approval on an individual subject basis.

5.8.3.2. Only activities which directly benefit the subject, or directly reduce risk to subjects, may continue.

5.8.3.3. The IRB will be notified of the exception at the next convened meeting.

5.9. If the investigator does not respond to the “Approval Expired” notification from the ORA that a study has expired within 20 business days, the study will be considered closed.

5.10. The convened IRB will conduct continuing review as per section 4.0 above.

5.11. The convened IRB will be notified in the detailed agenda of protocols approved by expedited review per section 5.1 above. Detailed information about the protocol will be available on RSS.

5.12. For research that requires FPBCC Scientific Review Committee (SRC) review, IRB continuing approval will be contingent of SRC review and approval.

5.12.1. The IRB Continuing Review Administrator, or designee, in consultation with the IRB Executive Chair, or one of the Chairs or Vice-Chairs will be responsible for assuring that no substantive changes have been made to the protocol or the consent forms by the SRC. If substantive changes have been made, re-review by the convened IRB will be required.

5.13. The expiration date for the next continuing review based on the date that the convened IRB gave conditional re-approval of the research (as per section 5.6 above)

5.14. In accordance with 45 CFR 46.115(a)(3) the ORA will keep appropriate records of all continuing review activity.

5.15. For research that is exempt, or for which continuing review is no longer required per section 3.3, the ORA will contact the investigator by email annually on the anniversary of the date that the convened IRB gave conditional approval of the research, or the research was determined by the ORA to be exempt. The email will ask the investigator whether the research is still on-going, or is completed, and whether there have been any unanticipated problems involving risk (per HRPP policy 8.3: IRB Review of Unanticipated Problems Involving Risk to the Subject or Others). In addition, the email will remind investigators of their continued responsibility to submit Change Requests, deviation requests, reports of noncompliance, and reports of adverse events and unanticipated problems, as well as a Completion report on completion of the research.

5.16. If the research is still active, the investigator will be instructed to update Clinicaltrials.gov as applicable, per HRPP policy 1.29 (Clinicaltrials.gov Reporting)

5.17. If the investigator reports any unanticipated problems, they will be handled as per HRPP policy 8.3 (IRB Review of Unanticipated Problems Involving Risk to the Subject or Others).

5.18. If the research is completed, ORA records will be updated and the investigator will be responsible for the activities described in HRPP policy 2.9 (Closure of On-Going Research).

5.19. If the investigator does not respond within 20 business days, the study will be considered closed, and ORA records will be updated. The investigator will be responsible for the activities described in HRPP policy 2.9 (Closure of On-Going Research).
Administrative Approval:
Bruce G. Gordon, MD  IRB Executive Chair & Assistant Vice Chancellor for Regulatory Affairs
Christopher Kratochvil, MD  Institutional Official

Policy Amended:
- Amended September 7, 2018
- Initial February 6, 2018
Note: This policy is NOT valid until after the effective date for the Revised Rule. Prior to that effective date the Organization does not perform limited IRB review.

1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements and procedure for limited IRB review.

2.0 Policy
It is the policy of the Organization that research which satisfy the criteria for exemption under 45 CFR 46.104(d)(2 or 3) undergo limited IRB review if information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects.

3.0 Limited IRB Review
3.1. Limited IRB review will be conducted for research which satisfy the criteria for exemption as follows:

3.1.1. Exempt Category 2 section (iii) [45 CFR 46.104(d)(2)(iii)]: that is research that only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior (including visual or auditory recording) … if the information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects.

3.1.2. Exempt Category 3 section (i)(C) [45 CFR 46.104(d)(3)(i)(C)]: that is, research involving benign behavioral interventions in conjunction with the collection of information from an adult subject through verbal or written responses (including data entry) or audiovisual recording if the subject prospectively agrees to the intervention and information collection and … the information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects.

3.1.3. The Organization does not currently utilize exempt categories 7 and 8 (secondary research for which broad consent is required); therefore, limited IRB review is not used in that context.

4.0 Criteria for Approval
4.1. For research to be approved under exempt category 2 section (iii) or category 3 section (i)(C) limited IRB review must find that there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data [45 CFR 46.111(a)(7)].

4.2. Since the adequacy of provisions to maintain confidentiality depend, in part, on the nature of the research, the methods involved, the characteristics of the subject population (including the
vulnerability of subjects) and the risks related to the research, limited IRB review will take into account all this additional factors.

5.0 Procedure

5.1. Research which appears to be eligible for approval under exempt categories 2 section (iii) or 3 section (i)(C) must be submitted on an Exempt Educational, Behavioral, and Social Science Research Application, and must contain enough information for limited IRB as described in section 4.0 above. The submission must include:

5.1.1. The full protocol or application containing the relevant information to determine whether the proposed research fulfills the criteria for approval.

5.1.2. Surveys, interview scripts

5.1.3. Proposed consent form(s).

5.1.4. Recruitment material.

5.2. Limited IRB review may be performed by expedited review, as described in HRPP policy 2.3 (Expedited Review).

5.2.1. If the expedited reviewer cannot determine that the criteria for approval defined in section 4.0 are satisfied, then the research will be referred to the convened IRB. The reviewer must document the rationale for this determination and the rationale for review by the convened IRB.

5.2.2. The expedited reviewer may not disapprove the research.

5.2.3. Limited IRB review determinations will be documented on the Limited IRB Review Checklist.

5.3. Limited IRB review determinations:

5.3.1. The research is no more than minimal risk.

5.3.2. For exemption Categories 2 section (iii) and 3 section (i)(C), there are adequate protections for privacy interests of participants and the confidentiality of the data.

Note: For exemption Category 7 and 8, UNMC does not currently allow investigators within the Organization to use broad consent for storage, maintenance or secondary use of identifiable private information or identifiable biospecimens.

5.3.3. The research fulfills the ethical standards of the Organization as per HRPP policy 1.1 (Human Research Protection Program).

5.3.4. The research does not involve minors.

5.3.5. Selection of subjects must be equitable.

5.3.6. The research does not involve prisoners, except for research aimed at involving a broader participant population that only incidentally includes prisoners.

5.3.7. The research is not regulated by the FDA.

5.4. The investigator will be informed of the findings of the limited IRB review as per HRPP policy 2.3 (Expedited Review).

5.5. Research approved by limited IRB review under exempt categories 2 section (iii) or 3 section (i)(C) does not require continuing review unless the expedited reviewer determines that such review would meaningfully protect the rights and welfare of human subjects of research.
5.6. The IRB retains the authority to suspend or terminate IRB approval of research approved with a limited review as per HRPP policy 8.6 (Study Hold, Suspension, and Termination).

Administrative Approval:
Bruce G. Gordon, MD  IRB Executive Chair & Assistant Vice Chancellor for Regulatory Affairs
Christopher Kratochvil, MD  Institutional Official

Policy Amended:
➢ Initial January 24, 2018
1.0 Purpose
The purpose of this policy is to describe the process of closing an on-going human research study, and to describe the Organization's requirements of investigators when studies are closed.

2.0 Policy
It is the policy of the Organization that all research activities must cease when a research study has closed.

3.0 Definitions
3.1. Closure of a study means that the research study is completed, and all research interventions have ceased. Completion may occur:
   3.1.1. When the aims of the study have been satisfied.
   3.1.2. As a decision by the investigator before study aims have been met (for example, due to lack of funds, poor accrual, departure of an investigator, demonstration of lack or efficacy or futility).
   3.1.3. As a decision by the sponsor or the granting agency.
   3.1.4. By the IRB or ORA if the investigator has failed to respond to the “Approval Expired” notification from the ORA that a study has expired, as per HRPP policy 2.7 (Continuing Review of Research).

3.2. Expiration means that approval is no longer valid because required continuing review has not received full approval by the IRB by the expiration date, per HRPP policy 2.7 (Continuing Review of Research). Approval expiration is not study suspension.

3.3. Suspension means that the research study is stopped, as a result of a directive of the IRB at a convened meeting, or a directive of the IRB Executive Chair (in consultation with the IO as appropriate), as per HRPP policy 8.6 (IRB Study Hold, Suspension and Termination). Suspension is usually temporary.

3.4. Termination means that the research study is stopped, as a result of a directive by the IRB at a convened meeting, or by the Organization, per HRPP policy 8.6 (IRB Study Hold, Suspension and Termination). Termination is permanent.

4.0 Procedures
4.1. When a study is closed, all research activities must cease. The investigator may not conduct any further research activities (including collection of existing or additional identifiable private information, or new analysis of existing identifiable private information), or allow any other person or organization to conduct any further research activities.

4.2. The investigator is responsible for notifying the IRB when a study is closed by him/her, or by the sponsor or the granting agency.
4.3. When a study is closed the investigator is responsible for revising the study status on ClinicalTrials.gov, and posting study results as appropriate, as per HRPP policy 1.29 (ClinicalTrials.gov Reporting).

4.4. After the effective date of the Revised Rule, when a study is closed the investigator is responsible for posting the consent forms on ClinicalTrials.gov as required.

4.5. If a study is closed by the IRB or ORA (per section 3.1.4 above), the investigator may request reactivation, with adequate justification, within two months from the date of completion. Reactivation after the two month grace period requires submission of a new IRB application.

ADMINISTRATIVE APPROVAL:
BRUCE G. GORDON, MD  IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS
CHRISTOPHER KRATOCHVIL, MD  INSTITUTIONAL OFFICIAL

POLICY AMENDED:
➢ Initial January 12, 2018
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. At the time of initial review, continuing review, or any other event, the IRB may decide that a research protocol requires increased monitoring and/or interim continuing review. Types of research which might require such actions include, but are not limited to:

3.1.1. Studies that utilize drugs or treatments associated with a higher than typical risk of toxicity.

3.1.2. Studies where there is an expectation of high morbidity and mortality due to the underlying medical condition of the subjects.

3.1.3. Studies whose design includes one or more group of subjects who will receive less than standard care (for example, use of placebo where there is an active alternative treatment, or withholding standard treatments during some point in the study), or where there is a significant risk intervention that is performed solely for research purposes.

3.1.4. Studies where the FPBCC Scientific Review Committee (SRC), or other equivalent scientific review body, has indicated the need for interim review or additional monitoring.

3.1.5. Any other situation where the IRB believes that increased monitoring or interim continuing review will meaningfully protect the rights and welfare of human subjects of the research.

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 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. At the time of initial review, continuing review, or any other event, the IRB may decide that a research protocol requires verification from sources other than the PI that no material changes
have occurred since the previous IRB review. Research that falls in any of the following categories may warrant consideration of verification from sources other than the PI:

4.1.1. Research performed by investigators with a history of significant noncompliance, recurrent delays in submitting amendments, high number of IRB approval expirations, or failure to respond to IRB review letters or other correspondence in a timely manner.

4.1.2. 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.
1.0 Purpose
The purpose of this policy is to describe the Organization’s requirements for data and safety monitoring for non-exempt research.

2.0 Policy
It is the policy of the Organization that all non-exempt research must have an appropriate plan for data and safety monitoring in consideration of the nature and risk level of the research. The Data and Safety Monitoring Plan (DSMP) may or may not include a formal Data and Safety Monitoring Board (DSMB).

3.0 Data and Safety Monitoring Plan
3.1. The DSMP must be developed to fit the design and risk profile of the research. It may include, as appropriate, elements such as:
   3.1.1. The frequency of data collection, including when safety data collection starts.
   3.1.2. Safety data collection (e.g., case report forms, study visits, subject telephone calls).
   3.1.3. Laboratory tests and radiographs to assess toxicity and efficacy
   3.1.4. Review of cumulative safety and efficacy data.
   3.1.5. Subject withdrawal criteria and stopping criteria
   3.1.6. Provisions for the oversight of safety data (e.g., by a data monitoring committee).

3.2. For studies that do not have or are not required to have a data monitoring committee and are blinded, have multiple sites, enter vulnerable populations, or employ high-risk interventions, the IRB will carefully review the data and safety monitoring plan and determine whether a data monitoring committee is needed.

3.3. If the DSMP does not include a formal DSMB, the protocol must have a plan for analyzing the safety data to determine whether harm is occurring.

3.4. The DSMP may include monitoring by the investigator and/or study staff, by faculty advisor, by a sponsor appointed medical monitor or CRO, by an independent monitor or monitoring group (not directly involved with the design and conduct of the study), or by a formal DSMB.

4.0 Data Safety Monitoring Board
4.1. Under certain circumstances, the IRB or the investigator may decide that the DSMP should include a formal DSMB.
   4.1.1. In general a formal DSMB is required for:
      4.1.1.1. Phase III clinical trials, with the exception of low-risk behavioral and nutritional studies (such as those where subjects are expected to experience only minor side effects, and interim analyses are not crucial for the protection of subjects).
**4.1.1.2.** Multicenter randomized phase II clinical trials, with the exception of low-risk behavioral and nutritional studies.

**4.1.1.3.** High risk phase II clinical trials (such as those involving interventions associated with risk of serious morbidity or death, studies involving diseases associated with high mortality or morbidity, and research involving highly experimental therapies).

**4.1.2.** In consideration of other trials, a formal DSMB should be considered for the following types of research:

**4.1.2.1.** Research involving a large study population, or multiple study sites.

**4.1.2.2.** Research intended to provide definitive information about effectiveness and/or safety of a medical intervention.

**4.1.2.3.** Research which involves an intervention with the potential to induce unacceptable toxicity.

**4.1.2.4.** Research which evaluates mortality or another major endpoint, such that inferiority of one treatment arm has safety as well as effectiveness implications.

**4.1.2.5.** Research for which it would ethically be important for the trial to stop early if the primary question addressed has been definitively answered, even if secondary questions or complete safety information were not yet fully addressed.

**5.0 Review of the DSMP by the IRB**

**5.1.** The DSMP must include at least a description of how data will be monitored to ensure the safety of subjects, who will perform the ongoing data and safety analysis, and the frequency of data analysis.

**5.2.** As appropriate based on the design and risk profile of the research, the DSMP may include subject withdrawal criteria, and study stopping rules based on efficacy, toxicity and futility.

**5.3.** If the research design or risk profile warrants a formal DSMB the investigator must provide the DSMB charter, or describe (1) the composition of the DSMB membership, (2) the frequency of DSMB meetings and reports. It is expected that most studies which require a formal DSMB will also have formal stopping rules for efficacy and toxicity.

**5.4.** The IRB will evaluate the DSMP in order to ensure that it represents adequate provision for monitoring the data collected to ensure the safety of subjects.

**6.0 Review of DSMB Reports by the IRB**

**6.1.** It is the responsibility of the investigator to obtain copies of, and review, DSMB reports, as they are produced, at the frequency described in section 5.3 above.

**6.2.** The PI is responsible for submitting copies of all DSMB reports to the IRB at the time of continuing review (or interim reporting period as mandated by the IRB).

**6.3.** If the DSMB report finds serious risks to the welfare of subjects, or recommends substantive changes to the protocol (including but not limited to halting of the protocol or accrual) or substantive changes to the informed consent document, then the investigator must submit the report promptly to the IRB. It is expected that such DSMB reports will be followed promptly by a Request for Change in protocol.
6.4. If the DSMB finds serious risks to the welfare of subjects, the IRB will take action in accordance with *HRPP policy 8.6 (Study Hold, Suspension, and Termination)*.

6.5. If the DSMB report is due but has not been submitted at the time of continuing review (or interim reporting period as mandated by the IRB), the IRB may table the Continuing Review, or may suspend the study in accordance with *HRPP policy 8.6 (Study Hold, Suspension, and Termination)*.

**Administrative Approval:**

Bruce G. Gordon, MD  IRB Executive Chair & Assistant Vice Chancellor for Regulatory Affairs
Christopher Kratochvil, MD  Institutional Official

*Policy Amended:*

- Revised February 2, 2018
- Initial April 4, 2016
**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**

2.1. It is the policy of the Organization that: 1) the privacy interests of participants are protected; and 2) the confidentiality of research data will be protected.

2.2. It is the policy of the Organization that Protected Health Information (PHI) will be protected in accordance with HRPP policy 3.4 (Use of Protected Health Information in Research).

**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).

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).

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.

**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 and the participants’ expectations of privacy. The board will make the following determinations:

4.1.1. The PI and other research personnel have ethical access to the participant’s private, identifiable information in accordance with HRPP policy 3.12 (Ethical Access).

4.1.2. The methods used to identify and contact potential participants minimize the risk to privacy.

4.1.3. The location where informed consent will be obtained is conducive to the privacy interests of participants.
4.1.4. No other persons are present during the informed consent process or during research activities unless the individual(s) is listed on the IRB application or is involved in the clinical care of the participant or is present to provide technical assistance. Other individuals can only be present with the consent of the participant.

4.1.5. The research activities are performed in as private a place as possible.

4.1.6. The minimum amount of PHI or other personal information necessary to complete the study will be maintained.

4.2. Protection of Confidentiality

4.2.1. The IRB will review all applications to determine whether there are adequate provisions to protect the confidentiality of data. The greater the risk to the subject associated with a breach of confidentiality, the more stringent must be the protections in place. During the course of review, the IRB will consider the participants’ expectations for confidentiality and the nature and degree of risk associated with loss of confidentiality. The board will make the following determinations as appropriate:

4.2.1.1. The physical and/or electronic safeguards and security measures for the entry, storage, and transfer of data are adequate in consideration of the nature of the data and the physical medium on which it is stored. PHI must be stored in a manner that is compliant with the HIPAA Privacy Rule, and other regulations and laws as applicable.

4.2.1.2. There is adequate justification for sharing identifiable private information, and PHI is shared in a manner that is compliant with the HIPAA Privacy Rule, and other regulations and laws as applicable.

4.2.1.3. The minimum amount of identifiable private information necessary to complete the study will be maintained, and access to identifiable private information will be restricted to the minimum number of persons with a legitimate need.

4.2.1.4. Identifiable private information will be appropriately and safely destroyed when it is no longer needed, as allowed under HRPP policy 1.17 (Retention of Research Records).

4.2.2. Certificate of Confidentiality

4.2.2.1. Research is automatically covered by a Certificate of Confidentiality whenever the study is funded in whole or in part by the NIH and involves identifiable, sensitive information.

4.2.2.1.1. Identifiable sensitive information means information about an individual, obtained during the course of biomedical, behavioral, clinical or other research, through which the individual is identified, or there is at least a very small risk that some combination of the information, a request for the information, and other available data sources could be used to determine the identity of an individual. This information may include name, address, social security or other identifying number; and fingerprints, voiceprints, photographs, genetic information, tissue samples, or data fields that when used in combination with other information may lead to identification of an individual.

4.2.2.2. Examples of research automatically covered by a Certificate of Confidentiality include:
4.2.2.2.1. Biomedical, behavioral, clinical or other research, including exempt research, except where the information obtained is recorded in such a manner that human participants cannot be identified or the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects.

4.2.2.2.2. The collection or use of biospecimens that are identifiable to an individual or for which there is at least a very small risk that some combination of the biospecimen, a request for the biospecimen, and other available data sources could be used to deduce the identity of an individual.

4.2.2.2.3. The generation of individual level, human genomic data from biospecimens, or the use of such data, regardless of whether the data is recorded in such a manner that human subjects can be identified or the identity of the human subjects can readily be ascertained.

4.2.2.2.4. Any other research that involves information about an individual for which there is at least a very small risk, as determined by current scientific practices or statistical methods, that some combination of the information, a request for the information, and other available data sources could be used to deduce the identity of an individual.

4.2.2.3. Researchers may also apply for a Certificate of Confidentiality for non-federally funded research if it would meaningfully enhance protection of confidentiality.

4.2.2.4. When research is covered by a Certificate of Confidentiality, researchers:

4.2.2.4.1. May not disclose or provide, in any Federal, State, or local civil, criminal, administrative, legislative, or other proceeding, the name of such individual or any such information, document, or biospecimen that contains identifiable, sensitive information about the individual and that was created or compiled for purposes of the research, unless such disclosure or use is made with the consent of the individual to whom the information, document, or biospecimen pertains; or

4.2.2.4.2. May not disclose or provide to any other person not connected with the research the name of such an individual or any information, document, or biospecimen that contains identifiable, sensitive information about such an individual and that was created or compiled for purposes of the research.

4.2.2.4.3. May disclose information only when:

4.2.2.4.3.1. Required by Federal, State, or local laws (e.g., as required by the Federal Food, Drug, and Cosmetic Act, or state laws requiring the reporting of communicable diseases to State and local health departments), excluding instances of disclosure in any Federal, State, or local civil, criminal, administrative, legislative, or other proceeding.

4.2.2.4.3.2. Necessary for the medical treatment of the individual to whom the information, document, or biospecimen pertains and made with the consent of such individual;

4.2.2.4.3.3. Made with the consent of the individual to whom the information, document, or biospecimen pertains; or

4.2.2.4.3.4. Made for the purposes of other scientific research that is in compliance with applicable Federal regulations governing the protection of human subjects in research.
4.2.2.4.4. Written materials require that when research is covered by a Certificate of Confidentiality, researchers must inform participants (for example, in the consent document) of the protections and limitations of certificates of confidentiality.

4.2.2.4.4.1. For studies that were previously issued a Certificate, and notified participants of the protections provided by that Certificate, NIH does not expect participants to be notified that the protections afforded by the Certificate have changed, although IRBs may determine whether it is appropriate to inform participants.

4.2.2.4.4.2. If part of the study cohort was recruited prior to issuance of the Certificate, but are no longer activity participating in the study, NIH does not expect participants consented prior to the change in authority, or prior to the issuance of a Certificate, to be notified that the protections afforded by the Certificate have changed, or that participants who were previously consented to be re-contacted to be informed of the Certificate, although IRBs may determine whether it is appropriate to inform participants.

4.2.2.4.5. Written materials require that researchers conducting NIH-supported research covered by a Certificate of Confidentiality must ensure that if identifiable, sensitive information is provided to other researchers or organizations, regardless of whether or not the research is federally funded, the other researcher or organization must comply with applicable requirements when research is covered by a certificate of confidentiality.
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 research.

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; and 4) UNMC Board of Regents Executive Memorandum No. 27 (HIPAA Compliance Policy).

2.2. It is the policy of the Organization that 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 HRPP policy 3.12 (Ethical Access).

2.3. It is the policy of the Organization that records containing PHI, in any form, are the property of the Organization, and that the PHI contained in the record is the property of the individual who is the subject of the record.

2.4. It is the policy of the Organization that, when using or disclosing PHI or when requesting PHI from another covered entity, the investigator must make reasonable efforts to limit protected health information to the minimum necessary to accomplish the research.

2.5. It is the policy of the Organization that a compound authorization process for research will be used where the HIPAA authorization is merged within the research ICF.

3.0 Definitions
3.1. Protected Health Information (PHI) is individually identifiable health information, whether oral or recorded in any medium, that:

3.1.1. Is created or received by the Organization; and

3.1.2. 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 (45 CFR 160.103).

3.2. HIPAA Identifiers are the characteristics of health information that make such information about the individual (or of relatives, employers, or household members of the individual) identifiable. Per the HIPAA Privacy Rule (45 CFR 164.51(b)(2)(i)), identifiers include the following:

3.2.1. Names

3.2.2. 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 publicly available data from the Bureau of the Census:

3.2.2.1. The geographic unit formed by combing all zip codes with the same three initial digits contains more than 20,000 people, and

3.2.2.2. The initial three digits of a zip code for all such geographic units containing 20,000 or fewer people are changed to 000.
3.2.3. 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;

3.2.4. Telephone numbers

3.2.5. Fax numbers

3.2.6. Electronic mail addresses

3.2.7. Social security numbers

3.2.8. Medical record numbers

3.2.9. Health plan beneficiary numbers

3.2.10. Account numbers

3.2.11. Certificate/license numbers

3.2.12. Vehicle identifiers and serious numbers, including license plate numbers

3.2.13. Device identifiers and serial numbers

3.2.14. Web Universal Resource Locators (URLs)

3.2.15. Internet Protocol (IP) address numbers

3.2.16. Biometric identifiers, including finger and voice prints

3.2.17. Full face photographic images and any comparable images

3.2.18. Any other unique identifying number, characteristic, or code

3.3. Limited Data Set means health information that excludes the direct HIPAA identifiers listed in section 3.2 above, except that it may include:

3.3.1. City; state; ZIP Code; and

3.3.2. Elements of date; and

3.3.3. Other numbers, characteristics, or codes not listed as direct identifiers

3.4. Honest Broker (as defined in UNMC Policy 6074 at https://wiki.unmc.edu/index.php/Honest_Broker) is a neutral intermediary (person or system), who is a workforce member and is certified to collect specified health information from the tissue or data bank, remove all patient identifiers, and provide the de-identified health information or tissue to research investigators, clinicians, or other healthcare workforce members, in such a manner that it would not be reasonably possible for any individual to identify the patients directly or indirectly.

4.0 Use or Disclosure of PHI for Research

The Privacy Rule permits the Organization to use or disclose PHI for research only under certain circumstances and conditions as described below:

4.1. The subject of the PHI has granted specific written authorization, in accordance with 45 CFR 164.508(c).

4.1.1. The Organization utilizes a compound authorization process for research in which the HIPAA authorization is merged within the research ICF
4.1.2. The HIPAA Authorization must include the following Core Elements per 45 CFR 164.508(c)(1):

4.1.2.1. Description of PHI to be used or disclosed (identifying the information in a specific and meaningful manner).

4.1.2.2. The name(s) or other specific identification of person(s) or class of persons authorized to make the requested use or disclosure.

4.1.2.3. The name(s) or other specific identification of the person(s) or class of persons who may use the PHI or to whom the covered entity may make the requested disclosure.

4.1.2.4. Description of each purpose of the requested use or disclosure. This section must "adequately describe such purposes such that it would be reasonable for the individual to expect that his or her protected health information could be used or disclosed for such future research." (78 FR 5612, 2013)

4.1.2.5. Authorization expiration date or event (for example, "end of the research study" or "none")

4.1.2.6. Signature of the individual and date. If the Authorization is signed by an individual's personal representative, a description of the representative's authority to act for the individual.

4.1.3. The HIPAA Authorization must include the following Required Statements, per 45 CFR 164.508(c)(2):

4.1.3.1. The individual's right to revoke his/her Authorization in writing and either (1) the exceptions to the right to revoke and a description of how the individual may revoke Authorization.

4.1.3.2. Notice of the covered entity's ability or inability to condition treatment, payment, enrollment, or eligibility for benefits on the Authorization, including research-related treatment, and, if applicable, consequences of refusing to sign the Authorization.

4.1.3.3. The potential for the PHI to be re-disclosed by the recipient and no longer protected by the Privacy Rule. This statement does not require an analysis of risk for re-disclosure but may be a general statement that the Privacy Rule may no longer protect health information.

Note: The templates for the ICFs are designed to meet all of the regulatory requirements required under the HIPAA regulations.

4.1.4. A research subject may revoke his/her Authorization at any time. However, the investigator may continue to use and disclose PHI that was obtained before the individual revoked Authorization. This would permit the investigator to continue using or disclosing the PHI as necessary to maintain the integrity of the research, as, for example, to account for a subject's withdrawal from the research study, to conduct investigations of scientific misconduct, or to report adverse events.

4.2. The PHI will be used for reviews preparatory to research per 164.512(i)(1)(ii)

4.2.1. Activities "preparatory to research" include, but are not limited to, (1) preparing a research protocol, (2) assisting in the development of a research hypothesis, or (3) aiding in research recruitment, such as identifying prospective research participants who would meet the eligibility criteria for enrollment into a research study.

4.2.2. The investigator must have ethical access to the PHI in accordance with HRPP policy 3.12 (Ethical Access).
4.2.3. PHI obtained and recorded may not be removed from the Organization during the course of the review.

4.2.4. PHI obtained and recorded may not be used for research purposes other than those described above without IRB approval.

4.2.5. Activities “preparatory to research” may still constitute “research” under 45 CFR 46, and therefore, may require informed consent under 45 CFR 46.116, even though HIPAA requirements are met.

4.3. The IRB or Privacy Board has granted a waiver of Authorization per 164.512(i) and HRPP policy 5.2 (Waiver or Alteration of Informed Consent and HIPAA Authorization).

4.4. The PHI has been de-identified per 45 CFR 164.514(b) or (c) (in which case, the health information is no longer PHI).

4.4.1. PHI is de-identified (and therefore becomes health information and no longer PHI) if either of the following applies:

4.4.1.1. A person with appropriate knowledge of and experience with generally accepted statistical and scientific principles and methods for rendering information not individually identifiable (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 determination; OR

4.4.1.2. The identifiers of the individual or of relatives, employers, or household members of the individual listed in section 3.2 (HIPAA Identifiers) are removed, and 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 a subject of the information 45 CFR 154.512(b)(2)(ii).

4.4.2. De-identification is performed by the designated “honest broker” in the Office of the Vice-Chancellor for Research, following the procedure described in UNMC Policy 6074.

4.5. The PHI is released in the form of a Limited Data Set (as defined in section 3.3 above), with a data use agreement between the researcher and the Organization per 45 CFR 164.514(e).

4.5.1. The Data Use Agreement (DUA): 1) establishes the permitted uses and disclosures of the information by the recipient of the Limited Data Set, and 2) establishes who is permitted use or receive the data set and (3) specifies that the recipient of the LDS will:

4.5.1.1. Not use or further disclose the information other than as permitted by the DUA/DTA or as otherwise required by law.

4.5.1.2. Use appropriate safeguards to prevent use or disclosure of the information other than as provided for by the DUA.

4.5.1.3. Report to the Organization (the ORA and the Privacy Office) any use or disclosure of the information not provided for by its DUA of which it becomes aware.

4.5.1.4. 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.

4.5.1.5. Not attempt to identify or contact the individuals.

4.5.2. The DUA will be negotiated through Sponsored Programs Administration.
4.5.3. The investigator must have ethical access to the PHI in accordance with *HRPP policy 3.12 (Ethical Access)*.

4.5.4. The LDS will be prepared by the designated “honest broker” in the Office of the Vice-Chancellor for Research, following the procedure described in *UNMC Policy 6074*.

5.0 Procedures

5.1. **Research Involving the Use of PHI**

5.1.1. The Investigator must submit the IRB application that is appropriate for the proposed research in accordance with *HRPP policy 2.1 (Submission of Items for Review by the IRB)*.

5.1.2. Applications requiring full IRB review will be reviewed in accordance with *HRPP policy 2.2 (Full IRB Review)*.

5.1.3. Applications that are eligible for review by the expedited method will be reviewed in accordance with *HRPP policy 2.3 (Expedited Review of Research)*.

5.1.4. Applications which are eligible for exemption under 45 CFR 46.101(b) (or rev 45 CFR 46.104(d)) or 21 CFR 56.104(d) will be processed and reviewed in accordance with *HRPP policy 2.6 (Exempt Research)*.

5.1.5. In all cases, the minimum amount of PHI should be recorded, and, whenever possible, data should be recorded without PHI.

5.1.6. Individuals who do not have ethical access to records containing PHI (as defined in *HRPP policy 3.12; Ethical Access*) must obtain data from the designated “honest broker” as described in section 4.4 above, or which has only a one-way code (for which the custodian of the records has the link and the code is not any part of the 18 HIPAA identifiers).

5.1.7. If the PHI will be sent to an external entity, a Data Use Agreement or sponsored agreement must be finalized by Sponsored Programs Administration prior to final IRB approval.

5.2. **Research Utilizing Decedent PHI**

5.2.1. Research involving decedents does not constitute human subject research under 45 CFR 46. However, HIPAA applies to PHI of individuals deceased for 50 years or less; therefore, the IRB, in its capacity as HIPAA Privacy Board, must review the use of such PHI.

5.2.2. To approve the use of PHI, the IRB, in its capacity as HIPAA Privacy Board, must obtain from the researcher who is seeking access to decedents' PHI:

5.2.2.1. Oral or written assurance that the use or disclosure sought is solely for research on the PHI of decedents.

5.2.2.2. Oral or written assurance that use or disclosure of the PHI is necessary for the purposes of the research.

5.2.2.3. Documentation, at the request of the Organization, of the death of the individuals whose PHI is sought.

5.2.3. An investigator conducting such research is not required to obtain Authorizations from the personal representative or next of kin under the Privacy Rule; however, permission may be required by State Law, and is certainly respectful of the survivors. Investigators should contact the UNMC Office of the General Counsel.

5.2.4. The HIPAA Privacy Rule does not apply to identifiable health information on individuals who have been deceased for more than 50 years (45 CFR 164.512(i)(1)(iii)).
Therefore, research involving health information from such individuals does not require review or approval of the Privacy Board.

**Administrative Approval:**

BRUCE G. GORDON, MD  IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS

CHRISTOPHER KRATOCHVIL, MD  INSTITUTIONAL OFFICIAL

**Policy Amended:**

- **Revised April 9, 2018**
- **Initial January 28, 2016**
1.0 Purpose

The purpose of this policy and procedure is to describe the Organization’s requirements for recruitment of subjects through advertisements. For the purpose of this policy, “advertisements” refer to printed advertisements (including bulletins, newsletters, posters, fliers, and magazine or newspaper ads); radio and television advertisements; and electronic advertisements (including social media or other on-line venue).

Note: Invitations to participate directed to specific persons are covered by HRPP policy 3.6 (Subject Recruitment Through Direct Invitation).

2.0 Policy

2.1. It is the policy of the Organization that all advertisements must be reviewed and approved by the IRB or ORA before the material can be used to recruit potential subjects.

2.2. It is the policy of the Organization that advertising be clear, promote equitable enrollment and not represent undue influence or coercion.

2.3. For the purpose of this policy, references to information provide to, or decisions made by, potential subjects also means information provided to, or decisions made by, parents, guardians or LARs as appropriate.

3.0 General Requirements and Prohibitions

3.1. Advertisements should be limited to information a potential subject may need to determine if he/she is interested and eligible to participate in a study.

3.2. Advertisements may not include any of the following:

3.2.1. Statements implying a certainty of a favorable outcome or other benefits beyond what was described in the consent document and the protocol.

3.2.2. Claims, either explicit or implicit, that the research procedures (e.g. drug, biologic or device) are safe or effective for the purposes under investigation.

3.2.3. Claims, either explicit or implicit, that the research procedures are known to be equivalent or superior to other interventions off-study.

3.2.4. Terms such as “new treatment”, “new medication”, or “new drug”.

3.2.5. Promises of “free medical treatment” regardless of whether the treatment will be provided without charge.

3.2.6. A stated amount of compensation for participation, or indication that compensation is available, in any font, font size, or manner that is intended to draw attention to the value or availability of compensation.

3.2.7. Any exculpatory language

3.2.8. Make claims, either explicitly or implicitly, about the drug, biologic, or device under investigation that are inconsistent with FDA labeling.
4.0 Printed Advertisement

4.1. All printed advertisements developed by the investigator or staff must be prepared within the RSS system. Advertisements developed by an outside sponsor may be used after review and approval by the IRB.

4.2. Printed advertisement must include the following items:
   4.2.1. Name and address of the PI and associated institution.
   4.2.2. A clear statement that the activity is research.
   4.2.3. Purpose of the research.
   4.2.4. IRB number.

4.3. Printed advertisement may include the following information, as appropriate:
   4.3.1. Brief relevant eligibility criteria (e.g., why a person might believe he/she is a potential subject).
   4.3.2. Time or other commitments required from the subject, including number of study visits and duration of the study.
   4.3.3. A brief list of potential benefits to the subject, and possible risks and discomforts, if any. Per FDA Guidance, if potential benefits are stated in recruitment material then the possible risks must also be stated.
   4.3.4. Location of the research, contact person, and phone number for further information.

4.4. The layout of the advertisements must conform to the Organization’s requirements regarding the use of logos and brands.

4.5. It is the responsibility of the investigator to ensure that the final published copy (including font and size) matches that approved by the IRB.

4.6. When accrual to the research is completed, the investigator must notify the IRB/ORA so that advertisements can be de-activated in RSS. The investigator is responsible for terminating newspaper or magazine ads.

5.0 Radio and Television Advertisements

5.1. Radio and Television advertisement must include the following items:
   5.1.1. Name of the PI and associated institution.
   5.1.2. A clear statement that activity is research.
   5.1.3. Purpose of the research.

5.2. Radio and Television advertisement may include the following information, as appropriate:
   5.2.1. Brief relevant eligibility criteria (e.g., why a person might believe he/she is a potential subject).
   5.2.2. Time or other commitments required from the subject.
   5.2.3. A brief list of potential benefits to the subject, and possible risks and discomforts, if any. Per FDA Guidance, if potential benefits are stated in recruitment material then the possible risks must also be stated.
5.2.4. Location of the research, contact person, and phone number for further information.

5.3. It is the responsibility of the investigator to ensure that the final broadcast matches that approved by the IRB.

5.4. When accrual to the research is completed, the investigator is responsible for assuring that radio or television ads cease.

6.0 Electronic Advertisements (including social media or other on-line venue)

6.1. Electronic advertisement must include the following items:
   6.1.1. Name and address of the PI and associated institution.
   6.1.2. A clear statement that the activity is research.
   6.1.3. Purpose of the research
   6.1.4. IRB number

6.2. Electronic advertisement may include the following information, as appropriate:
   6.2.1. Brief relevant eligibility criteria (e.g., why a person might believe he/she is a potential subject).
   6.2.2. Time or other commitments required from the subject.
   6.2.3. A brief list of potential benefits to the subject, and possible risks and discomforts, if any. Per FDA Guidance, if potential benefits are stated in recruitment material then the possible risks must also be stated.
   6.2.4. Location of the research, contact person, and phone number for further information.
   6.2.5. A link (and/or a URL) pointing to a site maintained by the Organization.
   6.2.6. A link (and/or a URL) pointing to a site maintained by an external organization with the domain “org”, “edu” or “gov”, that is relevant to the disease or condition which is being studied, or to the practice of human subject research or protection of human research subjects in general.

6.3. It is the responsibility of the investigator to ensure that the final published copy (including font and size) matches that approved by the IRB.

6.4. If the advertisement includes a link or a URL, it is the responsibility of the investigator to regularly check that link to be assured that it remains intact.

6.5. When accrual to the research is completed, the investigator must disable study-specific electronic advertising

7.0 Submission of Advertisements

7.1. All final versions of advertisements including print media, audio scripts for radio, video scripts for television, and screenshots of online advertising (including all webpages linked to the advertisement) must be submitted to the ORA in accordance with HRPP policy 2.1 (Submission of Items for Review) for review and approval. Copies will be maintained by the ORA.

7.2. Submission of planned advertising to the ORA must include a description of the location the advertisement will be placed (that is, the name of the publication [e.g., the Omaha World-Herald],
the specific media outlet [e.g., KETV] and/or the website or venue [e.g., specific Facebook page or community]), and the expected duration of the advertising.

8.0 IRB Review of Advertisements

8.1. 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) and HRPP policies 2.2 (Full IRB Review) and 2.3 (Expedited Review).

8.2. The IRB approval letter will cite the approved version of the advertisement.
1.0 Purpose
The purpose of this policy is to describe the Organization’s requirements for subject recruitment through direct invitations to participate.
Subject recruitment through advertisements is described in HRPP policy 3.5.

2.0 Policy
2.1. It is the policy of the Organization that all direct recruitment materials must be reviewed and approved before they can be used to recruit potential subjects.
2.2. It is the policy of the Organization that recruitment materials be clear, promote equitable enrollment and not represent undue influence or coercion.
2.3. It is the policy of the Organization that direct recruitment of subjects to research be respectful of the privacy of potential subject.

3.0 Definitions
3.1. “Opt-In” designation refers to agreement by the patient to be contacted for possible inclusion in biomedical research based on information in the patient’s EMR, as reflected in the UNMC/Nebraska Medicine [UNMC/NM] “Conditions of Treatment Form” (or, when available, the Children’s Hospital Medical Center [CHMC] “Conditions of Treatment Form”).
3.2. Honest Broker refers to a person, appropriately trained and designated by the Organization, whose responsibility is to de-identify protected health information and provide that de-identified information to investigators, in accordance with UNMC policy 6074.

4.0 Invitations to Patients
4.1. This section applies to patients (present and former) associated with UNMC/NM (including hospital and/or clinics), Bellevue Medical Center, or CHMC (including Children’s Physicians Clinics).
4.2. Distribution Lists based on Clinical Databases or Prior Research Subject Databases
   4.2.1. Potential subjects listed in these databases are either: (1) current or former patients of the investigator; or (2) patients to whom he/she has ethical access per HRPP policy 3.12 (Ethical Access); or (3) previous research subjects who have given express permission (usually as part of an IRB approved consent process) to be listed in the database for the purpose of being contacted for future research studies.
4.3. Distribution Lists based on the Conditions of Treatment Form designation (“opt-in” designation)
   4.3.1. The Associate Vice Chancellor must approve subject recruitment plans, which include directed invitations to former or present patients based on the Conditions of Treatment Form designation (“opt-in designation) for Clinical Research.
4.3.2. Once approved by the Associate Vice Chancellor for Clinical Research, the study personnel can add this documentation to their IRB submission.

4.3.3. After review and approval by the IRB, the Director of Electronic Health Record Access Core will authorize an “honest broker” to generate the distribution list based on the inclusion parameter defined in the Request for Electronic Health Data Form.

4.3.4. Only patients who have opted-in to be contacted for research on his/her Conditions of Treatment Form may be included in this search.

4.3.5. Once the distribution list is provided, it must be kept on a secure/encrypted UNMC/NM computer (reference End User Device Security procedure https://info.unmc.edu/its-security/policies/procedures/enduser.html or IM16 End User Device Policy) for no more than 3 months. After that time, the distribution list must be re-run to validate the opt-in recruitment status.

4.3.6. The list must be deleted/destroyed once it is no longer in use (Nebraska Medicine policy IM14-Destruction of Confidential Information).

4.3.7. Patients who have opted-out based on the Conditions of Treatment Form designation may still be contacted if they are either: (1) current or former patients of the investigator, or (2) patients to whom the investigator has ethical access per HRPP policy 3.12 (Ethical Access); or (3) previous research subjects who have given express permission to be contacted for future research studies.

4.3.8. Note that currently CHMC and Children’s Physicians clinics do not utilize an “opt-in” designation on the Conditions of Treatment form; therefore Distribution Lists based on the Conditions of Treatment Form designation described in this section (3.1) do not apply for potential subjects from those sites.

4.4. No more than three invitation attempts between all media channels (phone, mail, e-mail) for any specific study may be made from any Distribution List described above unless specific approval is given by the IRB or by the expedited reviewer as applicable. Specific parameters regarding frequency are noted below.

4.5. Contacting Patients by Email via MS Outlook (or future email system supported by the Organization)

4.5.1. If multiple recipients are included on the same email, the blind copy email function must be used to prevent recipients from seeing the email address of another subject or potential subject.

4.5.2. Emails must contain minimal PHI, limited to (a) Patient name, and (b) email address.

4.5.3. The subject line must clearly identify "UNMC/Nebraska Medicine (or CHMC) Research Opportunity". PHI or study information must not be contained in the subject line.

4.5.4. The sender of the email must be clearly identified as affiliated with the Organization.

4.5.5. The text of the email must include only the following items:

   4.5.5.1. Name and email address of the PI and associated institution.

   4.5.5.2. A clear statement that activity is research.

   4.5.5.3. Purpose of the research.

   4.5.5.4. IRB number.

   4.5.5.5. An invitation to contact the investigator for more information, with telephone number if applicable.
4.5.5.6. An explanation that the patients name and contact information were available because they had chosen to opt-in to be contacted for research on his/her Conditions of Treatment Form.

4.5.5.7. Information for the patient on how to change their research recruitment option in the conditions of treatment form and the contact information for the Research Subject Advocate.

4.5.6. Email invitations to UNMC/NM or BMC patients obtained through the Conditions of Treatment Distribution lists must be sent by the Clinical Research Outreach Coordinator (or equivalent position), via a central email address.

4.5.7. The Pediatric Research Office (PRO), via a central email address, must send email invitations to CHMC patients.

4.5.8. The reply back to sender will be reviewed by the Clinical Research Outreach Coordinator or the PRO coordinator, and then forwarded to research staff if appropriate.

4.5.9. The recruitment email invitation may be sent to potential subjects no more often than weekly unless specifically authorized by the IRB.

4.5.10. If a potential subject declines participation in a specific study, no further recruitment emails may be sent regarding that study.

4.6. **Contacting Patients by EPIC Email through One Chart**

4.6.1. The subject line must clearly identify "UNMC/Nebraska Medicine (or CHMC) Research Opportunity". PHI or study information must not be contained in the subject line.

4.6.2. The reply back to sender will be set to return all replies regarding recruitment to the investigator with ethical access.

4.6.3. The text of the email must include only the following items:

   4.6.3.1. Name and email address of the PI and associated institution.
   4.6.3.2. A clear statement that activity is research.
   4.6.3.3. Purpose of the research.
   4.6.3.4. IRB number.
   4.6.3.5. An invitation to contact the investigator for more information, with telephone number if applicable.

4.6.4. The recruitment email invitation may be sent to potential subjects no more often than weekly unless specifically authorized by the IRB.

4.6.5. If a potential subject declines participation in a specific study, no further recruitment emails may be sent regarding that study.

4.7. **Contacting Patients by Phone**

4.7.1. Telephone script must be approved by the IRB prior to use.

4.7.2. Recorded voice messages must go through the Clinical Research Outreach Coordinator (or equivalent position).

4.7.3. Frequency and number of calls must be specified by the investigator in the IRB application, and must be approved by the IRB.
4.7.4. If voicemails are left the message may only state that the call is about a research study for which the patient may be eligible and offer a call back number. The voicemail must not provide any additional details regarding the trial or the reason a patient may be eligible.

4.7.5. If a potential subject declines participation in a specific study, no further recruitment phone calls may be made regarding that study.

4.7.6. All recorded messages must follow the Telephone Consumer Protection Act.

4.8. Contacting Patients by Mail

4.8.1. Letters must contain minimal PHI, limited to (a) Patient name and (b) address.

4.8.2. All materials should be in an envelope with only patient’s name and address; the return address must include the Organization name, but no specific medical or surgical department.

4.8.3. If postcard format is appropriate, the postcard must fold and seal to cover any medical/trial information.

4.8.4. The text of the letter must include only the following items:
   4.8.4.1. Name and email address of the PI and associated institution.
   4.8.4.2. A clear statement that activity is research.
   4.8.4.3. Purpose of the research.
   4.8.4.4. IRB number.
   4.8.4.5. An invitation to contact the investigator for more information, with telephone number if applicable.
   4.8.4.6. An explanation of how the patients name and contact information were available to the investigator (for example, because they had chosen to opt-in to be contacted for research on his/her Conditions of Treatment Form, or because he/she had previously participated in research and had agreed to be contacted regarding additional research studies).
   4.8.4.7. If the patient had chosen to opt-in to be contacted for research on his/her Conditions of Treatment Form, information on how to change their research recruitment option, and the contact information for the Research Subject Advocate.

4.8.5. The recruitment letter may be sent to potential subjects no more often than weekly unless specifically authorized by the IRB.

4.8.6. If a potential subject declines participation in a specific study, no further recruitment letters may be sent regarding that study.

5.0 Invitations to Prospective Subjects who are not Patients

This section applies to prospective subjects who may be eligible for participation in research but who are not primarily eligible because they have a disease or condition being diagnosed or treated at UNMC/Nebraska Medicine (including hospital and/or clinics), Bellevue Medical Center, or Children’s Hospital & Medical Center (including Children’s Physicians Clinics). They may be patients or former patients, but that is not the primary reason they may be eligible.

Note: Examples of this subject population would be public or private school students; college, trade or professional school students (e.g., UNO freshman, enrollees at a particular trade school, UNMC
SOM students); cultural, ethnic or religious groups (e.g., Sudanese immigrants, members of a particular church); trades or professions (e.g., farmers, physicians, prison guards).

5.1. **Creation of Distribution Lists**

5.1.1. In most cases, unless the investigator has ethical access to names of potential subjects, or the names are obtained from publicly available databases, the distribution list must remain within the group, which has generated the list (that is, the investigator should not have access to the names or contact information on the list). The invitation to participate should come from the group, which generated the list.

5.1.2. In certain circumstances, when the group supplying the list cannot or will not be responsible for sending the invitation, the IRB may specifically approve that the list be transferred to the investigator. In making this exception, the IRB must be satisfied that:

   5.1.2.1. The risks of disclosure of the contact information constitutes no more than minimal risk to potential subjects (for example, disclosure would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects’ financial standing, employability, educational advancement, or reputation), and

   5.1.2.2. There are adequate safeguards to minimize the risk of disclosure beyond the investigator and study personnel, and

   5.1.2.3. There are adequate provisions to protect the privacy of subjects.

5.1.3. If the distribution list is provided to the investigator, it must be kept on a secure computer for no more than 3 months. The list must be deleted/destroyed once it is no longer in use (Nebraska Medicine policy IM14: Destruction of Confidential Information).

5.1.4. All information distributed to the investigator must be in compliance with applicable privacy laws and regulations, including The Family Educational Rights and Privacy Act (FERPA) (20 U.S.C. § 1232g; 34 CFR Part 99).

5.2. **Contacting Prospective Subjects by Email**

5.2.1. As noted above, in most cases the invitation to participate should come from the group, which generated the list. If the invitation comes directly from the investigator (as per section 5.2.2 above) emails must be sent from a UNMC/Nebraska Medicine, UNO, or CHMC, Outlook account.

5.2.2. If multiple recipients are included on the same email, the blind copy email function must be used to prevent recipients from seeing the email address of another potential subject.

5.2.3. The subject line must clearly identify UNMC, UNO or CHMC “Research Opportunity”. Study information must not be contained in the subject line.

5.2.4. The group sending the email must be clearly identified.

5.2.5. The affiliation of the investigator with the Organization must be clearly stated in the email.

5.2.6. The email must include an explanation why the prospective subject’s name and contact information were available.

5.2.7. The text of the email must include only the following items:

   5.2.7.1. Name and email address of the PI and associated institution.
5.2.7.2. A clear statement that activity is research.

5.2.7.3. Purpose of the research.

5.2.7.4. IRB number.

5.2.7.5. An invitation to contact the investigator for more information, with telephone number if applicable.

5.2.7.6. A description of why the prospective subject’s name and contact information were available.

5.2.8. The recruitment email invitation may be sent to potential subjects no more often than weekly unless specifically authorized by the IRB.

5.3. **Contacting Prospective Subjects by Phone**

5.3.1. Telephone script must be approved by the IRB prior to use.

5.3.2. Frequency and number of calls must be specified by the investigator in the IRB application, and must be approved by the IRB.

5.3.3. If voicemails are left, the message may only state that the call is about a research study for which the patient may be eligible and offer a call back number. The voicemail must not provide any additional details regarding the trial or the reason a prospective subject may be eligible.

5.3.4. All recorded messages must follow the Telephone Consumer Protection Act.

5.4. **Contacting Prospective Subjects by Mail**

5.4.1. All materials should be in an envelope with only prospective subject’s name and address; the return address must include the Organization name (if sent by the investigator), or the name of the group supplying the distribution list.

5.4.2. The affiliation of the investigator with the Organization must be clearly stated in the letter.

5.4.3. The mail must include an explanation why the prospective subject’s name and contact information were available.

5.4.4. The text of the letter must include only the following items:

5.4.4.1. Name and email address of the PI and associated institution.

5.4.4.2. A clear statement that activity is research.

5.4.4.3. Purpose of the research

5.4.4.4. IRB number

5.4.4.5. An invitation to contact the investigator for more information, with telephone number if applicable.

5.4.4.6. A description of why the prospective subject’s name and contact information were available.

5.4.5. The recruitment letter may be sent to potential subjects no more often than weekly unless specifically authorized by the IRB.
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. It is the view of the Organization that payment of finder’s fees or recruitment bonuses to investigators or to any representative of the Organization may create the perception that subjects or potential subjects could be unduly influenced or coerced to participate (or continue participation). Therefore, it is the policy of the Organization that such payments are not permitted.

3.0 Definitions
3.1. Finder’s Fee: Payment made by an investigator or sponsor to an organization or individual (including non-research personnel or a research participant) for identifying and/or referring potential participants for research.

3.2. Recruitment Bonus: Payment, merchandise, or other gift or service offered by a sponsor as an incentive or reward to an organization, investigator, or investigator’s staff designed to accelerate recruitment that is tied to enrollment rate, timing, or numbers.

4.0 Finder’s Fees
4.1. Finder’s fees, which are paid to investigators, investigator’s staff or to any representative of the Organization, for referring prospective research subjects, are not permitted.

4.2. Finder’s fee which are paid to non-research personnel or to research subjects for referring additional subjects are generally not permitted. Under limited circumstances the IRB may approve the payment of small amounts if such payment is necessary to recruit a population of subjects who would potentially benefit from the research, but would otherwise be difficult to recruit.

5.0 Recruitment Bonuses
5.1. Recruitment bonuses which are tied to the enrollment of a set number of subjects or accelerated enrollment, are not permitted.
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for, and limitations on, compensation of research subjects.

2.0 Policy
2.1. It is the policy of the Organization that 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.

2.2. It is the policy of the Organization that compensation in any form is not considered a benefit to be weighed against risks in the IRB’s assessment of the risk/benefit relationship of the research, and that compensation not be presented to the potential subject as a benefit in either the process of consent, 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. 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.

3.3. The amount or type of compensation should not serve as undue inducement to potential subjects.

3.4. Amount of compensation should reflect the amount of time required of the subject. The amount of compensation should not be tied to the degree of risk or discomfort associated with the study.

3.5. The IRB will not consider compensation as a benefit to offset risks (either quantitative or qualitative) associated with the research.

3.6. 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.

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.

4.7. The amount of total compensation should not be emphasized during the process of consent or in the ICF.

4.8. The IRB does not allow bonuses paid for completion of a study as it may offer undue influence to a subject to continue in a study when he/she would otherwise have chosen to withdraw.

4.9. 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 upon conclusion of the study. The IRB views this form of compensation to be an inappropriate marketing tool when associated with research participation.

4.10. 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.

4.11. 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. 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.

4.12. Payments for involvement of minors <16 years of age 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.

4.13. 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.

4.14. Due to the concerns relating to 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 for participation in greater than minimal risk research.

4.15. The IRB may allow use of a lottery (or raffle) as a mechanism to provide compensation to subjects for participation in minimal risk research on a case-by-case basis. This method of compensation must be approved by the IRB Executive Chair/designee.
1.0 Purpose
The purpose of this policy and procedure is to describe the contraception requirements for subjects participating in research.

2.0 Policy
3.0 It is the policy of the Organization that subjects must utilize appropriate contraception methods while participating in research with potential for reproductive toxicity.

3.1. Contraception requirements should be based on the FDA Pregnancy and Lactation Labeling Rule (for all investigational drug applications submitted after 6/30/2015). Drugs approved prior to 6/30/2015 contraception requirements may be based on FDA Use-in-Pregnancy Category until Pregnancy and Lactation Labelling has been submitted and approved by FDA.

3.2. Female study volunteers who are not of reproductive potential (premenarchal, postmenopausal, or surgically or otherwise sterile) are eligible to participate in research without requiring the use of contraception.

3.3. Male research subjects, including those who have undergone successful vasectomy with resulting azoospermia or have azoospermia for any other reason, should use barrier contraception, or their partners should use appropriate contraception, unless the agent has been shown not to be present in seminal fluid, or the agent has been shown to have no genotoxic, reproductive, or developmental effects in nonclinical or clinical studies.

3.4. It is the responsibility of the investigator with or without the Research Subject Advocate, to discuss the risks and benefits of each form of contraception with potential study participants to ensure that subjects are making an informed choice.

4.0 Categories based on FDA Pregnancy and Lactation Labeling Rule (PLLR)
4.1. Group 1: No systemic absorption of drug or biologic.

4.2. Group 2: Review of clinical trials conducted in pregnant women, pregnancy exposure registries, and other large scale epidemiologic studies show no evidence of adverse developmental outcomes.

4.3. Group 3: In the absence of human data, animal studies show no evidence of adverse developmental outcomes.

4.4. Group 4: Animal studies show evidence of adverse developmental outcomes, at dose levels higher than those to be used in this study.

4.5. Group 5:

4.5.1. Review of clinical trials conducted in pregnant women, pregnancy exposure registries, other large scale epidemiologic studies, or well described case-series show evidence of adverse developmental outcomes; OR

4.5.2. Animal studies show evidence of adverse developmental outcomes, at dose levels similar to those to be used in this study; OR
4.5.3. The mechanism of action of the drug suggests the possibility of adverse developmental outcomes.

5.0 Definitions of the FDA Use-In-Pregnancy Categories

5.1. **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.

5.2. **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.

5.3. **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.

5.4. **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.

5.5. **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.

6.0 Procedure

6.1. For drugs or biologics for which there is Pregnancy and Lactation Labelling available (all investigational drug applications submitted after 6/30/2015, and all approved drugs for which Pregnancy and Lactation Labelling has been submitted and approved by FDA), the ICFs must include the appropriate standard contraception language based upon the categories in section 3.0 (see Addendum 1 attached at the end of this policy).

6.1.1. **Studies Involving Group 1 Drugs**

6.1.1.1. Protocol may not require use of contraception. Exceptions to this policy must be approved by the full IRB after adequate justification by the PI.

6.1.2. **Studies involving Group 2 Drugs** (Human data shows no evidence of adverse developmental outcome)

6.1.2.1. The protocol may require the use of ONE form of contraception, with IRB approval, after justification by the PI.

6.1.3. **Studies involving Group 3 Drugs** (Animal Data shows no evidence of adverse developmental outcome)

6.1.3.1. The protocol may require the use of ONE form of contraception, with IRB approval, after justification by the PI.

6.1.4. **Studies involving Group 4 Drugs** (Animal studies show evidence of adverse developmental outcomes, at dose levels higher than those to be used in this study)

6.1.4.1. The protocol must require the use of ONE or TWO form(s) of concurrent contraception.
6.1.5. Studies involving Group 5 Drugs (Animal or Human studies show evidence of adverse developmental outcomes, or drug mechanism of action suggests the possibility of adverse developmental outcomes)

6.1.5.1. The protocol must require the use of TWO forms of concurrent contraception.

6.1.6. For all groups, the ICF must utilize the appropriate standard language.

6.1.7. The duration of contraception must be stated in the IRB Application and in the ICF. If contraception is required for longer than the time the drug is being administered, justification must be provided.

6.2. For drugs or biologics for which Pregnancy and Lactation Labeling is not available, the ICFs must include the appropriate standard contraception language based upon the categories in section 4.0 (see Addendum 1 attached at the end of this policy).

6.2.1. Studies Involving Category A Drugs:

6.2.1.1. Protocol may not require use of contraception. Exceptions to this policy must be approved by the full IRB after adequate justification by the PI.

6.2.2. Studies Involving Category B Drugs:

6.2.2.1. The protocol may require the use of ONE form of contraception, with IRB approval, after justification by the PI.

6.2.3. Studies Involving Category C Drugs:

6.2.3.1. The protocol must require the use of ONE or TWO form(s) of concurrent contraception.

6.2.4. Studies Involving Category D Drugs:

6.2.4.1. The protocol must require the use of TWO forms of concurrent contraception.

6.2.5. Studies Involving Category X Drugs:

6.2.5.1. The protocol must require the use of TWO forms of concurrent contraception.

6.3. For all groups and categories described above, the ICF must use the corresponding standard Contraception language in Addendum 1, except:

6.3.1. For Group 5 drugs, or category D or X drugs, if the sponsor mandates specific contraception language be included in the ICF this language may be used in lieu of the standard language in Addendum 1, provided the IRB determines that the specified language is as protective of the potential fetus, and does not create undue burden on the mother.

6.4. 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 (1) condoms (male or female) with or without a spermicidal agent and (2) diaphragm or cervical cap with spermicide, 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.

6.5. 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.
Policy #3.9
Contraception Requirements
Page 4 of 7

Administrative Approval:
Bruce G. Gordon, MD  IRB Executive Chair & Assistant Vice Chancellor for Regulatory Affairs
Christopher Kratochvil, MD  Institutional Official

Policy Amended:
- Revised November 21, 2017
- Initial December 28, 2015
ADDENDUM #1
ICF Pregnancy Risk Statements

Category A or Group 1 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 or Group 2 or Group 3 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 or Group 2 or Group 3 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 use birth control 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 or Group 4 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 possible risk to the fetus [OR an unborn child], methods of natural family planning are not, by themselves, reliable enough to avoid pregnancy.

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 use birth control 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 or Group 5 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 possible risks to a fetus [OR an unborn child], methods of natural family planning are not, by themselves, sufficiently reliable to avoid pregnancy.

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 use birth control 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. If the sponsor or FDA require inclusion of specific language relating to fetal risk, monitoring for pregnancy and prevention of pregnancy in the ICF, it may be included, and redundant category D language deleted.*
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 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 women 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. Woman of childbearing potential (WOCBP) for the purpose of this policy is a woman who has begun menstruating and not entered menopause. Women who are sterile due to history of hysterectomy, bilateral oophorectomy, or radical pelvic irradiation are not considered females of childbearing potential.
3.2. Menopause for the purpose of this policy is defined as lack of menses for 12 months in the absence of any reversible medical condition which could produce amenorrhea.

4.0 Procedures
4.1. Protocols that describe pregnancy as an exclusion criterion must describe how pregnancy status will be determined.
4.2. Protocols that include an intervention considered potentially harmful to a fetus must include pregnancy testing 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.
   4.3.1. Quantitative testing is not indicated for the purposes of this policy.
   4.3.2. Acceptable test results are those performed at Nebraska Medicine, BMC, CHMC, or a documented result from the subject’s provider.
   4.3.3. 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 (MS72). For ongoing interventions or exposures, testing should be done at a frequency consistent with clinical practice (and not more often than monthly).
4.6. The informed consent/assent process and the ICF must include:
   4.6.1. How often pregnancy testing will be done.
4.6.2. How often subjects will be informed of results.
4.6.3. Whether subjects will be removed from the study if they become pregnant.

4.7. Minor subjects should 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:

4.8.1. For protocols that require pregnancy testing, but are not expected to cause fetal harm, subjects may not be charged for pregnancy testing.

4.8.2. 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:**
BRUCE G. GORDON, MD IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS
CHRISTOPHER KRATOCHVIL, MD INSTITUTIONAL OFFICIAL

**Policy Amended:**
- REVISED JANUARY 8, 2018
- INITIAL DECEMBER 28, 2015
1.0 Purpose
The purpose of this policy is to describe the Organization’s requirements for obtaining informed consent, and collecting data from pregnant partners of research subjects and from their infants.

2.0 Policy
2.1. It is the policy of the organization that collection of identifiable private information about the pregnant partner of a research subject, or obtaining data about that subject through interaction with her, constitutes human subject research under 45 CFR 46, and is subject to the requirements of those regulations and of the HRPP.

2.2. It is the policy of the organization that collection of identifiable private information about the infant child (up to 3 months of age) conceived during the time that the mother was a partner of a research subject, or obtaining data about that child through interaction with the child, constitutes human subject research under 45 CFR 46, and is subject to the requirements of those regulations and of the HRPP.

3.0 General Considerations
3.1. There is considerable variation between IRBs regarding the interpretation of HHS and FDA regulations in respect to pregnant partners of research subjects. Generally, when the collection of pregnancy outcome data is limited to safety surveillance, neither the pregnant partner nor the infant is considered a human subject under FDA regulations. However, because researchers collect identifiable information about, and interact with, the pregnant partner and/or the infant, the collection of data in this context appears to constitute human subjects research under HHS regulations and the Common Rule.

3.2. Since obtaining pregnancy outcome data involves the use of protected health information of the mother and possibly the infant, the use and sharing of this information is subject to the HIPAA Privacy Rule. Consequently, authorization must be obtained, or waivers of authorization granted, as per regulation and HRPP policies 5.1 (Obtaining Informed Consent form Research Subjects) and 5.2 (Waiver or Alteration of Informed Consent and HIPAA Authorization).

3.3. Collection of pregnancy outcome data that is part of the clinical investigation, or is banked in a pregnancy exposure registry, constitutes human subject research, and is subject to HHS and/or FDA regulations.

4.0 IRB Review
4.1. Under most circumstances, protocol for collection of pregnancy outcome data should be submitted to the IRB on a Medical Records Research application.

4.2. If there is a high likelihood that subjects or partners of subjects will become pregnant during the course of the research, the collection of pregnancy outcome data may be included in the initial submission of the protocol.

4.2.1. The IRB application must include relevant information concerning the pregnant partners and the infant (if applicable) as subject populations distinct from the primary subject
of the research. The application must include a thorough description of the specific data to be collected regarding the pregnant partner, and the infant (if applicable), how privacy and confidentiality will be protected, how potential subjects will be identified and recruited, and how informed consent will be sought and documented.

4.3. Federally funded must satisfy requirements of subpart B. Non-Federally funded must be no more than minimal risk to mother and fetus, and satisfy requirements of HRPP policy 4.2: Research Involving Pregnant Women, Human Fetuses, and Neonates (Nonviable or of Uncertain Viability).

4.4. Federally funded or FDA regulated research must satisfy requirements of subpart D (45 CFR 46.404 and/or 21 CFR 50.51) if information about the infant is collected.

4.5. The Medical Records Research application may be reviewed through an expedited process (per HRPP policy 2.3; Expedited Review) provided it constitutes no more than minimal risk.

5.0 Informed Consent

5.1. Informed consent must be obtained and documented from the pregnant partner in accordance with HRPP policy 5.1 (Obtaining Informed Consent from Research Subjects).

5.2. If pregnancy outcome data includes identifiable private information regarding the infant, Parental permission must be obtained in accordance with HRPP policy 5.1 (Obtaining Informed Consent from Research Subjects). A separate “Parental Consent Form” is not required; the Pregnant Partner consent form should be structured such that it includes information relevant to the infant, and the partner’s signature on that form signifies her permission.

ADMINISTRATIVE APPROVAL:

BRUCE G. GORDON, MD IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS
CHRISTOPHER KRATOCHVIL, MD INSTITUTIONAL OFFICIAL

POLICY AMENDED:

Initial January 12, 2018
1.0 Purpose
The purpose of this policy is to define ethical access and to describe the Organization’s requirements to protect the privacy of patients in the context of recruitment for participation in research, or for identification of subjects for review of medical records.

2.0 Policy
It is the policy of the Organization that obtainment of information about a potential subject, and approach to the potential subject, must occur in a manner that respects the privacy of that person.

3.0 Ethical Access for Recruitment of Subjects
For the purposes of this policy, the recruitment of subjects requires two distinct activities, each of which must respect the privacy of patients: (1) obtainment of information about the patient which leads the investigator to believe or conclude that the patient is eligible for the research, and (2) subsequent approach to the patient to explain the research and obtain his/her consent to participate.

3.1. The obtainment of information about the patient which leads the investigator to believe or conclude that the patient is eligible for the research must occur in a manner that does not represent an invasion of his/her privacy. That is, the investigator must have ethical access to clinical information about the patient.

3.1.1. Ethical access, in this context, may occur in one of three ways:

3.1.1.1. The researcher has legitimate access to a patient’s information for clinical purposes, and therefore has legitimate access to that patient’s information for identifying potential research subjects

Specifically an investigator may have ethical access to this information in this context in one or more of the following manners:

3.1.1.1.1. The investigator has an existing clinical relationship with the patient; that is the information has been shared with the clinician for the primary purpose of care of the individual. The patient may or may not know this relationship exists; for example, a specialist consulted informally by the primary provider to assist in the care of the patient may never have met the patient, but the clinical relationship, and hence ethical access exists. Similarly, members of a “care team” (e.g., a hospital pharmacist, or nurse practitioner that rounds with the primary physician provider) have a clinical relationship and therefore ethical access.

Note that the “care team” does not usually include a research coordinator acting on behalf of the investigator. However, the IRB or expedited reviewer, or the IRB Chair or Executive Chair may extend “ethical access” to that person under limited circumstances (for example, when the risks associated with loss of confidentiality are low and the information sought is not sensitive). In general, these circumstances would be similar to the conditions of 45 CFR 46.116(d) (or rev 45 CFR 46.116(f)).
3.1.1.1.2. The investigator works with a provider who has an existing clinical relationship with the patient, and the relationship between the investigator and the provider is such that the investigator could reasonably be called upon to care for the patient in a clinical setting. For example, a physician partner of the investigator within the same specialty and clinical group might have the responsibility to care for the patient while on hospital service, or while taking night phone calls. Under these circumstances, for the purpose of this policy, the investigator has ethical access to information about the patient he/she would reasonably need to know to care for that patient.

3.1.1.1.3. The investigator’s professional responsibilities (independent of her role as a researcher) require that she has this information. For example, a hospital epidemiologist would have access to a list of inpatients with positive blood cultures, as part of her duties; an Operating Room Nursing supervisor would have a list of names and diagnoses of patients scheduled for surgical procedures on a given day.

3.1.1.2. The patient has given express consent for investigators to search medical records or other databases to determine potential eligibility (for example, Nebraska Medicine Conditions of Treatment Opt-in for Clinical Research utilizing the Electronic Health Record (EHR) Core).

3.1.1.3. The IRB has waived the requirement for the patient’s consent by finding that the conditions of 45 CFR 46.116(d) (or rev 45 CFR 46.116(f)) are met. Note that waiver of the requirement to obtain the patient’s consent to have access to the patient’s information to determine eligibility does not imply that, or require that, the requirement for consent to participate in the research is also waived.

3.2. Subsequent approach to the patient to explain the research and obtain his/her consent to participate must also occur in a manner that respects the patient’s privacy, and that minimizes the perception of dissemination of private information outside the clinical context (despite “ethical access” as described above.)

“Approach to the patient” may refer to physical approach to the potential subject (that is, a face-to-face contact), verbal contact (via telephone) or written contact (by letter or email addressed personally to the potential subject).

3.2.1. Physical approach: Potential subject may be approached by the investigator if one of two conditions applies:

3.2.1.1. The investigator has an existing clinical relationship with the patient. In contrast to section 2.1.1 above, the patient must be aware of this existing relationship; that is, the patient must already know the investigator in his clinical role; or

3.2.1.2. Someone with an existing clinical relationship has approached the patient, introduced the existence of the research study in question, and asked permission for the investigator (or her representative) to approach the subject to discuss the research.

Other personnel who may have access as described above (investigator with existing clinical relationship but who has never met the potential subject, or persons who have other professional access to identifiable information) may not directly approach the potential subject without introduction by a care provider and the express permission of the subject. Under limited circumstances, the IRB may approve approach by such persons without prior introduction.
3.2.2. **Verbal Contact**

3.2.2.1. Verbal contact initiated as a result of identification through existing clinical relationship will follow the same pattern as for physical approach described in 2.1.1 above.

3.2.2.2. Verbal contact initiated based on the Conditions of Treatment Form designation ("opt-in" designation) must follow procedures described in **HRPP policy 3.6 (Subject Recruitment Through Direct Invitation)** (which specifies the content and format of communication and frequency and timing of messages).

3.2.3. **Written contact:** Written contact must follow procedures described in **HRPP policy 3.6 (Subject Recruitment Through Direct Invitation)** (which specifies the content and format of communication, identification of recipient and sender, return contact information, and frequency and timing of messages).

4.0 **Ethical Access for Review of Medical Records**

4.1. For research that involves review of existing or prospective records, and where consent of the subject has been waived under HHS or FDA regulations, the requirement for ethical access will still apply to identification of potential subjects, as per section 3.1 above.

5.0 **IRB Procedure**

5.1. Investigators must describe how they have ethical access in the subject identification and recruitment section of the IRB application, or the appropriate section of the **Medical Records Application**.

5.2. The IRB (or the expedited reviewer) will evaluate ethical access as part of its determination whether or not the research satisfies the criteria for approval (45 CFR 46.111(a)(7); “When appropriate, there are adequate provisions to protect the privacy of subjects…”)

5.3. If the investigator does not have ethical access for the purposes of recruitment, the investigator may consider adding a co-investigator with the appropriate access, whose role would be to introduce the potential subject to the investigator (as per section 3.2.1.2).

5.4. If the investigator wishes to use a research coordinator acting on her behalf, the IRB or expedited reviewer, or IRB Chair or Executive Chair will determine whether ethical access can be extended to include that coordinator as per section 3.1.1.1.1.

5.5. If the investigator does not have ethical access for the purposes of review of medical records, the investigator may consider adding a co-investigator with the appropriate access, whose role would be to identify potential subjects and gather de-identified data for the investigator. This role can also be taken by an “honest broker” (per **HRPP policy 3.4; Use of Protected Health Information in Research**)

5.6. Review of medical records must also satisfy requirements of the HIPAA Privacy Rule per **HRPP policy 3.4 (Use of Protected Health Information in Research)**.
POLICY AMENDED:
- Revised February 18, 2019
- Revised November 20, 2018
- Initial April 16, 2018
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for IRB review and approval of clinical trials that utilize placebos or wash-out of effective therapy.

2.0 Policy
2.1. It is the policy of the Organization that use of placebo in a controlled clinical trial, or of a wash-out period from effective therapy, must be ethically and scientifically justified, and risks associated with placebo or wash-out must be minimized.
2.2. It is the policy of the Organization that subjects be adequately informed of the use of placebo or of wash-out of effective therapy, and of the associated risks.

3.0 Definition
3.1. Placebo is an inactive substance or treatment that may resemble an active medication or treatment, but has no therapeutic value.
The OHRP Institutional Review Board Guidebook Glossary defines placebo as “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.”
3.1.1. This policy refers use of a placebo in a RCT where the placebo is used as an alternative to the clinical intervention being tested (that is, intervention X vs placebo). The use of placebo when subject is also receiving the standard care (for example, standard treatment + intervention X vs standard treatment + placebo) generally does not pose an ethical concern in and of itself.
3.2. Randomization is assignment of subjects to different treatments, interventions, or conditions according to chance rather than systematically.
The OHRP Institutional Review Board Guidebook Glossary notes that “Random assignment of subjects to conditions is an essential element of experimental research because it makes it makes more likely the probability that differences observed between subject groups are the result of the experimental intervention.”
3.3. Wash-Out Period refers to a protocol required period of withdrawal from current treatment prior to initiation of placebo or active treatment arms. “Wash-out” of effective therapy prior to institution of “investigational therapy” in a clinical trial may be ethically problematic, especially if the clinical trial includes a placebo arm.

4.0 Ethical Justification
4.1. The use of a placebo as an alternative to “standard therapy” may be ethically justified in the following situations:
4.1.1. There is no standard therapy.
4.1.2. Standard therapy is known to be not effective (that is, standard therapy is no better than no treatment).

4.1.3. Standard therapy may be effective, but associated with significant toxicity such that there is doubt regarding the net therapeutic advantage of the standard treatment.

4.1.4. Standard treatment is unavailable.

4.1.5. There are compelling and scientifically sound methodological reasons the use of placebo is necessary AND the patients who receive placebo will not be subject to additional risks of serious or irreversible harm as a result of not receiving the best proven intervention (WMA Declaration of Helsinki (2013)).

4.2. The use of a “wash-out” of effective therapy may be ethically justified when there are compelling and scientifically sound methodological reasons for the wash-out AND subjects will not be placed at additional risks of serious or irreversible harm during the wash-out period (or during the duration of the trial if subsequently assigned to placebo).

5.0 Study Design Considerations

5.1. The investigator must demonstrate, and the IRB must find that:

5.1.1. The risk of placebo or of wash-out of effective therapy is minimized. Procedures to minimize risk may include, but are not limited to:

5.1.1.1. Careful and frequent monitoring for worsening of underlying condition

5.1.1.2. Early withdrawal of subjects for worsening of underlying condition, or for non-improvement

5.1.1.3. Early intervention or treatment (including, when appropriate, resumption of known effective therapy)

5.1.1.4. Exclusion of patients at increased risk of harm from wash-out, or non-response associated with placebo

5.1.1.5. Cross-over study design, where all subjects receive investigational treatment or intervention at some point in the study

5.1.1.6. Interim monitoring by DSMB

5.1.2. Possible assignment to the active study drug offers the prospect of at least equivalent direct subject benefit compared to standard treatment.

6.0 Informed Consent Requirements

6.1. For clinical trials utilizing placebo, the informed consent process and document must include:

6.1.1. A statement that a placebo is used in the study and an appropriate lay definition of “placebo” (for example “a pill or injection that has no medicine in it”).

6.1.2. The scientific rationale for use of a placebo, in lay terms.

6.1.3. The risks of non-treatment associated with placebo, including worsening of the subject’s disease or condition.

6.1.4. The plan for early withdrawal from the study if the subject’s clinical status worsens or fails to improve to a pre-defined level.
6.2. For clinical trials utilizing wash-out of effective therapy, the informed consent process and document must include:

6.2.1. A statement that the research will utilize a wash-out period where subject will be taken off therapy that has been effective.

6.2.2. The scientific rationale for the wash-out period, in lay terms.

6.2.3. The risks of the wash-out period, including worsening of the subject's disease or condition by discontinuing effective therapy.

6.2.4. The plan for early termination of the wash-out and resumption of effective therapy if the subject's clinical status worsens.
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for IRB review and approval of Phase I and First in Human Studies.

2.0 Policy
2.1. It is the policy of the Organization that, except in limited circumstances, phase I studies are assumed to represent no direct benefit to subjects/
2.2. It is the policy of the Organization that review of phase I studies requires a careful assessment of the risk-benefit relations, subject selection, study design, monitoring and the process and content of informed consent.

3.0 Definitions
3.1. Phase I studies represents the initial administration of an investigational new drug into humans, or into a specific population of humans (for example, elderly subjects, or children). The primary aim of a phase I study is determination of safety and tolerability, and assessment of maximum tolerated dose (MTD). Phase I studies may also assess pharmacokinetics, pharmacodynamics, drug metabolism, structure-activity relationships, and mechanism of action of the investigational agent. Participants in phase I trials may suffer from a disease or condition which could be the eventual target of the investigational agent (for example, an anti-neoplastic drug in patients with advanced cancer), or they may be healthy volunteers. In the former instance, early measurement of drug activity may be a secondary objective. Participants in phase I drug tests may receive a completely novel agent, an agent belonging to a class of drugs already studied in humans or a combination of new and approved drugs
3.2. First-in-Human (FIH) trials represent the subset of phase I studies where the investigational agent has not been previously used in humans. The starting dose for a FIH phase I trial is typically based on the No Observed Adverse Effect Level (NOAEL), the highest dose at which no statistically significant and/or biologically relevant adverse effect is observed in the most relevant animal species.
3.3. Phase 0 studies (also referred to as pre-phase I studies) are conducted prior to phase I trials to determine whether further human trials are worth pursuing. Objectives and endpoints of phase 0 studies conducted under an exploratory IND may include evaluating modulation of a presumed drug target in humans; optimizing target assay methodology using human samples; providing pharmacokinetic (PK) data; assessing PK/pharmacodynamics (PD) relationships; and selecting the most promising agent from several chemical entities or formulations. Study participants, who can be either patients or healthy volunteers, are administered sub-therapeutic but pharmacologically active doses of drug. Participant exposure to the agent is limited. Phase 0 studies have no therapeutic intent.

4.0 General Principles
4.1. Phase 0 studies have no potential for direct benefit.
4.2. Phase I studies of new agents alone generally are considered to have no potential for direct benefit. Assertions of potential benefit must be based on clear pre-clinical data, or preliminary clinical data in a different population of subjects, at the dose levels proposed in the research.

4.3. Phase I studies of a new agent in combination with an agent with known effectiveness, administered to subjects with a disease or condition, may be considered to have potential for direct benefit.

4.4. Phase I studies of approved agents administered to new specific population of subjects (for example, elderly subjects, or children) with a disease or condition, may be considered to have potential for direct benefit.

5.0 IRB Review

5.1. As a part of the analysis of the ethical basis for the research and the regulatory criteria for approval, the IRB should consider the following points

5.1.1. **Assessment of risk**

5.1.1.1. In most cases, risk assessment is based on pre-clinical data, and can be difficult. Pre-clinical data may fail to predict human risks, leading to adverse effects in human trials (for example, consider the TGN1412 trial). It may predict clinical benefits that then fail to materialize for human subjects. And it may predict nonexistent risks in humans with the result that a potentially useful agent is discarded (Dresser J. J Law Med Ethics 37:38, 2009)

5.1.1.2. When phase I trials involve healthy people, there should be stronger preclinical evidence that risks are low than there need be when trials involve people with an underlying serious disease.

5.1.2. **Assessment of potential benefit**

5.1.2.1. Potential direct subject benefit should be considered as noted above (section 4.0)

5.1.2.2. Potential benefit to an individual subject is usually conceptualized in the form of an improvement in health status derived from the agent being tested; however this is not always the sole potential therapeutic benefit. For example an improvement in the quality of life may qualify as a clinically relevant benefit (Chapman AR. J Clinic Res Bioeth 2:113, 2011).

5.1.2.3. Extraneous benefits such as payment or adjunctive medical services that might benefit individual participants should not be considered when conducting a risk-benefit analysis (Emanuel EJ, et al. JAMA 283: 2705, 2000)

5.1.3. **Subject Selection**

5.1.3.1. Choice of subject population (healthy volunteers vs patients with a disease or condition) should depend on the scientific objectives of the trial, as well as the risks associated with the intervention and the consequences of those harms should they occur.

5.1.3.2. If patients with a disease or condition are considered the appropriate subjects, careful consideration should be given to the choice of “stable well-managed patients” vs those with poor managed, debilitating or end-stage disease. The former group may be more likely to benefit, may provide better data, and may be likely to make a free and deliberate choice. However the consequences of harm arising from participation may be
greater than for those for whom there are limited other choices, or for whom death or disability is inevitable.

5.1.3.3. When healthy volunteers are considered as appropriate subjects, care must be taken to assure payment (if offered) does not constitute undue inducement and is not exploitative, and that potential subjects do not conceal personal information that could disqualify them from trial enrollment in order to receive payment.

5.1.4. Study design and toxicity monitoring

5.1.4.1. Trials should be designed with sequential, rather than concurrent, enrollment. There must be an adequate interval for monitoring effect of the agent on a subject before the next subject is enrolled, and before a dose escalation is made.

5.1.4.2. The data and safety monitoring plan should be sufficiently robust to assure that subjects are not exposed unnecessarily to harm. The plan should include frequent and clear safety evaluations, well defined dose limiting toxicities, and adequate oversight.

5.1.5. Informed consent

5.1.5.1. Extreme care must be taken to avoid therapeutic misconception and unrealistic optimism.

5.1.5.1.1. “Therapeutic misconception exists when individuals do not understand that the defining purpose of clinical research is to produce generalizable knowledge, regardless of whether the subjects enrolled in the trial may potentially benefit from the intervention under study or from other aspects of the clinical trial.” (Henderson GE. PLoS Med 4(11):e324, 2007). Two core concepts are (1) subjects need to understand that the main purpose of the research protocol is to produce generalizable knowledge; and (2) conducting a research protocol differs from providing individualized care (Pentz RD. Cancer 118(18):4571, 2012).

5.1.5.1.2. Unrealistic optimism “occurs when people perceive their own personal outcomes as being more positive than those of other people in similar circumstances when, in fact, there is no good reason to do so.” Unrealistic optimism may compromise autonomous decision making when it interferes with the appreciation and processing of information related to risks and benefits (Crites JS. J Med Ethics 39(6):403, 2013)

5.1.5.2. General concepts and specific language for ICFs are described in section 6.0 below

6.0 Informed Consent Model Language

6.1. Methods

6.1.1. For Phase I studies conducted in classic 3 + 3 design, or similar dose escalation design, CF language should reflect the escalation of dose (between cohorts) to toxicity.

For example: “The purpose of the study is to find the highest dose of X that can be given safely. To do this a small number of subjects are given a low dose of X, and side effects are noted. If the side effects are tolerable, then the next group will get a higher dose, and this will be repeated with successive groups until some patients get certain side effects. The particular dose you get will depend on when you enter the study. The dose you get will not increase.”
6.2. **Risks**

6.2.1. For Phase I studies conducted in classic 3 + 3 design, or similar dose escalation design, CF language should reflect the escalation of dose, with development of worse or new adverse effects in higher dose cohorts.

*For example: “The dose of X will be increased with each successive group of subjects in order to see what dose causes side effects. Therefore, depending on when you enter the study (which group you are in) you may get more side effects, or new side effects, not seen with lower doses.”*

6.3. **Potential Benefits to the Subject:**

6.3.1. CF language should reflect General Principles above (section 4.0).

6.3.2. When there is potential for direct benefit, it should reflect the disease stage of the target population. For example, while use of a new agent in combination with an agent with an approved chemotherapy regimen may have potential for direct benefit, such benefit is unlikely to be significant or long-lasting in a patient with late stage cancer.

6.3.3. When potential benefits are suggested, the CF language should highlight differences between the study definition of positive response and the way that patients would define it.

*For example, a phase I oncology trial CF should alert subjects to the fact that tumor response is not equivalent to clinical improvement.*

*For example: “It is possible that X [the investigational agent] would make your tumor shrink. However, it is important to understand that the tumor shrinking might not mean you will live longer, or even that your symptoms will improve”*

6.3.4. When potential benefits arise from combination of an effective therapy with the investigational agent, CF language should clearly state that the benefit arises from the approved effective agent (which may be available outside the study) unless there is pre-clinical data to suggest the investigational agent augments the efficacy of the approved drug.

*For example: “It is possible that the combination of [standard therapy] with X [the investigational agent] would make your tumor shrink. However, it is important to understand that the [standard therapy] might cause your tumor to shrink even if you didn’t get X.”*

6.3.5. CF language should minimize description of collateral benefit (for example, avoid phrases like “satisfaction associated with helping find a cure for X”)

6.3.6. CF language can include such benefits as improvement in quality of life, or relief of pain, if such benefits are realistic at the lowest dose levels to be administered.

6.4. **Potential Benefits to Others**

6.4.1. CF language should describe realistic potential scientific benefits associated with the research, and should avoid framing benefits in terms of FDA approval.

*For example “The research may help us determine the safest dose of investigational drug X” is acceptable, as opposed to “This research will help develop a new treatment for disease” or “… provide information to allow FDA approval of drug X”*

7.0 **Phase I Studies in Children**

7.1. Use of early phase investigational agents in children may pose ethical challenges. Investigators need to be especially alert to the risks of unreasonable optimism and therapeutic misconception on behalf of the parents who are asked to provide consent (permission). When
older children are involved, investigators must pay close attention to eliciting assent and respecting dissent.

7.2. In general, phase I studies in children hold out greater potential for direct benefit, since there is usually already data from adults suggesting efficacy, and starting dose in pediatric trials is usually close to the adult MTD, thereby suggesting less likelihood of a sub-therapeutic dose (Berg SL. Oncologist 12:1336, 2007). Therefore, pediatric phase I trials may potentially be approvable under 21 CFR 50.52 (Clinical investigations involving greater than minimal risk but presenting the prospect of direct benefit to individual subjects) and 45 CFR 46.405.

8.0 Phase I Studies in Decisionally Impaired Persons

8.1. Use of early phase investigational agents in decisionally impaired persons may pose ethical challenges, to the extent that these potential subjects may not be able to provide consent for themselves. Investigators must actively assess capacity to provide consent and assent, especially when capacity may wax and wane. Investigators must structure the consent/assent process in a fashion that maximizes the ability of the prospective subject to provide his/her voluntary, informed agreement to participate.

8.2. Phase I studies in decisionally impaired persons may be more problematic than those conducted in children (section 7.2 above), since there may not be preliminary efficacy data and starting doses may be at the NOAEL (see section 3.2 above). Therefore, there may be no or limited potential direct benefit.

8.3. Criteria for inclusion of decisionally impaired persons, based on risk-benefit relationship, are described in HRPP policy 4,6 (IRB Review of Research Involving Subjects with Impaired Decision-Making Capacity), sections 7.2 (Category 2 – Greater than minimal risk with the prospect of direct benefit) and 7.3 (Category 3 - Greater than minimal risk with no prospect of direct benefit).

Note that the latter category requires that the research represent only a minor increase over minimal risk, which is unlikely to be true when conducting research with a novel agent.

ADMINISTRATIVE APPROVAL:
BRUCE G. GORDON, MD  IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS
CHRISTOPHER KRATOCHVIL, MD  INSTITUTIONAL OFFICIAL

POLICY AMENDED:
★ Initial February 5, 2018
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for disclosure, or nondisclosure, of radiographic incidental findings that may affect the management of a subject’s current or future health or welfare.

2.0 Policy
2.1. It is the policy of the Organization that all human subject research must include provisions for management of unexpected incidental findings.

2.2. This policy applies to radiographs (including but not limited to MRI, fMRI, CT scan, ultrasound, nuclear medicine scans, PET scans, and plain radiographs) that are performed solely for research purposes, when there is not a formal radiologist’s report generated and saved in the medical record. This includes research scans performed as a screening procedure to determine whether a potential subject meets eligibility requirements for inclusion, or as a baseline evaluation prior to beginning the research intervention.

3.0 Definitions:
3.1. Incidental Finding (IF) is a finding concerning an individual research participant that has potential health implications and is discovered in the course of conducting research but is beyond the aims of the study.

4.0 Procedures
4.1. Plan for Review and Disclosure of IFs to Subjects
   4.1.1. The PI has an obligation to handle IFs responsibly and promptly. The time frame of the initial communication with the subject should be consistent with the suspected severity of the finding and the net benefit of the disclosure.

   4.1.2. Prior to commencing the research, the PI must have a plan to validate any IF and confirm its importance for the health and wellbeing of the subject. If the researcher does not have the expertise to make this assessment, he/she must identify an individual who does have this competence. The plan and time course of the review must take into account the type and resolution of scans or tests performed (e.g., anatomic imaging more urgent than functional imaging), and the age and health status (and likelihood of an abnormality) of the subject population.

   4.1.3. During the process of consent, the PI must explain the potential for discovering IFs, describe the steps researchers will follow to evaluate IFs, (including consultation with a qualified clinician), describe what types IFs the PI intends to disclose or withhold, describe the process of disclosure, and inform the prospective subject of their right to refuse to receive information regarding incidental findings.

   4.1.4. The PI has a responsibility for ensuring subjects are well informed regarding the potential risks and benefits of disclosure of incidental findings.
4.2. When to Disclose IF Results

4.2.1. Whether IFs are disclosed to subjects will depend on the investigator’s (and, if necessary, the consultant’s) assessment of the “net benefit of disclosure.”

4.2.1.1. **Category A (Strong net benefit):** (1) information revealing a condition likely to be life-threatening; or (2) information revealing a serious condition that can be avoided or ameliorated. Category A IFs must be disclosed, unless the subject explicitly refuses to receive the information.

4.2.1.2. **Category B (Possible Net Benefit):** (1) information revealing a nonfatal condition that is likely to be serious but that cannot be avoided or ameliorated, when a research participant is likely to deem that information important. Category B IFs may be disclosed, at the discretion of the investigator, unless the subject explicitly refuses to receive the information.

4.2.1.3. **Category C (Unlikely Net Benefit):** (1) information revealing a condition that is not likely to be of serious health importance; or (2) information whose likely health importance cannot be ascertained. Category C IFs should not be disclosed to subjects.

4.3. Process of Disclosure to Subject

4.3.1. The time frame of the initial communication with the subject should be consistent with the suspected severity of the finding and the net benefit of the disclosure.

4.3.2. Subjects may refuse to receive information regarding incidental findings. As appropriate, the PI is responsible for explaining to the subject the consequences of non-disclosure.

4.3.3. Disclosure of IFs should include a medical professional who is knowledgeable about the type of IF found and who is experienced in communicating sensitive medical information.

4.3.4. IFs should be disclosed directly to the research participant. Investigators may offer to disclose to the subject’s PCP (in addition to, or in lieu of disclosure to subject), but this decision must be made by the subject.

4.4. All IFs must be reported promptly to the IRB. All Category A IFs must be reported to the IRB as soon as possible. The report must include the plan to disclose the results to the subject (for categories A and B), or a description of how the results were disclosed if expeditious disclosure was warranted (for example, for a life-threatening finding).

4.5. The PI generally has no obligation to affirmatively search for IFs. The goal of research is to seek generalizable knowledge, not to provide health information to individuals. Thus, in the context of imaging studies, the PI is not obligated to perform extra scans or modify scans to provide clinical information.

4.6. IFs in Pediatric and Adolescent Research Participants

4.6.1. If incidental findings detected in pediatric or adolescent subjects are to be disclosed (per section 4.2 above) disclosure should be made to parent or guardian.

4.6.2. If the disclosed minor subject has been judged mature enough to provide assent, then offer of disclosure should also be made to the subject. These subjects may refuse to receive this information.
4.7. **IFs in Adult Research Participants without Decisional Capacity**

4.7.1. If incidental findings detected subjects who lack decisional capacity are to be disclosed (per section 4.2 above) disclosure should be made to LAR.

4.7.2. If the subject has been judged competent enough to provide assent, then offer of disclosure should also be made to the subject. These subjects may refuse to receive this information.

5.0 **Model CF Language**

5.1. The following information must appear in the consent forms where the determination is made to disclose IF (as indicated in Section 4.2 above):

“In the course of this research, you will undergo [type of study or studies]. These tests are done for research purposes, and not to look for any specific abnormalities. The scans/tests are not the same as you might get to diagnose a medical condition. However, occasionally, scans/tests will find something unexpected which the research was not looking for. This is called an “incidental finding.” Incidental findings may be nothing to worry about, or they may be significant or even life-threatening.

If one of the researchers sees something on your test which he/she is concerned about, he/she may review the scan/test with an expert. The expert review will be supplied if needed with no cost to you. If the researcher and/or the expert thinks the finding may be of importance to you the researcher will tell you. You can refuse to get this information. If you agree he/she will also tell your doctor.

There may be benefits to learning such results (such as early detection and treatment of a medical condition), but there are also risks. These include anxiety over a finding which may not be real or may not require treatment.

You and/or your insurance company may be billed for follow-up to the incidental finding to see if the abnormality is real or a medical problem.”

6.0 **IRB Review**

6.1. Prior to approval of the research, the IRB must review:

6.1.1. The plan to validate any IF and confirm its importance for the health and well-being of the subject (per 4.1.2 above).

6.1.2. The criteria for deciding whether an IF will be disclosed to subjects

6.1.3. The proposed process of disclosure (per 4.3 above), including the qualifications of the persons who will be disclosing information to the subject

6.2. All category A IFs must be reviewed by the full IRB. The IRB will determine whether the IF represents an unanticipated problem involving risk to the subject, whether the risk benefit relationship of the research is still acceptable, whether risks have been minimized, and whether the CF is adequate

**Administrative Approval:**

Bruce G. Gordon, MD
IRB Executive Chair & Assistant Vice Chancellor for Regulatory Affairs
Christopher Kratochvil, MD Institutional Official

Policy Amended:

- Initial February 28, 2018
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 vulnerable populations will be afforded additional protections, in accordance with the ethical principles described in the Belmont Report, and the requirements of 45 CFR 46.111(b) and 21 CFR 56.111(b).

2.2. It is the policy of the Organization that 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) will be applied for research funded by any of the Common Rule agencies or departments.

2.3. It is the policy of the Organization that equivalent protections will be provided for the vulnerable populations described above who are participating in research not funded by any of the Common Rule agencies or departments. Equivalent protections will be based upon the ethical principles in the Belmont Report, and 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.

2.4. It is the policy of the Organization that the additional safeguards for children in clinical investigations under FDA regulations at 21 CFR 50 Subpart D will be applied for research regulated by the FDA.

2.5. It is the policy of the Organization that additional protections will be provided for other vulnerable populations including, but not limited to, decisionally-impaired persons, terminally ill, or economically or educationally disadvantaged persons. 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 principles of the Belmont Report, the nature of the research, and other factors determining vulnerability.

3.0 Definition
3.1. **Vulnerable Persons** are defined as individuals or groups of individuals “with diminished autonomy” (National Commission, 1979) or as individuals or groups of individuals who “have difficulty providing voluntary, informed consent arising from limitations in decision-making capacity … or situational circumstances …, or because they are especially at risk for exploitation” (National Bioethics Advisory Committee, 2001). Within any group of vulnerable subjects, individuals may have different levels of vulnerability based on the level of capacity, circumstance, or condition. In addition, “vulnerability is sensitive to context, and individuals may be vulnerable in one situation but not in another” (National Bioethics Advisory Committee, 2001).

4.0 Categories of Vulnerability
4.1. Broadly, vulnerabilities in the context of research may be considered to fall into one or more of the following types:
4.1.1. Cognitive or Communicative: diminished capacity to understand or communicate.

4.1.2. Institutional: subject to the formal authority of others.

4.1.3. Deferential: informal subordination to others (gender, race or class inequalities; inequalities of power and knowledge).

4.1.4. Medical: serious health conditions.

4.1.5. Economic and/or Social - disadvantaged in the distribution of social goods and services, or belonging to an undervalued group.

4.2. Vulnerable person may also be considered as belonging to certain groups or populations. Though useful, categorization in this manner needs to consider context and situation. Groups include, but are not limited to:

4.2.1. Pregnant women (Subpart B) (see HRPP policy 4.2).
4.2.2. Fetuses and neonates (Subpart B) (see HRPP policy 4.2).
4.2.3. Prisoners (Subpart C) (see HRPP policy 4.3).
4.2.4. Children (Subpart D) (see HRPP policy 4.4).
4.2.5. Decisionally impaired (see HRPP policy 4.6).
4.2.6. Critically ill persons
4.2.7. Terminally ill persons
4.2.8. Blind or deaf persons, or persons with other disabilities
4.2.9. Economically or socially disadvantaged persons
4.2.10. Educationally disadvantaged persons
4.2.11. Employees and students (see HRPP policy 4.7).
4.2.12. Non-English speaking persons

5.0 Additional Protections for Vulnerable Populations

5.1. Investigators must consider whether subjects to be enrolled in their research might be vulnerable, and if so, what additional protections might be appropriate to provide additional protections.

In making the latter determination, investigators should consider:

5.1.1. Is inclusion of the vulnerable person or population necessary? That is, could the aims of the research be accomplished by enrolling persons or a population that is not (or less) vulnerable?

Note: Investigators should be aware that there are competing ethical imperative related to enrollment of vulnerable persons. The Belmont Principle of Respect for Persons requires that investigators protect those with limited autonomy (even to the extent of excluding them from the research); however, the Belmont Principles of Beneficence and Justice require that researchers provide the benefit of research, and distribute those benefits fairly.

Investigators should also be cognizant of the risks of not including certain populations in research. For example, considering children as research subjects, the National commission noted “The argument in favor of conducting research involving children rests on … the consequences of not conducting research involving children in those instances. Such
consequences might include the perpetuation of harmful practices, the introduction of untested practices, and the failure to develop new treatments …” (National Commission: Research Involving Children. Report and Recommendations, 1977; page 21).

5.1.2. If so, then are protections afforded to subjects adequate?

5.1.2.1. Do prospective subjects have difficulty providing voluntary, informed consent? Are condition for informed consent satisfied? (Is information presented in an understandable manner? Do subjects comprehend the details of the research and their rights as research subjects? Is the process of consent conducive to true voluntariness?)

5.1.2.2. Are prospective subjects at risk for exploitation?

5.2. Specific additional protections that might be considered include (but are not limited to):

5.2.1. The use of an extended consent process.
5.2.2. The use of a consent monitor.
5.2.3. Appointment of a subject advocate.
5.2.4. Involvement of the subject’s family and/or friends.
5.2.5. The requirement for re-consenting of subjects/LARs.
5.2.6. Limits placed on risk.
5.2.7. Increased monitoring of the research through use of a Data Safety Monitoring Board or other mechanisms.
5.2.8. More stringent withdrawal criteria.
5.2.9. Longer study follow-up.
5.2.10. Exclusion from participating in the research.

6.0 Investigator and IRB Procedures Regarding Inclusion of Vulnerable Persons or Populations

6.1. The investigator must identify whether research will include any population which is directly subject to the additional protections in 45 CFR 46 subpart B, C or D, or 21 CFR 56 subpart D.

6.2. The investigator must identify whether subject eligibility criteria will specifically target other potentially vulnerable populations, or whether there is a high likelihood that a sizable number of subjects will come from a vulnerable population.

Note: the intent here is to identify research proposals for which it would be reasonable to have additional protections in place prior to enrollment. The intent is not to identify situations when a vulnerable person would incidentally be enrolled. In the latter case, it is expected that the investigator would identify that person and take appropriate actions.

6.3. The investigator must specifically describe additional protections for persons or populations identified in sections 7.1 and 7.2.

6.4. The IRB will consider whether inclusion of vulnerable subjects or populations is appropriate, and whether the additional protections proposed as adequate, as required in HRPP policy 2.5 (Criteria for Approval).

6.5. The IRB will consider whether the inclusion of vulnerable subjects satisfies the requirements of 45 CFR 46 subpart B, C or D, or 21 CFR 56 subpart D, and of HRPP policies 4.2 (Research Involving Pregnant Women, Human Fetuses, and Neonates – Nonviable or of Uncertain Viability),
4.3 (Research Involving Prisoners), 4.4 (Research Involving Children), 4.6 (Research Involving Subjects with Impaired Decision Making Capacity) and/or 4.7 (Research Involving Employees and Students).

6.6. If the IRB reviews and approves a protocol which does not involve vulnerable subjects but a subject, after enrollment, becomes vulnerable (for example, by being incarcerated, or becoming pregnant or homeless), the PI must notify the IRB and revise the IRB Application as applicable. The IRB will review the submission in order to determine that the vulnerable subject(s) has appropriate additional protections.

6.6.1. 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 continued participation is in compliance with that Subpart.

6.6.2. The IRB determinations regarding inclusion of pregnant women, prisoners, and children will be documented in accordance with HRPP policies 2.2 (Full IRB Review), 2.3 (Expedited IRB Review), 4.2 (Research Involving Pregnant Women, Human Fetuses, and Neonates-Nonviable or of Uncertain Viability), 4.3 (Research Involving Prisoners), and/or 4.4 (Research Involving Children).

7.0 7.8 The IRB determinations regarding inclusion of other vulnerable populations will documented in accordance with HRPP policies 2.2 (Full IRB Review) and 2.3 (Expedited Review).

ADMINISTRATIVE APPROVAL:
BRUCE G. GORDON, MD        IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS
CHRISTOPHER KRATOCHVIL, MD    INSTITUTIONAL OFFICIAL

POLICY AMENDED:
- REVISED JANUARY 26, 2018
- INITIAL JANUARY 6, 2016
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. It is the policy of the Organization that federally funded research involving pregnant women, fetuses, and neonates (nonviable or of uncertain viability) will be reviewed and approved in accordance with the requirements of 45 CFR 46 Subpart B.

2.2. It is the policy of the Organization that 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.

2.3. It is the policy of the Organization that women 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, the protocol must include a valid way to screen for pregnancy in accordance with HRPP policy 3.10 (Pregnancy Testing).

3.0 Definitions

3.1. *Pregnancy* encompasses the period of time from implantation until delivery. A woman shall be assumed to be pregnant if she exhibits any of the pertinent presumptive signs of pregnancy, such as missed menses, until the results of a pregnancy test are negative or until delivery.

3.2. *Fetus* means the product of conception from implantation until delivery.

3.3. *Viable neonate* means a neonate, after delivery, which can survive (given the benefit of available medical therapy) 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* is 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*

4.1.1. Pregnant women may be involved in research if all of the following conditions are met:

   4.1.1.1. For research subject to HHS regulations at 45 CFR 46 subpart B, where scientifically appropriate, preclinical studies, including studies on pregnant animals and
clinical studies involving non-pregnant women, have been conducted and provide data for assessing potential risks for the enrollment of pregnant women and fetuses.

4.1.1.1. For research which is not subject to this subpart, the IRB may decide that preclinical studies on pregnant animals and clinical studies involving non-pregnant women are not reasonable requirements to protect subjects. For example, this requirement would likely be of limited value in social and behavioral science research, or minimal risk biomedical research.

4.1.1.2. For research subject to HHS regulations at 45 CFR 46 subpart 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 the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means.

4.1.1.2.1. For research that is not subject to this subpart, the IRB may decide that the purpose of the research need only be the development of knowledge which has sufficient value which justifies the enrollment of pregnant women.

4.1.1.3. Any risk to the pregnant woman or the fetus is the least possible to achieve the research objectives.

4.1.1.4. The consent of the pregnant woman alone is obtained when the research holds out (1) the prospect of direct benefit to the pregnant woman, (2) the prospect of a direct benefit both to the pregnant woman and the fetus, or (3) no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means.

4.1.1.5. The consent of both the pregnant woman and the father is obtained when the research holds out the prospect of direct benefit solely to the fetus. The father’s consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest.

4.1.1.6. Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate.

4.1.1.7. For children who are pregnant assent of the pregnant minor and permission of the pregnant minor’s parent(s) are obtained in accordance with HHS regulations 45 CFR 46, Subpart D and HRPP policy 4.4 (Research Involving Children).

4.1.1.8. No inducements, monetary or otherwise, will be offered to terminate a pregnancy.

4.1.1.9. Individuals engaged in research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy.

4.1.1.10. Individuals engaged in research will have no part in determining the viability of a neonate.

4.2. Research Involving Neonates

4.2.1. Neonates of uncertain viability and nonviable neonates may be involved in research if:

4.2.1.1. Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.
4.2.1.2. Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate.

4.2.1.3. Individuals involved in the research will have no part in determining the viability of the neonate.

4.2.1.4. The additional requirements listed below for uncertain and nonviable neonates have been met.

4.2.2. Neonates of Uncertain Viability may be involved in research only if, in addition to the conditions listed above in Section 4.2.1, the following requirements are met:

4.2.2.1. 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.

4.2.2.2. 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.

4.2.3. Nonviable Neonates may be involved in research only if, in addition to the conditions listed above in Section 4.2.1, the following requirements are met:

4.2.3.1. The vital functions of the neonate will not be artificially maintained.

4.2.3.2. The research will not terminate the heartbeat or respiration of the neonate.

4.2.3.3. There is no additional risk to the neonate resulting from the research.

4.2.3.4. The purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means.

4.2.3.5. The legally effective informed consent of both parents of the neonate is required. 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.

4.2.3.5.1. The waiver and alteration provisions at 45 CFR 46.116(e) and 45 CFR 46.116(d) (or rev 45 CFR 46.116(e) and rev 45 CFR 46116(f)) do not apply.

4.2.3.5.2. The consent of the father is not required where the pregnancy resulted from rape or incest.

4.2.3.5.3. The consent of a legally authorized representative of either or both of the parents of a nonviable neonate is not permitted.

4.2.4. A neonate, after delivery, that has been determined to be viable may be included in research only to the extent permitted by and in accord with the requirements of HHS regulations 45 CFR 46, Subpart D and HRPP policy 4.4 (Research Involving Children).

4.3. Research involving placenta, dead fetus(s) or fetal material

4.3.1. Research involving the placenta, dead fetus, or fetal material after delivery does not constitute human subject research under 45 CFR 46 (unless any information associated with the material used in the research can be linked in any way to a living person). Research involving the placenta may occur if all federal, state, or local laws and regulations are met.
Research involving dead fetus, or fetal material, is prohibited under University of Nebraska Board of Regents policies.

4.4. Research not otherwise approvable

4.4.1. The Secretary of HHS may conduct or fund research that the IRB does not feel meets the above policy if the following conditions are met:

4.4.1.1. 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 in pertinent disciplines and following opportunity for public review and comment, that the research either:

4.4.1.1.1. Does, in fact, meet the requirements of 45 CFR 46.204, OR

4.4.1.1.2. 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.

4.4.2. For research that is not subject to this subpart (that is, not conducted or funded by HHS), but which the IRB finds satisfies the requirements of section 4.4.A.1 above, the IRB may convene an equivalent panel of experts to advise the board in determining whether the requirements of 4.4.A.1.a and b are met.

5.0 Non-pregnant subjects who become pregnant during research

5.1. If a subject becomes pregnant while actively participating in a research protocol, 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 has determined that it is in the best interest of the pregnant subject to continue participating in the study and has provided justification to the IRB Chair who is authorized to make the final determination.

5.1.1. If the investigator or the IRB chair determines that it is not in the best interest of the pregnant subject to remain in the study, participation will be terminated and the PI must make provisions for the continuation of any necessary treatment of the subject as appropriate.

5.1.2. If the investigator and the IRB chair determines that it is in the best interest of the pregnant subject to continue participating, research activities may continue but 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

6.1. For research reviewed by the convened IRB, compliance with Subpart B (or with the equivalent protections described in this policy) will be documented in the letter to the investigator which is part of the meeting minutes.

6.2. For research reviewed through the expedited mechanism, compliance with Subpart B (or with the equivalent protections described in this policy) will be documented in the letter to the investigator which is available for review by the IRB in RSS.
POLICY #4.2
RESEARCH INVOLVING PREGNANT WOMEN, HUMAN FETUSES AND
NEONATES (NONViable OR OF UNCERTAIN VIABILITY

ADMINISTRATIVE APPROVAL:
BRUCE G. GORDON, MD  IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS
CHRISTOPHER KRATOVIL, MD  INSTITUTIONAL OFFICIAL

POLICY AMENDED:

- FEBRUARY 20, 2018
- INITIAL JANUARY 6, 2016
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for review and approval of research involving prisoners.

2.0 Policy
2.1. It is the policy of the Organization that federally funded research involving prisoners will be reviewed and approved in accordance with the requirements of 45 CFR 46 Subpart C.

2.2. It is the policy of the Organization that 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.

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, such subjects 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 a prisoner.*

4.0 Additional IRB Requirements
4.1. When reviewing research involving prisoners, the IRB will satisfy the following additional requirements:

4.1.1. The majority of the members of the IRB will not have an association with the prison involved in the study (excluding the prisoner members).
4.1.2. At least one member of the IRB will be a prisoner or a prisoner representative. The prisoner or prisoner representative must have a close working knowledge, understanding, and appreciation of prison conditions from the perspective of the prisoner.

4.2. A prisoner or prisoner representative must be involved in all IRB actions pertaining to protocols involving prisoners, including (but not limited to) a) initial review of the protocol, b) continuing review, c) protocol and/or consent changes, d) review of reports of unanticipated problems involving risks to subjects. When research involving prisoners is reviewed by the convened IRB the prisoner representative must be present as part of the quorum.

5.0 Permitted Research Involving Prisoners

5.1. 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:

5.1.1. 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.

5.1.2. 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.

5.1.3. 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).

5.1.4. Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subject.

5.2. If HHS-funded research fits either category C or D above 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.

5.3. For research which is not funded by HHS, neither certification to OHRP nor expert review for Categories C and D above is required. The IRB may however, at its discretion convene an equivalent expert review body to review studies classified under those categories.

5.4. Waiver of Requirements for Epidemiological Studies

5.4.1. Epidemiologic studies involving prisoners as subjects need not meet the requirements of section 5.1, 5.2 and 5.3 of this policy provided:

5.4.1.1. 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.

5.4.1.2. The research presents no more than minimal risk and no more than inconvenience to the prisoner-subjects, and

5.4.1.3. 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.

6.0 Procedures for IRB Review of Research Involving Prisoners

6.1. If a research protocol will involve prisoners (per section 3.1 of this policy), the IRB application must also include completion of Addendum C: Research Involving Prisoners as Subjects.

6.2. The UNMC IRB will normally not use expedited review for protocols, changes, or continuing review of research involving prisoners.

6.3. The UNMC IRB does not allow exemption from IRB review of research involving prisoners.

6.4. The UNMC IRB does not allow monetary compensation of prisoners who serve as research participants.

7.0 IRB Findings

7.1. The IRB will make the following additional findings for research involving prisoners (per 45 CFR 46.305(a)):

7.1.1. The research represents one of the categories permissible under Section 5.0 of this policy.

7.1.2. 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.

7.1.3. The risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers.

7.1.4. 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.

7.1.5. The information is presented in language which is understandable to the subject population.

7.1.6. 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.

7.1.7. 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.

7.2. The IRB may grant a waiver or alteration of informed consent in accordance with HRPP policies 5.2 (Waiver or Alteration of Informed Consent and HIPAA Authorization).
7.3. The IRB may grant a waiver of signed consent in accordance with **HRPP policy 5.5 (Waiver of the Requirement to Obtain Signed Consent Form)**.

8.0 Documentation of Compliance with Subpart C

8.1. For research reviewed by the convened IRB, compliance with Subpart C (or with the equivalent protections described in this policy) will be documented in the letter to the investigator which is part of the meeting minutes.

8.2. If the IRB approves research involving prisoners funded by HHS that has been, the IRB will provide written certification to OHRP that it fulfilled the responsibilities described in this policy and in 45 CFR 46 subpart C. Specifically the certifications will include:

- **8.2.1.** The name and address of the institution.
- **8.2.2.** Identification of the research protocol and relevant HHS grant application or protocol.
- **8.2.3.** A copy of all paperwork necessary for IRB initial review (including detailed protocol, relevant HHS grant application or proposal, IRB application, ICF).
- **8.2.4.** Verification of the presence of a prisoner representative during consideration of the study.
- **8.2.5.** Verification of the required findings per section 7.1 of this policy, and 45 CFR 46.305(a).
- **8.2.6.** Determination that the research falls into one of the permitted categories of research per section 5.1 of this policy, and 45 CFR 46.306(a).

8.3. For epidemiologic studies described in section 5.4 above funded by HHS, the IRB will provide written certification to OHRP as above, except that it will only verify that the requirements of 45 CFR 46.305(a)(2) through (7) were met.

9.0 Special Circumstances

9.1. **When a previously enrolled subject becomes a prisoner**

- **9.1.1.** 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. All research activities and interventions for the now incarcerated prisoner-subject must stop until the protocol is reviewed under the requirements of this policy.

  - **9.1.1.1.** If the investigator believes that it would be in the best interests of the subject to continue research activities while incarcerated, a request may be made to the IRB. 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.

  - **9.1.1.2.** The IRB will be notified of the exception at the next convened meeting.

- **9.1.2.** 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.

9.2. **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 this policy and HRPP policy 4.4 (Research Involving Children).

9.3. 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)

9.4. 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 must determine that there are appropriate additional protections in accordance with 45 CFR 46.111(b).

**Administrative Approval:**

BRUCE G. GORDON, MD  IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS

CHRISTOPHER KRATOCHVIL, MD  INSTITUTIONAL OFFICIAL

**Policy Amended:**

- DECEMBER 10, 2019
- FEBRUARY 19, 2018
- INITIAL APRIL 14, 2016
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. It is the policy of the Organization that 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. It is the policy of the Organization that 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.

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.

   3.1.1. 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.”

   3.1.2. 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.

   3.1.3. 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 in consultation with the investigator, 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 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 and magnitude of harm or discomfort associated with the research are not greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests." For the purpose of this policy "daily life" refers to the daily life of an average healthy child, not the daily life of the subject.

*Note: 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. Specifically "The increase in the probability and magnitude of harm is only slightly more than minimal risk. Any potential harms associated with the procedure will be transient and reversible in consideration of the nature of the harm (restricted to time of procedure or short post-experimental period). There is no or an extremely small probability that participants will experience as severe the potential pain, discomfort, stress, or harm associated with the procedure." (SACHRP 2005).

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 categories and meet the specified criteria:

4.1. **Research not involving greater than minimal risk** (45 CFR 46.404; 21 CFR 50.51)

   4.1.1. The IRB will determine and document (including protocol-specific information justifying each IRB finding) that the research presents no greater than minimal risk to children.

   4.1.2. 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)

   4.2.1. 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.

   4.2.2. The IRB finds that:

      4.2.2.1. The risk is justified by the anticipated benefit to the subjects.
4.2.2.2. The relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches.

4.2.2.3. 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)

4.3.1. 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.

4.3.2. The IRB finds that:

4.3.2.1. The risk represents a minor increase over minimal risk.

4.3.2.2. 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.

4.3.2.3. 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.

4.3.2.4. 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)

4.4.1. 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.

4.4.2. In order to determine that the research should be submitted for review at the Federal level, the IRB must find and document the following:

4.4.2.1. The research does not qualify under 45 CFR 46.404, 405, 406; 21 CFR 50.51, 52, 53.

4.4.2.2. The research presents a reasonable opportunity to further the understanding, prevention or alleviation of a serious problem affecting the health or welfare of children.

4.4.2.3. The research meets applicable requirements of 45 CFR 46; 46.408; 46.409; 21 CFR 50, 56, (as applicable).

4.4.2.4. Research will be conducted in accordance with sound ethical principles.

4.4.2.5. Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians.

4.4.3. If the research is not HHS-funded or subject to FDA regulations, the ORA will, at the IRB’s discretion, convene an equivalent Local 407 Panel, as per HRPP policy 4.5 (Local 407 Panel Review of Pediatric Research).
4.5. Research Involving Wards

4.5.1. 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.

4.5.1.1. 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.

4.5.1.2. 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:

4.5.1.2.1. 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.

4.5.1.2.2. 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:

4.5.1.2.2.1. 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.

4.5.1.2.2.2. 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.

4.5.1.2.2.3. 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.

4.5.1.2.2.4. The advocate must promptly notify the investigator and the IRB of any concerns about the child’s participation in research.

4.5.2. Children who are wards of the state or any other agency, institution, or entity, can be included in research only if the investigator demonstrates sufficient scientific justification for including this vulnerable population.

4.5.3. In the State of Nebraska, children who are wards of the state can be included in research only if the ward would receive direct treatment or therapy that might benefit him/her and Nebraska DHHS allows an exception to policy (390 NAC 11-002.04K).

4.5.4. If a child becomes a ward while participating in the research, the IRB must be promptly notified and Request for Change submitted justifying the inclusion of Wards.
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 one of the following:

5.1.1. The IRB determines that a research satisfies the criteria for a waiver of parental permission under 45 CFR 45.408(c); that is, the 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), and provided further that the waiver is not inconsistent with federal, state, or local law.

5.1.1.1. If the IRB waives parental permission under 45 CFR 46.408(c) there must be an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted. 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.

5.1.2. The IRB determines that the research satisfies the criteria for a waiver of parental permission under the provisions of 45 CFR 46.116(d) (or rev 45 CFR 46.116(f)).

Note: Waiver of parental consent is not applicable for FDA regulated research.

5.2. 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.

5.2.1. 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

5.2.2. 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.

5.2.3. 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.

5.2.4. 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.

5.3. Permission by parents/guardian must be documented in accordance with and to the extent required by 45 CFR 46.117 and 21 CFR 56.109

5.4. Documentation of permission by parents/guardians may be waived if the IRB determines the conditions of 45 CFR 46.117(c); 21 CFR 56.109(c) are satisfied.

5.5. 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, in consideration of their cognitive ability and maturity, 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 provides justification for a waiver, and the IRB finds that:

6.3.1. 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

6.3.2. 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

6.3.3. The research meets the requirements for a waiver of assent under 45 CFR 46.116(f); 21 CFR 50.55(d).

6.4. Unless assent has been waived as above, children who do not provide assent, or who actively dissent may not be enrolled in the research.

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:

7.1.1. 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.

7.1.2. 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.

7.1.3. 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:

7.2.1. 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.

7.2.2. 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.

7.2.3. 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.

8.4. If, upon reaching the age of majority, the now adult subject refuses consent to continue participation in the study, no additional research interventions may be performed, and no additional data may be collected. Existing data collected under the parent/guardian consent process may still be used.

9.0 Assent of Subjects Reaching the Age of 13 Years (Age of Assent)

9.1. Children who reach the age of assent while actively participating in an IRB-approved study must give their assent to continue participation in the research at the first visit after reaching that age if they are capable of providing assent. Assent will be obtained in the manner described in IRB application. Subjects must then sign an IRB-approved parental informed consent document (though it does not have to be the same consent form his/her parent signed).

9.2. If the study only involves data analysis (that is, all research interventions have been completed) children who reach the age of assent do not need to provide assent.

9.3. If, upon reaching the age of assent the subject is not capable of providing assent the parental/legal guardian consent remains in effect. This must be documented in the study records or patient medical record.

9.4. If, upon reaching the age of assent, the subject refuses to provide assent to continue participation in the study, no additional research interventions may be performed, and no additional data may be collected, unless the conditions of section 6.3 are met. Existing data collected under the parent/guardian consent process may still be used.

10.0 Procedures for IRB Review

10.1. IRB Assignment:

10.1.1. The IRB-04 will review research that only involves children conducted within the Organization in accordance with the authority granted in HRPP policy 1.2 (Authority Granted to the IRB by the Organization).

10.1.2. 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 CHMC. The IRB Executive Chair/designee, or the full IRB, may request appropriate consultation to assist in review of protocols involving adults.
10.1.3. In general, where the majority of subjects are adults but also include children, the research will be reviewed by IRB-01 or IRB-02.

10.2. **IRB Review Process:**

10.2.1. Applications which require review by the full IRB will be processed and reviewed in accordance with HRPP policy 2.2 (Full IRB Review).

10.2.2. Applications that are eligible for review by the expedited method will be processed and reviewed in accordance with HRPP policy 2.3 (Expedited Review).

10.2.3. 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.

11.0 **Documentation of Compliance with Subpart D**

11.1. For research reviewed by the convened IRB, compliance with Subpart D (or with the equivalent protections described in this policy) will be documented in the letter to the investigator which is part of the meeting minutes.

11.2. For research reviewed through the expedited mechanism, compliance with Subpart D (or with the equivalent protections described in this policy) will be documented in the letter to the investigator which is available for review by the IRB in RSS.

**Administrative Approval:**

BRUCE G. GORDON, MD IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS
CHRISTOPHER KRATOCHVIL, MD INSTITUTIONAL OFFICIAL

**Policy Amended:**

- **Revised February 19, 2018**
- **Initial January 6, 2018**
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 research involving minors which is neither funded by HHS nor regulated by FDA, and which presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children but does not meet the requirements of HHS regulations at 45 CFR 46.404, 46.405, or 46.406 may be reviewed by a local 407 panel.

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. See HRPP policy 4.4 (Research Involving Children), section 3.1 for additional details.

4.0 Eligibility for Local 407 Panel Review
4.1. The Executive Chair or the Chair IRB-04 (Joint Pediatric IRB) may convene a local 407 Panel if all of the following conditions are met:
   4.1.1. The research neither funded by HHS nor regulated by FDA; and
   4.1.2. The IRB determines, by two-thirds majority vote, that:
      4.1.2.1. 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
      4.1.2.2. The IRB does not believe the research meets the requirements of HHS regulations at 45 CFR 46.404, 46.405, or 46.406.

5.0 Local 407 Panel Membership
5.1. The local 407 Panel will include at least 5 voting members and 1 non-voting member:
   5.1.1. Two or more members in a discipline relevant to the research being reviewed. At least one must be unaffiliated with the institution.
   5.1.2. Two or more members with general pediatrics experience. If possible, these members will have been present at the IRB-04 meeting during which the protocol was previously reviewed.
   5.1.3. One non-scientist
5.1.4. The IRB Executive Chair or the Chair of IRB-04 will serve as the Chair of the local 407 panel, and will be non-voting

5.2. 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.

5.3. The role of the Local 407 Panel Chair will be to:
   5.3.1. Chair the meeting and focus relevant discussion.
   5.3.2. Provide relevant regulatory information and guidance to the 407 Panel to assist their analysis.
   5.3.3. Present a summary of the research.
   5.3.4. Present the analysis of the IRB with respect to classification under 45 CFR 46.404, 405, and 406.
   5.3.5. Answer questions from the panel relevant to the deliberations of the IRB.

6.0 407 Panel Review

6.1. Prior to the Local 407 Panel Review, the investigator will be informed the panel will be convened and will be given the opportunity to present written comments to the Panel in support of the criteria described in section 6.4B and 6.4C below (that is, 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 the research will be conducted in accordance with sound ethical principles).

6.2. The following materials will be distributed to the 407 Panel members, at least one week prior to the meeting:
   6.2.1. A copy of the IRB application, full protocol, ICF and information sheet, and all other relevant protocol related documents.
   6.2.2. Any relevant questions for consideration.
   6.2.3. Any additional written materials provided by the investigator

6.3. 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.

6.4. The Local 407 Panel will determine whether the research satisfies the following criteria:
   6.4.1. The research does not meet the requirements of 46.404, 405 or 406; and
   6.4.2. The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; and
   6.4.3. The research will be conducted in accordance with sound ethical principles

6.5. Recommendations from the Panel whether the research satisfies the criteria in section 6.4 above will be made based on a simple majority vote. The Panel may also comment, as a group or individually, on the specific criteria in section 6.4.

6.6. The recommendations of the Local 407 Panel, including individual comments and findings, will be transmitted to the full IRB.
7.0 Full IRB Review

7.1. At its subsequent convened meeting, the IRB will re-review the research, utilizing the findings of the Local 407 Panel in its deliberations, and make one of the following determinations:

7.1.1. The research, in fact, satisfies the regulatory criteria for approval under HHS regulations at 45 CFR 46.404, 405, or 406.

7.1.2. The research satisfies the criteria for approval under 45 CFR 46.407; specifically:

7.1.2.1. 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

7.1.2.2. The research will be conducted in accordance with sound ethical principles; and

7.1.2.3. Adequate provisions have been made for soliciting the assent of children and the permission of their parents or guardians, as set forth in 45 CFR 46.408.

7.1.3. The research is not approved.

7.2. A two-thirds majority vote will be required to approve the research under section 7.1.1 or 7.1.2 above. If a two-thirds majority vote is not obtained then the research is not approved.

7.3. The investigator will be informed, in writing, of the decision of the IRB promptly after the meeting of the convened IRB.

ADMINISTRATIVE APPROVAL:

BRUCE G. GORDON, MD  IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS
CHRISTOPHER KRATOVIL, MD  INSTITUTIONAL OFFICIAL

POLICY AMENDED:

- Revised February 19, 2018
- Initial January 28, 2016
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.

2.0 Policy
It is the policy of the Organization that research involving subjects who have impaired decision-making capacity must include appropriate additional protections in accordance with the ethical principles described in the Belmont Report, and the requirements of 45 CFR 46.111(b) and 21 CFR 56.111(a)(3), as applicable.

3.0 Definitions
3.1. Decisionally impaired person, in the context of human subject research, means an adult with diminished capacity for judgment and reasoning such that he/she is unable to make an informed, voluntary decision to participate in research. The impairment which leads to this diminished capacity may be a temporary acute condition, may fluctuate, or may be a more long-term or permanent condition. It may be the result of any psychiatric disorder, an organic impairment, a developmental disorder, or severe acute illnesses associated with cognitive impairment.

Note: Capacity, defined as an individual's ability to make an informed decision should not be confused with competence. Competence is a legal state, not a medical one. Competence refers to the degree of mental soundness necessary to make decisions about a specific issue or to carry out a specific act. All adults are presumed to be competent unless adjudicated otherwise by a court. Incompetence is defined by one's functional deficits, which are judged to be sufficiently great that the person cannot meet the demands of a specific decision-making situation, weighed in light of its potential consequences. Only a court can make a determination of incompetence.

3.2. Legally Authorized Representative (LAR) is defined as “an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedures involved in the research” (45 CFR 46.102(c)). “Legally authorized representative” in the context of research is, however, not defined in the Nebraska revised statutes.

OHRP Guidance (https://www.hhs.gov/ohrp/regulations-and-policy/guidance/faq/informed-consent/index.html) notes that “In these states [that have no law specifically addressing the issue of consent in the research context], law that addresses who is authorized to give consent on behalf of another person to specific medical procedures or generally to medical treatment may be relevant if the research involves those medical procedures or medical treatment. When the laws of the jurisdiction in which the research is being conducted provide a reasonable basis for authorizing an individual to consent on behalf of a prospective subject to their participation in the research procedure(s), OHRP would consider such an individual to be an LAR as defined by HHS regulations at 45 CFR 46.102(c).”

3.2.1. Under Nebraska law, the following persons may serve as a Legally Authorized Representative
3.2.1.1. Parents and guardians having legal custody of the decisionally impaired person.

3.2.1.2. The court-appointed legal guardian of the decisionally impaired person in accordance with Neb. Rev. Stat. 30-2627.

3.2.1.3. The individual authorized to consent on behalf of a decisionally impaired person pursuant to a legally effective Health Care Power of Attorney (POA-HC).

3.2.2. In addition, Institutionally Authorized Surrogate, as defined per Section 3.3 below, may serve as a LAR for the purpose of this policy.

3.2.3. Following the effective date of the Revised Rule, Legally Authorized Representative will be further defined to include “an individual recognized by institutional policy as acceptable for providing consent in the non-research context on behalf of the prospective subject to the subject’s participation in the procedure(s) involved in the research” (rev 45 CFR 46.102(i)).

3.3. **Institutionally Authorized Surrogate (IAS)** is defined in the priority order listed below in accordance with *Nebraska Medicine policy MS14*:

3.3.1. 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.

3.3.2. A spouse.

3.3.3. An adult child.

3.3.4. A parent, or the written nominee of a deceased parent.

3.3.5. Any relative the incapacitated person with whom he or she has resided for more than six months.

3.3.6. An adult sibling.

3.3.7. An adult person in the next degree of kindred in the order named by the succession laws in the state of Nebraska.

3.3.8. Significant others who have a current sustained relationship with the decisionally impaired person and can present the person’s preferences.

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 capacity, or by an independent assessor.

4.2. The method utilized to determine capacity may vary depending on the characteristics of the from research protocol (including the risks and the risk-benefit relationship) and of the subject population. In general, with increasing risks, less favorable risk-benefit relationship, expected higher proportion of cognitively impaired subjects, or expected greater depth of impairment, the assessment of capacity should utilize more formal tools. Standard tools include, in order of stringency and reliability:

4.2.1. Clinical interviews

4.2.2. Mini-Mental Status Exam (MMSE)
4.2.3. “Assessment of Capacity to Consent to Participate in Research” instrument available on the IRB website at http://unmc.edu/irb.

4.2.4. MacArthur Competency Assessment Tool for Clinical Research (MacCat-CR).

4.3. For research studies involving higher risks, less favorable risk-benefit relationship, expected higher proportion of cognitively impaired subjects, or expected greater depth of impairment, the investigator should consider the use of an independent, experienced assessor or a consent monitor who can observe the process of informed consent.

4.4. Researchers should reassess capacity for individuals who exhibit fluctuating capacity levels, or if the research involves a population where it would be reasonably expected that capacity would be regained for at least some of the subjects.

5.0 Appointment and Authority of the LAR

5.1. If an individual lacks the capacity to consent, they can only be enrolled in research if an LAR provides consent on their behalf.

5.2. If a prospective subject does not have an LAR as defined in Section 3.2.1, 3.2.2., or 3.2.3 above, an IAS should be appointed.

5.3. The prospective subject’s capacity to choose an IAS should be assessed and, when possible, the subject’s choice should be honored.

5.4. Availability, willingness and capacity to serve as a responsible surrogate decision-maker should be considered in the appointment of an IAS.

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.

6.0 Assent and Dissent

6.1. The investigator must make adequate provisions for soliciting the assent of the decisionally impaired persons, when in the judgment of the investigator and the IRB they are capable of providing assent.

6.2. If the investigator and the IRB determine that the capability of some or all of the potential subjects of the research is so limited that they cannot reasonably be consulted or 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 potential subjects and is available only in the context of the research, the assent of the decisionally impaired persons is not a necessary condition for proceeding with the research.

6.3. 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. The full IRB will be notified of the IRB Executive Chair’s decision, and the board has the authority to accept the IRB Executive Chair’s decision, require additional actions, or require withdrawal of the subject.
6.4. 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 will be notified of the IRB Executive Chair’s decision, and the board has the authority 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. Category 1 - Minimal risk
A decisionally impaired subject may participate in research involving minimal risk with no direct subject benefit if an LAR or IAS provides consent, and the decisionally impaired person provides assent (as described in 6.1 and 6.2 above).

7.2. Category 2 – Greater than minimal risk with the prospect of direct benefit
A decisionally impaired subject may participate in research involving greater than minimal risk and a prospect of direct benefit if:

7.2.1. The risk-benefit relationship is favorable, and
7.2.2. The risk-benefit relationship is at least as favorable as available alternative therapies, and
7.2.3. An LAR or IAS provides consent, and the decisionally impaired person provides assent (as described in 6.1 and 6.2 above).

7.3. Category 3 - Greater than minimal risk with no prospect of direct benefit
A decisionally impaired subject may participate in research involving greater than minimal risk without prospect of direct benefit only if:

7.3.1. The research represents only a minor increase over minimal risk, and
7.3.2. The intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual medical, dental, psychological, social, or educational situations; and
7.3.3. 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; and
7.3.4. An LAR provides consent, and the decisionally impaired person provides assent (as described in 6.1 and 6.2 above).

Note: An IAS is not authorized to provide consent for category 3 research

7.4. Cognitively impaired persons may not be enrolled into research which does not fall into one of the above 3 categories.

7.5. Cognitively impaired persons 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 (Additional Protections for Vulnerable Populations).

9.0 IRB Review

9.1. Applications which require review by the full IRB will be processed and reviewed in accordance with HRPP policy 2.2 (Full IRB Review). 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.

9.2. Applications that are eligible for review by the expedited method will be processed and reviewed in accordance with HRPP policy 2.3 (Expedited Review). 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.

9.3. The IRB will determine whether the research is allowable as per section 7.0 above, whether there are adequate additional protections for vulnerable populations, whether assent and dissent will be managed in accordance with section 6.0, whether capacity is being assessed adequately, and whether there are adequate plans for re-consent or withdrawal should a subject regain capacity.

10.0 Disclosure and Consent for Continuing Participation

10.1. If a person with diminished capacity regains capacity during the conduct of the research, he/she must be fully informed about the research and the circumstances of his/her enrollment. His/her consent to continue in the research protocol must be obtained in accordance with HRPP policy 5.1 (Obtaining Informed Consent from Research Subjects).

11.0 Disclosure After the Research has Been Completed

If a person with diminished capacity regains capacity following completion of the conduct of the research, he/she must be fully informed about the research and the circumstances of his/her enrollment.

12.0 Consent Forms/Adult Information Sheet

12.1. **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 ICF Template).

12.2. **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.
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 employees of the Organization, and/or students as subjects. These persons are considered vulnerable because of the potential for undue influence or coercion.

2.0 Policy

2.1. It is the policy of the Organization that students, and employees of the Organization, may be recruited for research participation. To the extent that these subjects are vulnerable, the research plan must include additional safeguards to protect the rights and welfare of these subjects.

2.2. It is the policy of the Organization that the recruitment of employees working directly for, or under the supervision of, the PI or other study personnel, is discouraged.

2.3. It is the policy of the Organization that the recruitment of students taking classes from the PI or other study personnel, is discouraged.

3.0 Students as Research Participants

3.1. Students (for example, undergraduates, graduate students, medical students, residents, fellows, doctoral students) may be recruited for research participation.

3.2. A student may not be required to participate in research without a comparable non-research alternative offered as a course requirement.

3.3. Students (individuals or groups) should not be selected solely on the basis of convenience when they would not otherwise be appropriate for inclusion.

3.4. Recruitment of students taking classes from the PI or other study personnel is strongly discouraged; when such recruitment is scientifically justified and important to the conduct of the research, there must be additional safeguards in place to reduce the risk of undue influence or coercion.

3.5. A student’s decision about research participation may not affect grades or other such assessments of opportunities for the student.

3.6. Attention must be paid by the investigator to the risks to the student’s privacy, since the classroom situation may make it difficult to keep an individual’s participation confidential.

3.7. Use of student education records for research must comply with the requirements of the Family Educational and Rights Privacy Act (FERPA) at 34 CFR 99 (https://www2.ed.gov/policy/gen/quir/fpco/ferpa/index.html)

3.8. Research involving surveys with students in elementary and secondary schools that receive funding from the Department of Education must also comply with the Protection of Pupil Rights Amendment (PPRA) at 34 CFR 98 (http://www2.ed.gov/policy/gen/quir/fpco/ppra/index.html).

3.9. UNO Students may participate in the SONA Research Participation System. All preceding requirements must be met. Any other student database or registry used for recruitment purposes...
must have procedures in place to exclude students that have enacted a FERPA hold on their registry information.

4.0 Research Involving Employees of the Organization as Research Participants

4.1. Employees (full-time, part time or student) of the Organization may be recruited for research participation.

4.2. An employee may not be required to participate in research as a condition of employment.

4.3. Employees should not be selected solely on the basis of convenience when they would not otherwise be appropriate for inclusion.

4.4. Recruitment of employees under the supervision of the PI or other study personnel is strongly discouraged; when such recruitment is scientifically justified and important to the conduct of the research, there must be additional safeguards in place to reduce the risk of undue influence or coercion.

4.5. An employee’s decision about research participation may not affect performance evaluations or other such assessments or opportunities for the employee.

4.6. Attention must be paid by the investigator to the risks to the employee’s privacy, since the workplace situation may make it difficult to keep an individual’s participation confidential.

5.0 IRB Review

5.1. Research involving employees of the Organization, or students may be reviewed by the full convened IRB (as per HRPP policy 2.2) or using an expedited procedure (as per HRPP policy 2.3). The IRB application must clearly address:

   5.1.1. Justification of the need to recruit the particular subject population

   5.1.2. A description of any additional safeguards have been included in the study to protect the rights and welfare of these subjects.

5.2. If an investigator proposes to recruit employees working for, or under the supervision of, the PI or other study personnel; or students taking classes from the PI or other study personnel, the IRB application must clearly address:

   5.2.1. The nature of the professional relationship.

   5.2.2. Justification of the need to recruit the particular subject population. This justification must be particularly strong for any study which involves greater than minimal risk procedures.

   5.2.3. The plan for minimizing the risk of undue influence and/or coercion is the process of recruitment and consent.

   5.2.4. A description of any additional safeguards have been included in the study to protect the rights and welfare of these subjects.

Administrative Approval:

BRUCE G. GORDON, MD  IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS
CHRISTOPHER KRATOCHVIL, MD INSTITUTIONAL OFFICIAL

Policy Amended:
- Revised January 29, 2018
- Initial January 7, 2016
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, their Legally Authorized Representatives (LARs), or a minor subject’s parents or legal guardians 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.

2.3. For this policy reference to “subject” also refers to a subject’s LAR, or a minor subject’s parent or legal guardian, as appropriate.

3.0 General Requirements
3.1. No human being may be enrolled as a subject in research unless the PI or authorized designee (see section 3.3 below) has prospectively obtained the legally effective 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 (Waiver or Alteration of Informed Consent and HIPAA Authorization).

3.2. The PI, in accordance with HRPP policy 1.26 (PI Qualifications and Responsibilities), is ultimately responsible for the obtainment, and documentation of valid informed consent from the subject (or LAR) prior to participation in the research, unless these requirements have been waived by the IRB.

3.3. The PI may authorize other study personnel (secondary investigator, participating personnel or research coordinator) to participate in the process of consent, providing those persons have adequate knowledge of the research protocol, of UNMC HRPP policies, and of their responsibility to protect the rights and welfare of subjects.

3.4. Except as provided in HRPP policy 5.4 (Waiver of the Requirement to Obtained Signed Consent Form), 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.

3.5. The information contained in the ICF and conveyed to the subject during the process of consent shall be in language understandable to the subject. 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.
3.6. The subject (or LAR) must be provided with the information that a reasonable person would want to have in order to make an informed decision about whether to participate, and must be provided with an opportunity to discuss that information.

3.7. Informed consent must begin with a concise and focused presentation (summary) of the key information that is most likely to assist a prospective subject (or LAR) in understanding the reasons why one might or might not want to participate in the research. This part of the informed consent must be organized and presented in a way that facilitates comprehension.

3.7.1. The summary must include at least the following information:

3.7.1.1. A statement that consent is being sought for research, and participation is voluntary.

3.7.1.2. The purpose and expected duration of the subject’s participation, and a description of the procedures to be followed.

3.7.1.3. The reasonably foreseeable risks and discomforts to the subject. This section should only include the most important reasonably foreseeable risks.

3.7.1.4. The benefits to the prospective subject or to others that may reasonably be expected.

3.7.1.5. Appropriate alternative procedures or courses of treatment, if any, which might be advantageous to the prospective subject.

3.7.2. The summary should not exceed two pages in length.

3.7.3. Information included in the summary need not be repeated later in the body of the informed consent form.

3.8. Informed consent as a whole must present information in sufficient detail relating to the research, and must be organized and presented in a way that does not merely provide lists of isolated facts, but rather facilitates the prospective subject’s (or LAR’s) understanding of the reasons why one might or might not want to participate.

3.9. 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.

3.10. The consent process minimizes the potential for coercion and undue influence.

3.11. The obtainment 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 (Research Involving Pregnant Women, Human Fetuses, and Neonates-Nonviable or of Uncertain Viability).

3.12. The obtainment of consent for the participation of prisoners in research must be conducted in accordance with this policy and HRPP policy 4.3 (Research Involving Prisoners).

3.13. 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 (Research Involving Children).

3.14. The obtainment of assent for the participation of minors in research must be conducted in accordance with HRPP policy 4.4 (Research Involving Children).
3.15. 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 (Research Involving Subjects with Impaired Decision-Making Capacity).

4.0 Elements of Informed Consent

4.1 Basic Elements of Informed Consent

4.1.1. The consent process and form must provide the following information, in accordance with Federal Regulations at 45 CFR 46.116 and 21 CFR 50.25, other laws and regulations, and/or HRPP policy. 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).

4.1.1.1. 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.

4.1.1.2. A description of any benefits to the subject or to others which may reasonably be expected from the research.

4.1.1.3. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.

4.1.1.4. A statement describing the extent, if any, to which confidentiality of records identifying the subject must be maintained.

4.1.1.5. 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.

4.1.1.6. For any research that involves the collection of identifiable private information or identifiable biospecimens:

4.1.1.6.1. A statement that identifiers might be removed from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the subject (or LAR) authorized representative, if this might be a possibility; OR

4.1.1.6.2. A statement that the subject's information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research.

4.1.1.7. 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.

4.1.1.8. Provision of contact information for the IRB and Research Subject Advocate (as applicable) in the event the subject wishes to talk to someone other than the research staff or to obtain assistance in the event the research staff cannot be reached. The subject may wish to obtain answers to questions about the research or their rights as a research subject, or for resolution of problems, concerns, complaints or offer input about the research.

4.1.1.9. 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.

4.1.1.10. A statement which indicates that the IRB, institutional officials designated by the IRB, OHRP, and, as appropriate, FDA, NIH, sponsors/CROs, other institutions and investigators, third party payers, the FPBCC SRC, or others will, as necessary, have access to research records containing PHI.

4.1.1.11. A statement that FDA-regulated clinical trials and federally funded interventional and observational trials must be listed on http://ClinicalTrials.gov.

4.2. Additional Elements of Informed Consent [45 CFR 46.116(b), 21 CFR 50.25(b)]

When appropriate, the consent process and form must provide some or all of the following information, in accordance with Federal Regulations at 45 CFR 46.116 and 21 CFR 50.25, other laws and regulations, and/or HRPP policy. 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).

4.2.1. A statement that the particular treatment or procedure may involve risks to the subject, which are currently unforeseeable (for example, when the research involves investigational test articles or other procedures in which the risks to the subject are not well known).

4.2.2. 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 (for example, 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.

4.2.3. Anticipated circumstances under which the subject’s participation may be terminated by the investigator without regard to the subject’s/LAR’s consent (for example, when there are medical circumstances or compliance requirements that would necessitate involuntary withdrawal of the subject from the research).

4.2.4. Any additional costs to the subject/LAR that may result from participation in the research.

4.2.5. The consequence(s) of a subject/LAR decision to withdraw from the research (for example, when withdrawal from the research is associated with adverse medical consequences, such as an interruption of treatment).

4.2.6. Procedures for orderly termination of the subject’s research participation (for example, voluntary notification of the PI, follow up and treatment substitution).

4.2.7. 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.

4.2.8. 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 and/or the LAR.

4.2.9. The approximate number of subjects involved in the study. It may be appropriate to inform subjects when there is a small number of participants or a large number of subjects.
4.2.10. A statement that the subject’s biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit.

4.2.11. A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions.

4.2.12. For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing.

4.2.13. The amount and schedule for compensation of subjects.

4.2.14. When a subject withdraws from the interventional portion of the study, ask if the subject wishes to continue into the follow-up portion of the study where there are no direct study interventions. This portion of the study involves collection of associated clinical outcome information, such as medical course or laboratory results obtained through non-invasive chart review, and address the maintenance of privacy and confidentiality of the participant’s information.

4.2.14.1. If this is not in the original consent form, the subject must provide additional written consent for this limited participation in the study.

4.2.14.2. If a participant withdraws from the interventional portion of a study and does not consent to continued follow-up collection of associated clinical outcome information, the researcher must not access for purposes related to the study the participant’s medical record or other confidential records requiring the participant’s consent. However, a researcher may review study data related to the participant collected prior to the participant’s withdrawal from the study, and may consult public records, such as those establishing survival status.

4.2.15. For research subject to ICH GCP, a description of the additional elements for informed consent are found in HRPP policy 1.13; Section 4.2.5 (Compliance with ICH Guidelines).

4.2.16. For Department of Defense research, a description of the additional elements for informed consent are found in HRPP policy 1.14; Section 4.11.10 (Research Subject to Department of Defense Regulatory Requirements).

4.2.17. For Department of Justice research, a description of the additional elements for informed consent are found in HRPP policy 1.15; Sections 4.1.3 and 4.2.9 (Research Subject to Department of Justice Regulatory Requirements).

5.0 ICF Templates

All investigators are required to utilize one or more of the following ICF templates as applicable:

5.1. Adult biomedical research ICF template

5.2. Adult social and behavioral research ICF template

5.3. Adult tissue banking ICF template

5.4. Adult registry ICF template

5.5. Parental biomedical research ICF template

5.6. Parental social and behavioral research ICF template

5.7. Parental tissue banking ICF template
6.0 Study Information Sheet Templates
All investigators are required to utilize one or more of the following information sheet templates as applicable:

6.1. Youth information sheet
6.2. Child information sheet
6.3. Adult information sheet (for the decisionally impaired)

7.0 Other Consent Templates
All investigators are required to utilize one or more of the following other consent templates as applicable:

7.1. Cover letter consent template
7.2. Narrative ICF template
7.3. National Cancer Institute Central IRB or other Central IRB ICF templates

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, as described in HRPP policy 4.6 (Research Involving Subjects with Impaired Decision-Making Capacity).

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 whether or not to participate in the study.

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/designee and the prospective subject (or LAR) should occur by face-to-face contact. However, depending upon the nature and risks of the study or other factors, the IRB may permit an alternate method of communication and consent, such as, telephone, video conference (for example, Skype), other form of electronic communication, mail or fax.
8.5. The PI/designee must fully explain all elements of informed consent (as described in sections 4.1 and 4.2 above) to the prospective subject (or LAR).

8.6. The PI/designee 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 that 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 consent, reading the consent to the subject, and use of teaching aids.

8.8. The PI/designee 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/designee must provide the prospective subject (or LAR) with 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 and to 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 others. 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/designee 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 after signing. If the IRB has approved a waiver of signed informed consent, each subject (or LAR) must be offered a copy of the unsigned ICF.
8.14. The IRB is authorized to randomly audit any on-going process of informed consent, as per HRPP policies 1.21 (Post-Approval Monitoring of Research) and 8.4 (Review of Noncompliance Involving the PI and Study Personnel).

9.0 Documentation of Informed Consent

9.1. Unless a waiver of the requirement to obtain signed consent in accordance with HRPP policy 5.4 (Waiver of the Requirement to Obtain Signed Consent Form), informed consent must be documented by the use of a written or electronic ICF approved by the IRB.

9.2. Study personnel who are permitted to document informed consent must be:

   9.2.1. Authorized by the PI.
   9.2.2. Listed by name in the documentation of consent section of the IRB Application and consent form.
   9.2.3. Approved by the IRB.

9.3. Individuals authorized to document consent must have the:

   9.3.1. Sufficient knowledge of the protocol.
   9.3.2. Sufficient knowledge of UNMC HRPP policies and of their responsibility to protect the rights and welfare of subjects.
   9.3.3. Required licensure to perform the procedures described in the protocol, as applicable.
   9.3.4. Authorization per hospital policy to perform the procedures in a non-research context, as applicable.

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. Provided the IRB has not approved an alternate method of communication and consent (per section 8.4 above) the subject (or LAR), PI (or other person authorized to document consent), and the witness (if required per section 9.6 below) must sign and date the ICF in the physical presence of each other. The PI (or other person authorized to document consent) must be present at this time to certify that the subject (or LAR) provided valid informed consent.

9.6. The signature of a witness is required for all research studies involving populations where the IRB has determined that a witness provides additional protection. The witness should be someone who is not listed on the IRB Application and ICF as study personnel.

9.7. For clinical studies involving significant risk, only licensed physicians or dentists are authorized to obtain and document consent.

9.8. For studies involving an FDA unapproved drug or biologic, or an FDA unapproved significant risk device, only licensed physicians or dentists are authorized to obtain and document consent.

10.0 Documentation in the Research and Medical Records

10.1. The research record must contain the original signed ICF.
10.2. For any protocol where a research procedure or intervention 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), except as below:

10.2.1. Consent forms for research which includes genetic testing will not be placed in the subject’s medical record if the IRB determines that (1) the subject’s health insurance status or employability may be jeopardized, and (2) the subject’s medical safety will not be compromised by excluding the ICF from the medical record.

10.2.2. Consent forms for research where breach of confidentiality constitutes a significant risk will not be placed in the subject’s medical record.

10.3. For all studies greater than minimal risk, the process of consent must be documented in the medical or individual study subject record, if applicable, or in a separate consent log. This documentation should include the names of the individuals involved in the process of consent, and the period of time over which the process of consent was conducted.

11.0 Special Consent Circumstances

11.1. Non-English Speaking Subjects

11.1.1. Expected Enrollment of Non-English Speaking Subjects

11.1.1.1. For research where it is reasonable to expect that a significant number of non-English speaking persons will participate, the IRB may require that a translated CF be prepared and used.

11.1.1.2. Consent forms must be prepared by a certified translator, or must be back-translated by a certified translator.

11.1.1.3. Consent Forms prepared by a commercial sponsor, or by an NIH or equivalent funded cooperative group may be used without back-translation.

11.1.1.4. 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:

11.1.1.4.1. 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.

11.1.1.4.2. A commercial interpretation/translation service (such as CyraCom).

11.1.1.5. If a prospective subject/LAR/parent wishes to designate their own interpreter, then:

11.1.1.5.1. This must be documented in the medical/research record.

11.1.1.5.2. The Official Interpreter that qualifies under 11.1.1.1 and 11.1.1.2 above must be present to ensure the quality and accuracy of the interpretation and this must also be documented.

11.1.1.5.3. A minor cannot be used as an interpreter.

11.1.1.6. Procedures for Using an Interpreter

11.1.1.6.1. Interpreters should be provided with a copy of the IRB-approved ICF. Whenever possible, the ICF(s) should be provided in advance of initiating the consent process with the subject/LAR.
11.1.1.6.2. Upon conclusion of the consent process the subject/LAR and the interpreter must sign and date the non-English version of the ICF.

11.1.1.6.3. The person obtaining consent must sign and date the English version of the ICF.

11.1.1.6.4. A copy of the signed and dated non-English and English version of the ICFs must be given to the subject/LAR.

11.1.1.6.5. The process of consent must be fully documented and maintained on file which includes the following:

   11.1.1.6.5.1. The time over which the process of consent was conducted.
   11.1.1.6.5.2. The name and contact information of the interpreter.

11.1.2. 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:

11.1.2.1. 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.

11.1.2.2. 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 5.5 (Use of the Short Form Consent Document) are satisfied.

11.2. Braille consent

For research where it is reasonable to expect that a significant number of blind or low vision subjects who read Braille will participate, 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 oral consent will be obtained, witnessed and documented in accordance with Section 11.4 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

11.4.1. When a subject (or LAR) is unable to read an ICF (such as blind or illiterate subjects), the IRB chair may approve an oral consent process.
11.4.2. 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.

11.4.3. 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.

11.4.4. 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.

11.4.4.1. By signing the consent document, the witness attests that the information in the consent document and any other written information was accurately explained to, and apparently understood by, the participant or the participant’s legally acceptable representative, and that consent was freely given by the participant or the participant’s legally acceptable representative.

11.4.5. 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).

11.4.6. For research that is no more than minimal risk, documentation of consent may be waived if it satisfies the additional requirements as described in HRPP policy 5.4 (Waiver of the Requirement to Obtain Signed Consent Form).

11.4.7. 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 2.4: IRB Review of Changes in Previously Approved Research).

12.0 Requirements for Re-Consent of Subjects

12.1. A formal re-consent procedure is not required for minor changes in protocol or the ICF. Examples of “minor changes are provided in HRPP policy 2.4 (IRB Review of Changes in Previously Approved Research). In general, minor changes are those that do not alter the risk-benefit relationship and that a reasonable person would not consider justification for withdrawing from the research. This new information may be presented, as necessary, through a verbal exchange between the subject/LAR and PI/designee), for example at the time of the next planned interaction with the subject.

12.2. Changes in the protocol or in the ICF that are more significant than those described in section 12.1, or new information relevant to the subject, 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. Depending on the nature of the new information or changes, re-consent may occur at the time of the next planned interaction with the subject.

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 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 regularly 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).

12.7. 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.

13.0 Telephone Consent
Refer to HRPP policy 5.3 (Use of a Telephone Consent Process).

14.0 Short Form
Refer to HRPP policy 5.5 (Use of the Short Form Consent Document).

15.0 Waiver or Alteration of Informed Consent
Refer to HRPP policy 5.2 (Waiver or Alteration of Informed Consent and HIPAA Authorization).

16.0 Waiver of the Requirement to Obtain a Signed ICF
Refer to HRPP policy 5.4 (Waiver of the Requirement to Obtain Signed Consent Form).
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 with or without waiver of HIPAA authorization requirements in research.

2.0 Policy
2.1. It is the policy of the Organization that the IRB serves as the Privacy Board for human subject research, and that HIPAA requirements are applied to all research involving protected health information (PHI).

2.2. It is the policy of the Organization that a waiver or alteration of the requirement for informed consent and for authorization under the HIPAA Privacy Rule may be approved, provided that the IRB finds and documents the criteria specified in 45 CFR 46.116(d) (or rev CFR 46.116(f)), and 45 CFR 164.512(I)(2)(ii) [HIPAA] have been satisfied.

2.3. It is the policy of the Organization that a waiver of the requirement for informed consent from parents of minor subjects (parental permission) may be approved provided that the IRB finds and documents the criteria specified in 45 CFR 46.408(c) or 21 CFR 50.55 have been satisfied.

2.4. It is the policy of the Organization that waiver or alteration of the requirement for informed consent for FDA regulated minimal risk research may be approved provided the IRB finds and documents the criteria described in “FDA Guidance: IRB Waiver or Alteration of Informed Consent for Clinical Investigations Involving No More Than Minimal Risk to Human Subjects; July 2017”.

2.5. It is the policy of the Organization that the IRB will acknowledge an exception to FDA’s general requirements for informed consent for emergency use of a test article in accordance with 21 CFR 50.23(a), and HRPP policy 6.4 (Emergency Use of a Test Article).

2.6. It is the policy of the Organization that an exception from informed consent requirements for emergency research involving an FDA regulated test article must be in full compliance with the requirements of 21 CFR 50.24, and HRPP policy 5.6 (Exception from Informed Consent Requirements for Emergency Research).

2.7. It is the policy of the Organization that complete waiver of informed consent is not allowed for research involving subjects who are prisoners. The Organization will allow the alteration of informed consent provided the criteria at 45 CFR 46.116(d) (or rev 45 CFR 46.116(f)) and 45 CFR 512(l)(2)(ii) are met, and prisoners are 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)].

3.0 Criteria for Waiver or Alteration of Consent under HHS regulations and HIPAA regulations
3.1. Prior to the effective date of the Revised Rule 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).

3.1.1. The research involves no more than minimal risk to the subjects (45 CFR 46.116(d)(1)).
3.1.1.1. Within this criterion the IRB must find that the use or disclosure of protected health information involves no more than a minimal risk to the privacy of individuals, based on, at least, the presence of the following elements: (1) An adequate plan to protect the identifiers from improper use and disclosure; (2) An adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law; and (3) Adequate written assurances that the protected health information will not be reused or disclosed to any other person or entity (45 CFR 512(l)(2)(ii)(A)).

Note: Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests (45 CFR 46.102(i)). The Organization interprets “daily life” to be the “daily life of the average person in the general population” as opposed to the daily life of the subject.

3.1.2. The waiver or alteration will not adversely affect the rights and welfare of the subjects (45 CFR 46.116(d)(2)).

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.

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.

3.1.3. The research could not practicably be carried out without the waiver or alteration (45 CFR 46.116(d)(3); (45 CFR 512(l)(2)(ii)(B)).

Note: In some research projects it would not be practicable to perform the research if informed consent was required. For example:

(1) The sample size required is so large (for example, with 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.
(3) 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.

(4) There is a risk of inflicting psychological, social, or other harm by contacting individuals or families with particular conditions.

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.

3.1.4. Whenever appropriate, the subjects or legally authorized representatives will be provided with additional pertinent information after participation (45 CFR 46.116(d)(4)).

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 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.

3.1.5. For research involving PHI, the research could not practicably be conducted without access to and use of the protected health information (45 CFR 164.512(l)(2)(ii)(C)).

3.2. Following the effective date of the Revised Rule, 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 rev 46.116(f) and HIPAA regulations at 45 CFR 164.514(l)(2)(ii):

3.2.1. The research involves no more than minimal risk to the subjects (rev 45 CFR 46.116(f)(3)(i)).

3.2.1.1. Within this criterion the IRB must find that the use or disclosure of protected health information involves no more than a minimal risk to the privacy of individuals, based on, at least, the presence of the following elements: (1) An adequate plan to protect the identifiers from improper use and disclosure; (2) An adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law; and (3) Adequate written assurances that the protected health information will not be reused or disclosed to any other person or entity (45 CFR 164.512(l)(2)(ii)(A))

Note: Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests (rev 45 CFR 46.102(j)). The Organization interprets “daily life” to be the “daily life of the average person in the general population” as opposed to the daily life of the subject.

3.2.2. The research could not practicably be carried out without the requested waiver or alteration (rev 45 CFR 46.116(f)(3)(iii); (45 CFR 164.512(l)(2)(ii)(B)).

Note: In some research projects it would not be practicable to perform the research if informed consent was required. For example:

(1) The sample size required is so large (for example, with 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.

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.

3.2.3. If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format (rev 45 CFR 46.116(f)(3)(iii)).

3.2.3.1. Within this criterion the IRB must find that the research could not practicably be conducted without access to and use of the protected health information (45 CFR 164.512(l)(2)(ii)(C)).

3.2.4. The waiver or alteration will not adversely affect the rights and welfare of the subjects (rev 45 CFR 46.116(f)(3)(iv)).

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.

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.

3.2.5. Whenever appropriate, the subjects or legally authorized representatives will be provided with additional pertinent information after participation (45 CFR 46.116(f)(3)(v)).

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.

4.0 Criteria for Waiver of Parental/Guardian Consent (Permission) 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 consent (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.

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.

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 Criteria for Waiver or Alteration of Consent in research involving public benefit and service programs conducted by or subject to the approval of state or local officials

5.1. 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) (or rev 45 CFR 46.116(e)): 
5.1.1. 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:

5.1.1.1. Public benefit of service programs
5.1.1.2. Procedures for obtaining benefits or services under those programs
5.1.1.3. Possible changes in or alternatives to those programs or procedures
5.1.1.4. Possible changes in methods or levels of payment for benefits or services under those programs.

5.1.2. The research could not practicably be carried out without the waiver or alteration.

5.1.3. The research is not regulated by the FDA.

6.0 Criteria for Waiver or Alteration of Consent for FDA Regulated Minimal Risk Research

6.1. The following are the IRB requirements that must be met in order to approve a waiver or alteration of informed consent for FDA regulated minimal risk research:

6.1.1. The clinical investigation involves no more than minimal risk (as defined in 21 CFR 50.3(k) or 56.102(i)) to the subjects.

6.1.2. The waiver or alteration will not adversely affect the rights and welfare of the subjects.

6.1.3. The clinical investigation could not practicably be carried out without the waiver or alteration.

6.1.4. Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

Note: As per FDA Guidance: “IRB Waiver or Alteration of Informed Consent for Clinical Investigations Involving No More Than Minimal Risk to Human Subjects (July 2017)”, FDA intends to revise its informed consent regulations to add this waiver or alteration under appropriate human subject protection safeguards to the two existing exceptions from informed consent. However, until FDA promulgates these regulations, they do not intend to object to an IRB approving a consent procedure that does not include, or that alters, some or all of the elements of informed consent set forth in 21 CFR 50.25, or waiving the requirements to obtain informed consent when the IRB makes the findings described above.

7.0 Process of Review

7.1. For research which does not involve PHI, the IRB will review the proposed waiver or alteration of informed consent in accordance with HRPP policy 2.2 (Full Board Review) or HRPP policy 2.3 (Expedited Review).

7.2. If the research involves PHI it may only be reviewed by the convened IRB, unless the research represents no more than minimal risk to the privacy of the individuals who are the subject of the PHI, in which case it may qualify for expedited review.

7.3. 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.
7.4. Documentation and justification for IRB approval of waiver or alteration of informed consent and HIPAA authorization will appear in the IRB review letter and in the meeting minutes.

**Administrative Approval:**
BRUCE G. GORDON, MD  IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS
CHRISTOPHER KRATOCHVIL, MD  INSTITUTIONAL OFFICIAL

**Policy Amended:**
- **Revised January 29, 2018**
- **Initial January 11, 2016**
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for use of telephone informed consent process. For the purpose of this policy “telephone” includes video-conferencing or similar technologies.

2.0 Policy
2.1. It is the policy of the Organization that telephone consent may be used in both clinical and non-clinical research, at the discretion of the convened IRB, or of a qualified expedited reviewer (if the research or change in protocol qualifies for expedited review), provided such communication satisfies requirements of HHS regulations at 45 CFR 46.116 and 45 CFR 46.117 and FDA regulations at 21 CFR 50.20 and 21 CFR 50.27, and satisfies the additional requirements in the policy.

2.1.1. The convened IRB or a qualified expedited reviewer may authorize use of telephone consent or documentation for new subjects if:

2.1.1.1. Enrollment of new subjects provided the research constitutes no more than minimal risk, OR
2.1.1.2. Screening of new subjects to determine eligibility for a greater than minimal risk study, provided the screening procedures are all minimal risk. In this case the subject must be re-consented in person before performance of any greater than minimal risk research interventions, or any additional screening procedures conducted within the Organization.

2.2. It is the policy of the Organization that telephone consent may be used in both clinical and non-clinical research, on a single subject basis, at the discretion of the IRB Executive Chair or designee, provided such communication satisfies requirements of HHS regulations at 45 CFR 46.116 and 45 CFR 46.117 and FDA regulations at 21 CFR 50.20 and 21 CFR 50.27, and satisfies the additional requirements in the policy.

2.2.1. The IRB Executive Chair or designee may authorize use of telephone consent or documentation for a single subject if:

2.2.1.1. Direct face-to-face contact with the research staff would place an unreasonable burden on the subject (for example, because of distance), or
2.2.1.2. Requirement for direct face-to-face contact would prohibit enrollment of a potential subject in research with the prospect of direct benefit, or
2.2.1.3. Provision of new information to the subject would be inappropriately delayed by requiring direct face-to-face contact with the research staff

3.0 Process for Utilizing Telephone Consent
3.1. Enrollment of new subjects in clinical research

3.1.1. The informed consent form (as well as all protocol related ancillary materials) and a copy of “The Rights of Research Subjects” and “What Do I Need to Know?” must be provided
to the subject for review prior to the telephone consent process. These items can be provided to the subject by mail, fax or email.

3.1.2. The process of consent will be conducted as per the requirements of HRPP policy 5.1 (Obtaining Informed Consent from Research Subjects), HHS regulations (45 CFR 46.116(a)) and FDA regulations (21 CFR 50.20).

3.1.3. If the subject agrees to participate in the research or the screening:

3.1.3.1. The subject is instructed to sign and date the ICF and return the signed document to the investigator by mail, fax or a scanned copy via email. No research interventions (including screening) can be conducted until a signed copy of the ICF has been received by the investigator by email, fax or mail.

3.1.3.2. The ICF must be signed and dated by the investigator 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”).

3.1.3.3. A copy of the ICF signed by the investigator must be provided to the subject.

3.1.4. If the research satisfies the requirement for waiver of documentation of informed consent under 45 CFR 46.117(c) the ICF does not need to be signed and returned by the subject to the investigator and research interventions may begin as soon as verbal consent is obtained. In addition, ICF does not need to be signed and dated by the investigator.

3.1.5. The process of telephone consent must be documented in the medical or individual study subject record, if applicable, or in a separate consent log. The documentation must include:

3.1.5.1. The rationale for use of telephone consent.

3.1.5.2. The date and time of telephone consent.

3.1.5.3. Identification of all personnel involved in obtaining and documenting informed consent.

3.2. Enrollment of new subjects in non-clinical research

3.2.1. Telephone Consent may be utilized for enrollment of new subjects provided the research constitutes no more than minimal risk and the subjects are not required nor expected to come into personal contact with the researchers at any time during the conduct of the research.

3.2.2. Procedure will be as per section 3.1 above.

3.3. Re-consent to disclose new information or protocol changes

3.3.1. Telephone Consent may be utilized for the purpose of disclosing new information which may relate to the subject’s willingness to continue participation in the research, or protocol changes that may affect the subject directly.

3.3.2. Procedure will be as per sections 3.1 above.

3.3.3. If new information requires immediate verbal transmission to the subject (for example, a serious adverse event, or significant change in protocol which is required immediately) the subject may be notified by phone prior to supplying the revised ICF. The phone conversation
between the investigator and the subject should be witnessed by a member of the Organization not associated with the research. Written re-consent as per section 3.1 items B thru F should follow promptly.

3.4. Enrollment of decisionally impaired subjects whose LAR is unavailable in person

3.4.1. Telephone Consent may be utilized for the purpose of enrolling decisionally impaired subjects whose LAR is unavailable in person, even if that research constitutes greater than minimal risk as long as there is the possibility of direct benefit.

3.4.2. Procedure will be as per section 3.1 above.

3.4.3. The phone conversation between the investigator and the LAR should be witnessed by a member of the Organization not associated with the research.

3.4.4. Assent of the decisionally impaired person must be obtained as required in HRPP policy 4.6 (Research Involving Subjects with Impaired Decision-Making Capacity).

ADMINISTRATIVE APPROVAL:
BRUCE G. GORDON, MD IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS
CHRISTOPHER KRATOCHVIL, MD INSTITUTIONAL OFFICIAL

POLICY AMENDED:
- REVISED JULY 27, 2018
- INITIAL JANUARY 12, 2016
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s process for 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 45 CFR 46.117(c) are satisfied.

2.2. 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 for FDA regulated research only provided that the IRB finds and documents the criteria specified in FDA regulations at 21 CFR 56.109(c) are satisfied.

2.3. It is the policy of the Organization that, for research where the IRB has waived the requirement to obtain signed informed consent, the PI/authorized study personnel must still perform an adequate informed consent process in accordance with HRPP policy 5.1 (Obtaining Informed Consent from Research Subjects).

3.0 Criteria for IRB Approval of a Waiver of Requirement to Obtain a Signed ICF

3.1. The IRB may waive the requirement for the investigator to obtain a signed informed consent form for some or all subjects if it finds any of the following:

3.1.1. The only record linking the subject and the research would be the informed consent form and the principal risk would be potential harm resulting from a breach of confidentiality (45 CFR 46.117(c)(1) (or rev 45 CFR 46.117(c)(1)(i)).

3.1.1.1. Each subject (or legally authorized representative) will be asked whether the subject wants documentation linking the subject with the research, and the subject’s wishes will govern.

3.1.1.2. The oral or written information provided to subjects includes all required and additional elements of consent,

3.1.1.3. This justification for waiver applies only to non-FDA regulated research.

3.1.2. The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context (45 CFR 46.117(c)(2) (or rev 45 CFR 46.117(c)(1)(ii)), or 21 CFR 56.109(c)).

3.1.2.1. For research not regulated by FDA, there are no additional requirements.

3.1.2.2. For research regulated by FDA, the subject will be provided with a written statement regarding the research. This statement can be in the form of an informed consent form without signature blanks, or a narrative

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.
3.1.3. Following the effective date of the Revised Rule, the subjects or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not the norm and the research presents no more than minimal risk of harm to subjects and there is an appropriate alternative mechanism for documenting that informed consent was obtained

3.1.3.1. This justification for waiver applies only to non-FDA regulated research

3.2. In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects or legally authorized representatives with a written statement regarding the research. If required, this statement must be

*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 3.1.1 above.*

4.0 Process of Review

4.1. To request a waiver of the requirement to obtain signed informed consent the investigator must complete and submit with the appropriate sections of the IRB application.

4.2. The IRB will review the proposed waiver in accordance with HRPP policies 2.2 (Full Board Review) or 2.3 (Expedited Review).

4.3. Documentation and justification for IRB approval of waiver of requirement to obtain signed ICF will appear in the IRB review letter.

**Administrative Approval:**

BRUCE G. GORDON, MD  IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS

CHRISTOPHER KRATOCHVIL, MD  INSTITUTIONAL OFFICIAL

**Policy Amended:**

- **REVISED JANUARY 25, 2018**
- **INITIAL JANUARY 12, 2016**
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:

2.1.1. A subject/LAR who cannot understand English is unexpectedly encountered.

2.1.2. There is not sufficient time to develop and obtain IRB approval for a complete ICF written in language understandable to the subject/LAR.

2.1.3. The research presents the prospect of direct therapeutic benefit to the subject.

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. For research where it is reasonable to expect that a significant number of non-English speaking persons will participate, the IRB may require that a translated CF be prepared and used.

2.3. The short form is restricted to enrollment of no more than three subjects per language in a given protocol. In order to enroll more than three subjects, the PI is required to have the complete ICF translated into the appropriate language and reviewed and approved by the IRB.

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.

2.5. It is the policy of the Organization that the use of a short form written consent document is permissible when an external IRB acts as the IRB of record for clinical trials conducted on the premises of the Organization provided the IRB of record approves the use of the short form written consent document.

3.0 Procedure

3.1. The Short Form states that the elements of informed consent required by 45 CFR 46.116 have been presented orally to the subject or the subject’s LAR

3.1.1. Following the effective date of the Revised Rule the short form will also state that a concise and focused presentation of the key information that is most likely to assist a prospective subject or LAR in understanding the reasons why one might or might not want to participate in the research (as required by rev 45 CFR 46.116(a)(5)(i)) was presented first to the subject, before other information, if any, was provided.

3.1.2. IRB-approved short forms are available on the IRB website (www.unmc.edu/irb) in the following languages: Arabic, Bosnian, Croatian, French, Hmong, Khmer, Laotian, Oromo, Russian, Somali, Spanish, and Vietnamese.
3.2. Investigators must complete a *Short Form Request* (available on the IRB website at www.unmc.edu/irb) for each subject, and submit to the ORA.

3.3. If an IRB-approved short form is not available in a language understandable to the subject/LAR, the investigator may 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 *Short Form Request* and the translated Short Form must be submitted to ORA for expedited review and approval before use.

3.4. The IRB Executive Chair/designee must approve each *Short Form Request* prior to use of the requested short form.

3.5. The approved short form (IRB stamped) must be used within two weeks. The approval period can be extended by the Executive Chair/designee with adequate justification.

3.6. The IRB number and title of the protocol (in English) and contact information must be typed in the appropriate spaces provided on the Short Form.

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:

   3.7.1. A Nebraska Medicine, CH&MC 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 medical or other scientific terminology related to the research.

   3.7.2. A commercial interpretation/translation service (such as CyraCom).

3.8. If a prospective subject/LAR/parent wishes to designate his/her own interpreter:

   3.8.1. This must be documented in the medical/research record.

   3.8.2. The Official Interpreter that qualifies under 3.7 above must also be present to ensure the quality and accuracy of the interpretation and this must also be documented.

   3.8.3. A minor cannot be used as an 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:

   3.9.1. An official Nebraska Medicine, CH&MC, or study site hospital interpreter/translator.

   3.9.2. A commercial interpretation/translation service (such as CyraCom).

   3.9.3. If the Official Interpreter qualifies under 3.7, then they may also serve as the witness (with the exception that study staff may not serve as witness).

3.10. The interpreter must be involved in the process of consent as follows:

   3.10.1. The subject/LAR should be given a copy of the short form.

   3.10.2. The person obtaining consent, with the assistance of the interpreter, should explain the use of the short form.

   3.10.3. The person obtaining consent, with the assistance of the interpreter, must

       3.10.3.1. Provide a concise and focused presentation of the key information that is most likely to assist a prospective subject or LAR in understanding the reasons why one might or might not want to participate in the research (as required by rev 45 CFR 46.116(a)(5)(i)) before other information about the research.
3.10.3.2. Describe the research and the prospective subject’s rights (including elements of consent required by 45 CFR 46.116), using the IRB-approved English version of the complete ICF as a guide. As long as the above information is provided, the complete ICF need not be translated word-for-word.

3.10.4. The complete ICF, which has been approved by the IRB, will serve as the summary required by 45 CFR 46.117(b)(2).

3.10.5. 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.

3.10.6. 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 in advance of initiating the consent process with the subject/LAR.

3.11. Upon conclusion of the consent process the subject/LAR must sign and date the short form.

3.12. The person obtaining consent must sign and date the English version of the complete ICF.

3.13. 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.

3.14. A copy of the signed and dated short form and the English version of the complete ICF must be given to the subject/LAR.

3.15. Depending on the nature and duration of the research, the IRB Executive 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.

3.16. The process of consent using the short form must be fully documented and maintained on file which includes the following:

3.16.1. The time over which the process of consent was conducted.

3.16.2. The name and contact information of the interpreter.

3.16.3. The name and contact information of the witness.

3.17. Both the investigator and interpreter must document the informed consent process utilizing the short form in the medical/research record.

Administrative Approval:

Bruce G. Gordon, MD IRB Executive Chair & Assistant Vice Chancellor for Regulatory Affairs
Christopher Kratochvil, MD Institutional Official

Policy Amended:

- Revised June 18, 2018
- Initial February 5, 2016
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
2.1. 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.

2.2. It is the policy of the Organization that the informed consent requirements of 45 CFR 46.116 and 45 CFR 46.408 may be waived for emergency research not subject to 21 CFR 50, provided the IRB has approved both the research and a waiver of informed consent and has found and documented that conditions for emergency research contained in the Secretarial waiver document have been met [61 FR 51531, 1996].

3.0 Definition
3.1. **Emergency Research** means a planned clinical investigation that requires prior written FDA authorization to proceed and involves subject(s) who are in a life-threatening situation for which available treatments or in vitro diagnostic tests are unproven or unsatisfactory.

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 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 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:

4.3.1. 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.

4.3.2. Obtaining informed consent is not feasible because:
4.3.2.1. The subjects will not be able to give their informed consent as a result of their medical condition, and

4.3.2.2. The intervention under investigation must be administered before informed consent from the subjects’ legally authorized representatives is feasible, and

4.3.2.3. There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation or research.

4.3.3. Participation in the research holds out the prospect of direct benefit to the subjects because:

4.3.3.1. Subjects are facing a life-threatening situation that necessitates intervention, and

4.3.3.2. 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

4.3.3.3. 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.

4.3.4. The clinical investigation could not practicable be carried out without the waiver.

4.3.5. The protocol defines the length of the potential therapeutic window based on scientific evidence.

4.3.6. 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.

4.3.7. The PI will summarize efforts made to contact LARs and make this information available to the IRB at the time of continuing review.

4.3.8. 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.

4.3.9. 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.

4.3.10. Additional protections of the rights and welfare of the subjects will be provided, including, at least:

4.3.10.1. 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.

4.3.10.2. 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.

4.3.10.3. 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.
4.3.10.4. Establishment of an independent data monitoring committee to exercise oversight of the clinical investigation.

4.3.10.5. 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.

4.3.10.6. 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.

4.4.1. 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.

4.4.2. 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.

4.4.3. 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.

Administrative Approval:

Bruce G. Gordon, MD  IRB Executive Chair & Assistant Vice Chancellor for Regulatory Affairs
Christopher Kratochvil, MD  Institutional Official

Policy Amended:
- Revised March 5, 2018
- Initial January 8, 2016
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for research involving investigational and marketed drugs.

2.0 Policy
2.1. It is the policy of the Organization that the IRB will review all research involving the use of investigational drugs, biologics, and marketed drugs (test articles) in full accordance with 21 CFR 50, 56; 21 CFR 312, 314; and 45 CFR 46, and with HRPP policies.

2.2. It is the policy of the Organization that investigators will conduct such research in full accordance with 21 CFR 50, 56; 21 CFR 312, 314; and 45 CFR 46, and with HRPP policies.

2.3. It is the policy of the Organization that sponsors and any CRO acting on behalf of the sponsor will fully comply with FDA regulations at 21 CFR 312.50-59

3.0 Definitions
3.1. **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 clinical trial.

3.2. **Clinical Investigation** means any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the FDA under Section 505(i) or 520(g) of the Food, Drug and Cosmetics Act or need not meet the requirements for prior submission to the FDA under these sections of the Act but the results of which are intended to be later submitted as part of an application for a research or marketing permit. The terms research, clinical research, clinical study, and clinical investigation are deemed to be synonymous.

3.3. **Investigator** means the individual under which immediate direction the test article is administered or dispersed to a subject (21 CFR 56.102(h)). Under HRPP policy 1.26 (PI Qualifications and Responsibilities), this individual is referred to as the Principal Investigator (PI).

3.4. **Human Subject** means an individual who is or becomes a participant in a clinical investigation either as a recipient of the test article or as a control. A subject may be either a patient or a healthy individual.

3.5. **Investigational New Drug (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.

3.6. **Marketed Drug** is a drug or biologic approved by FDA for marketing and is generally in use for treatment purposes.

3.7. **Sponsor** is a person or organization 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** 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 serves as a sponsor must comply with all FDA requirements applicable to both an investigator as well as a sponsor.

3.9. **Emergency Use** is 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.

3.10. **Expanded Access** is the use of an investigational agent outside of a clinical trial. The terms expanded access and treatment use are used interchangeably to refer to use of an investigational drug when the primary purpose is to diagnose, monitor, or treat a patient’s disease or condition. The term compassionate use is also occasionally used in the context of the use of an investigational drug to treat a patient. Although these terms have been used informally they are not defined or described in FDA regulations.

4.0 Procedures

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

4.2. All contracts between sponsors and CHMC for investigational drug studies must be reviewed and approved by UNMC Sponsored Programs Administration (SPA) or by UNeHealth, or by CHMC Administration, in compliance with **HRPP policy 1.12 (Sponsored Research)**. If the contract is reviewed and approved by CHMC Administration it will also be reviewed by UNMC SPA to assure the requirements of **HRPP policy 1.12, section 4.3** are met.

4.3. The Organization has determined clinical investigations involving drugs should be reviewed by the full IRB in accordance with **HRPP policy 2.2 (Full IRB Review)**. However, the IRB may determine select clinical investigations involving no more than minimal risk may be eligible for expedited review in accordance with **HRPP policy 2.3 ( Expedited Review)**.

4.4. If the contract agreement requires compliance with ICH GCP, the IRB will review the submission in accordance with **HRPP policy 1.13 (Compliance with ICH-GCP)**. The investigator will designate the need for ICH GCP compliance in the IRB application.

4.5. The IRB will review the information in the application to ensure that investigational drugs are securely stored and dispensed in accordance with FDA regulations at 21 CFR 312.60-62.

4.5.1. 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.

4.5.2. For research conducted at CH&MC investigational drugs must be stored and dispensed in accordance with **CH&MC Policy 204.00**.

4.5.3. For research conducted at an external site, a copy of the policy of the external site(s) which satisfies the requirements of FDA regulations at 21 CFR 312.60-62 must be submitted to the ORA.

4.6. 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.
4.7. 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.

4.8. The PI must promptly inform the IRB and Investigational Drug Pharmacist when a study involving investigational drugs has been terminated.

5.0 Studies Requiring an IND

5.1. Prior to IRB approval of the study, 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 be the industry sponsored protocol with the IND number, written determination from the FDA, or other documentation or communication verifying the IND number.

5.2. 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 Sponsor-Investigator.

5.3. 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).

5.4. All protocol-related documents, including FDA notification, must contain matching IND numbers.

5.5. A clinical investigation involving an exception to the informed consent requirement under 21 CFR 50.24 must be performed under a separate IND (even if an IND for the same drug product already exists (21 CFR 50.24(d)).

5.6. 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.

6.0 Exemptions from IND Requirements

6.1. A clinical investigation of a drug product that is lawfully marketed is exempt from the requirements of an IND if:

   6.1.1. The investigation is not intended to be reported to FDA in support of a new indication for use or any other significant change in the labeling for the drug; AND

   6.1.2. The investigation is not intended to support a significant change in the advertising for the product; AND

   6.1.3. The investigation does not involve a 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; AND

   6.1.4. The investigation is conducted in compliance with 21 CFR 50, 56, and 21 CFR 312.7 (Promotion of investigational drugs)
6.2. A clinical investigation involving blood grouping serum, reagent red blood cell and anti-human globulin is exempt from the requirements of an IND if the conditions of (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 312.160 (per 21 CFR 312.2(b)(2)).

6.3. A drug intended solely for tests in vitro or in laboratory research animals is exempt from the requirements of an IND if it is shipped in accordance with 21 CFR 312.160 (per 21 CFR 312.2(b)(3))

7.0 Expanded Access to Investigational Drugs

7.1. FDA regulations at 21 CFR 312.300 (subpart I) allow certain individuals not enrolled in clinical trials to obtain expanded access to investigational drugs through various expanded access programs (EAPs).

7.1.1. All expanded access programs must meet the basic criteria in 21 CFR 312.305(a). Specifically the FDA must determine:

7.1.1.1. The patient or patients to be treated have a serious or immediately life-threatening disease or condition, and there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition;

7.1.1.2. The potential patient benefit justifies the potential risks of the treatment use and those potential risks are not unreasonable in the context of the disease or condition to be treated; and (3) Providing the investigational drug for the requested use will not interfere with the initiation, conduct, or completion of clinical investigations that could support marketing approval of the expanded access use or otherwise compromise the potential development of the expanded access use.

7.1.2. All expanded access programs described below require prior IRB approval and informed consent of the subject.

7.1.3. Specific EAPs:

7.1.3.1. Single (Individual) Patients

7.1.3.1.1. Treatment is generally limited to a single course of therapy for a specified duration, though FDA may authorize multiple courses or chronic therapy. Use of this EAP requires an individual patient IND for treatment use.

7.1.3.1.2. The following determinations must be made (21 CFR 312.310):

7.1.3.1.2.1. The requesting physician determine the probable risk to the person from the investigational drug is not greater than the probable risk from the disease or condition

7.1.3.1.2.2. (FDA must determine that the patient cannot obtain the drug under another IND or protocol

7.1.3.2. Intermediate-Size Patient Populations

7.1.3.2.1. Investigational drug may be used for the treatment of a patient population smaller than that typical of a treatment IND or treatment protocol, as per 21 CFR 312.315.

7.1.3.2.2. The FDA must determine:
7.1.3.2.2.1. There is enough evidence that the drug is safe at the dose and duration proposed for expanded access use.

7.1.3.2.2.2. There is at least preliminary clinical evidence of effectiveness of the drug, or of a plausible pharmacologic effect of the drug to make expanded access use a reasonable therapeutic option in the anticipated patient population.

7.1.3.3. Treatment IND or Treatment Protocol (widespread treatment use)

7.1.3.3.1. FDA may permit widespread use of an investigational drug under 21 CFR 312.320.

7.1.3.3.2. FDA must determine:

7.1.3.3.2.1. The drug is being investigated in a controlled clinical trial under an IND designed to support a marketing application for the expanded access use, or all clinical trials of the drug have been completed;

7.1.3.3.2.2. The sponsor is actively pursuing marketing approval of the drug for the expanded access use with due diligence.

7.1.3.3.2.3. When the expanded access use is for a serious disease or condition, there is sufficient clinical evidence of safety and effectiveness to support the expanded access use; or when the expanded access use is for an immediately life-threatening disease or condition, the available scientific evidence, taken as a whole, provides a reasonable basis to conclude that the investigational drug may be effective for the expanded access use and would not expose patients to an unreasonable and significant risk of illness or injury.

7.1.3.4. Group C Treatment IND

7.1.3.4.1. “Group C” is a special class of Treatment IND that has been established by the FDA and the National Cancer Institute (NCI) for the distribution of certain investigational agents (generally Phase 3 study drugs) to oncologists for the treatment of cancer under protocols outside the controlled clinical trial. Group C drugs are distributed only by the National Institutes of Health (NIH) under NCI protocols.

7.1.3.4.2. Though the FDA has generally granted a waiver from the IRB review requirements (21 CFR 56.105) the Organization has decided to require review and approval by the convened IRB in accordance with HRPP policy 5.2 (Waiver or Alteration of Informed Consent and HIPAA Authorization).

7.1.3.5. Parallel Track Policy

7.1.3.5.1. The FDA’s “Parallel Track” policy facilitates early access to promising new drugs for AIDS/HIV related diseases under a separate expanded access protocol that “parallels” the controlled clinical trials that are essential to establish the safety and effectiveness of new drugs.

7.2. Although an investigational article used under the FDA expanded access mechanism is intended for the purpose of clinical treatment, the FDA may consider the treatment to constitute a “clinical investigation” (i.e., research), and require that data from the treatment be reportable in a marketing application. Conversely, under the U.S. Department of Health and Human Services (HHS) human research protection rules, patients who receive investigational articles through the expanded access mechanism are not considered research subjects, and outcomes of expanded access treatments may not be included in reports of research funded by federal agencies that follow HHS rules.
8.0 Emergency Waiver of IND

8.1. FDA regulations at 21 CFR 312.310(d) 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.

8.2. 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).

9.0 Emergency Use of Investigational Drugs

Emergency use of an investigational drug will be administered to subjects in accordance with HRPP policy 6.4 (Emergency Use of a Test Article).

10.0 Waiver of Informed Consent for Planned Emergency Research

Waiver of informed consent for planned emergency research will be reviewed and approved by the full IRB in accordance with HRPP policy 5.6 (Exception from Informed Consent Requirements for Emergency Research).

ADMINISTRATIVE APPROVAL:
BRUCE G. GORDON, MD  IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS
CHRISTOPHER KRATOCHVIL, MD  INSTITUTIONAL OFFICIAL

POLICY AMENDED:
- REVISED MARCH 2, 2018
- INITIAL JANUARY 25, 2016
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization's requirements for research involving investigational and marketed devices.

2.0 Policy
2.1. It is the policy of the Organization that the IRB will review all research involving investigational devices and FDA-approved devices (test articles) in full accordance with the following: 21 CFR 50, 56; 21 CFR 812, 814; 45 CFR 46.

2.2. It is the policy of the Organization that investigators will conduct such research in full accordance with the above cited regulations and applicable HRPP policies.

2.3. It is the policy of the Organization that sponsors and any CRO acting on behalf of the sponsor will fully comply with FDA regulations at 21 CFR 812.

3.0 Definitions
3.1. **Investigational Device** means a device, including a transitional device, which is the object of a clinical investigation. As further defined, a device is any healthcare product that does not achieve its primary intended purpose by chemical action or by being metabolized.

3.2. **Clinical Investigation** means any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the FDA under Section 505(i) or 520(g) of the Act or need not meet the requirements for prior submission to the FDA under these sections of the Act but the results of which are intended to be later submitted as part of an application for a research or marketing permit. The terms research, clinical research, clinical study, and clinical investigation are deemed to be synonymous.

3.3. **Investigator** means the individual under which immediate direction the test article is administered or dispersed to a subject. Under HRPP policy 1.26 (PI Qualifications and Responsibilities), this individual is referred to as the PI.

3.4. **Human Subject** means an individual who is or becomes a participant in a clinical investigation either as a recipient of the test article or as a control. A subject may be either a patient or a healthy individual.

3.5. **Significant risk device (SRD)** is a device that

3.5.1. Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject; or

3.5.2. Is purported or represented to be for a use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject; or

3.5.3. Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety or welfare of a subject; or

3.5.4. Otherwise presents a potential to the health, safety or welfare of a subject.
Note: SR device studies must follow all the IDE regulations at 21 CFR 812, and must have an IDE application approved by FDA before they may proceed.

3.6. **Non-significant risk device (NSRD)** is a device that does not meet the definition of an SRD.

Note: NSR device studies must follow the abbreviated requirements at 21 CFR 812.2(b). These abbreviated requirements address labeling, IRB approval, informed consent, monitoring, records, reports, and prohibition against promotion. However, there is no need to make progress reports or final reports to FDA. NSR device studies do not have to have an IDE application approved by FDA.

Note. FDA is the final arbiter as to whether a device study is SR or NSR and makes the determination when an IDE is submitted to FDA or if asked by the sponsor, clinical investigator, or IRB. See 21 CFR § 812.2(b)(1).

3.7. **Investigational New Device Exemption (IDE)** is an application submitted to FDA to conduct a clinical investigation with an investigational device that is subject to 21 CFR 812.2 and is classified as an SRD. The IDE is submitted by the sponsor of the research. The FDA will provide a written authorization to conduct a clinical investigation within 30 days after receipt of the IDE. If the device is not an SRD, the investigation is considered by FDA to have an approved IDE unless FDA notifies the sponsor otherwise.

3.8. **Marketed Device** is a device approved by FDA for marketing and is generally in use for treatment or diagnostic purposes.

Note: When a marketed device is used in a clinical investigation, it is subject to 21 CFR 812.2 unless it qualifies as an exempted investigation. IRB review and approval, however, is required.

3.9. **Sponsor** is the person who initiates, but does not actually conduct the investigation. The sponsor is responsible for complying with the requirements under FDA regulations at 21 CFR 812.40-47. The sponsor may be a device company, governmental agency, academic institution, private organization or an individual investigator.

3.10. **Sponsor-Investigator** is an individual that initiates and conducts an investigation, that is, under whose immediate direction the investigational device is administered, dispensed or used. An investigator who also serves as a sponsor must comply with all FDA requirements applicable to an investigator as well as a sponsor.

3.11. **Treatment Use of an Investigational Device** means use of a device that is not approved for marketing, but may be under clinical investigational, for a serious or immediately life-threatening disease or condition in patients for whom no comparable or satisfactory alternative device or other therapy is available. Under a treatment IDE, patients not in a clinical investigation may be treated utilizing the device in accordance with 21 CFR 812.36. IRB approval is required for treatment use of an investigational device.

3.12. **Emergency Use** means use of a test article on a human patient in a life-threatening or severely debilitating circumstance where no standard medically acceptable treatment is available and there is not sufficient time to obtain full IRB approval for use of the test article to treat the patient.

3.13. **Unanticipated Adverse Device Effect (UADE)** means an adverse effect caused by, or associated with, a device, if that effect was: 1) not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), and 2) the adverse effect relates to or impacts the rights, safety, or welfare of subjects.
4.0 Requirements

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

4.2. All contracts between sponsors and CHMC for investigational drug studies must be reviewed and approved by UNMC Sponsored Programs Administration (SPA) or by UNeHealth, or by CHMC Administration, in compliance with HRPP policy 1.12 (Sponsored Research). If the contract is reviewed and approved by CHMC Administration it will also be reviewed by UNMC SPA to assure the requirements of HRPP policy 1.12, section 4.3 are met.

4.3. Clinical investigations involving SR devices must be reviewed and approved by the full IRB in accordance with HRPP policy 2.2 (Full IRB Review). However, the IRB may determine select clinical investigations involving NSR devices and exempt devices that are no more than minimal risk may be eligible for expedited review in accordance with HRPP policy 2.3 (Expedited Review).

4.4. If the contract agreement requires compliance with ICH GCP, the IRB will review the submission in accordance with HRPP policy 1.13 (Compliance with ICH-GCP). The investigator will designate the need for ICH GCP compliance in the IRB application.

4.5. If a study involves an investigator-initiated IDE, it is the expectation of the Organization that the PI will also comply with the FDA-mandated sponsor requirements (21 CFR 812) and certify compliance by submitting Addendum P (Principal Investigator Responsibilities: Investigator-Initiated Device Trials) which specifies all of the responsibilities of the Sponsor-Investigator.

4.6. Any PI who has a study that is audited by the sponsor, a CRO or FDA must immediately notify the UNMC Chief Compliance Officer and provide the IRB with a copy of the report following the audit. When the study is audited by the Fred & Pamela Buffett Cancer Center Protocol Review Monitoring System (PRMS) Audit Committee, a copy of the report must be provided to the IRB.

4.7. If a study involves an investigator-initiated IDE, the PI must also comply with the FDA-mandated sponsor requirements.

5.0 IRB Procedures

5.1. The IRB will review the information in the application to ensure that the PI has adequate controls in place for storage, security, and dispensing of investigational devices in accordance with 21 CFR 812.110. The IRB will assess whether:

5.1.1. The device is stored and secured in a manner that restricts access to investigators. As appropriate this may be a cabinet that has a physical lock to which only an investigator has a key (physical or electronic), or some other equivalent process.

5.1.2. The device is dispensed in a manner that assures that only subjects who have provided informed consent will be treated or tested/examined using the investigational device. This should involve marking the device in an easily visible manner that it is for investigational use only, and, as appropriate, include a mechanism to have a second party review the signed consent form prior to dispensing the device from a storage location, or some other equivalent process.

5.1.3. The investigator and the departments, sections, or operating rooms where device is used maintains records sufficient to document that the storage, security and dispensing of investigational devices has been in accordance with 21 CFR 812.110. These records may be physical or electronic, as long as they satisfy the requirements of 21 CFR 812.140, including, but limited to records of receipt, use or disposition of a device that relate to: (i) The type and
quantity of the device, the dates of its receipt, and the batch number or code mark; (ii) The names of all persons who received, used, or disposed of each device, and (iii) Why and how many units of the device have been returned to the sponsor, repaired, or otherwise disposed of.

5.2. Unless the research is exempt from the FDA IDE regulations, the IRB will review the sponsor’s determination of the risk classification of the device (SR or NSR) and make a determination of risk based upon the following:

5.2.1. The potential harm associated with the device itself
5.2.2. The proposed use of the device
5.2.3. Any procedure necessary for implantation of the device
5.2.4. A comparison of the risks of the device against the risks of alternative devices or procedures.

5.3. The IRBs determination of risk classification of the device and the rationale for the classification will be documented in the IRB minutes.

5.4. If the IRB has any question or concern about whether a study is SR and, therefore, requires an IDE, the PI will be instructed to contact the Food and Drug Administration (FDA) Center for Devices and Radiologic Health (CDRH) and obtain a written determination.

5.5. The IRB will notify the PI of the Board’s SR/NSR determination. If the IRB disagrees with the sponsor or PI’s determination that a device is NSR, the study can only be conducted within the Organization if an IDE is obtained. The PI is responsible for notifying the sponsor of the IRB’s determination. The PI must provide the IRB with confirmation of this action.

Note: In accordance with 21 CFR 812.150(b)(9), if the IRB determines that a device is SR and the sponsor had classified the device as NSR, the sponsor must submit to FDA a report of the IRB’s determination within 5 work days after the sponsor first learns of the IRB determination. If FDA does not agree with the IRB’s SR determination, the IRB will re-review the study. However, the IRB retains the ultimate authority in deciding whether or not to accept FDA’s NSR classification.

5.6. NSR device studies do not require submission of an IDE application to the FDA before starting the study. The FDA considers an NSR device study to have an approved IDE application after obtaining and maintaining IRB approval. Sponsors and the PI must meet the abbreviated requirements at 21 CFR 812.2(b). These abbreviated requirements address labeling, IRB approval, informed consent, monitoring, records, reports, and prohibition against promotion.

5.7. If the IRB classifies a device as NSR, the IRB will continue to follow procedures in accordance with the IRB approval criteria (HRPP policy 2.5) used in considering approval of any research involving an FDA-regulated product including all applicable local and regulatory requirements.

5.8. SR devices require submission of an IDE application to the FDA before starting the study. Final IRB approval and release of IDE studies is contingent upon the assigned IRB administrator’s receipt of FDA notification approving the IDE. All protocol-related documents, including FDA notification, must contain matching IDE numbers.

5.9. For studies involving marketed SR devices for potential new indications, the IRB may require submission of an IDE application to the FDA upon consultation with both the sponsor and the FDA.

5.10. All unanticipated adverse device effects (UADEs) will be reported in accordance with HRPP policy 8.1 (IRB Review of Adverse Events and Adverse Device Effects).
6.0 Exemptions from IDE Requirements

6.1. Any of the following types of clinical investigations are exempt from IDE requirements (21 CFR 812.2(c)):

6.1.1. A clinical investigation with approved devices used in accordance with labeling. The device may have been approved for commercial distribution before May 28, 1976 or deemed substantially equivalent to a device commercially approved before May 28, 1976.

6.1.2. A clinical investigation with in vitro diagnostic devices, if the sponsor complies with applicable labelling requirements in 21 CFR 809.10(c) and if the testing:
   6.1.2.1. Is noninvasive; and
   6.1.2.2. Does not require an invasive sampling procedure that presents significant risk; and
   6.1.2.3. Does not by design or intention introduce energy into a subject; and
   6.1.2.4. Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure.

6.1.3. A clinical investigation with a marketed device undergoing consumer preference testing, testing of a modification, or testing of a combination of two or more devices in commercial distribution, unless testing is for determining safety and efficacy and/or puts subjects at risk.

6.2. Exemption from IDE regulations does not mean the study is exempt from IRB review and approval. If the study involves use of a device, whether or not the device has been approved by the FDA, the IRB’s review and approval of the study must comply with all applicable local and federal regulations.

ADMINISTRATIVE APPROVAL:
BRUCE G. GORDON, MD  IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS
CHRISTOPHER KRATOCHVIL, MD  INSTITUTIONAL OFFICIAL

POLICY AMENDED:
➢ REVISED MARCH 2, 2018
➢ INITIAL JANUARY 12, 2016
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 an 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 not more than 8,000 individuals in the US per year. An HUD is a legally marketed device and is not investigational.

3.2. Humanitarian Device Exemption (HDE): HDE is a Pre-Market Approval (PMA) application which is exempt from the requirement of establishing a reasonable assurance of effectiveness. HDE approval is based upon, among other criteria, a determination by FDA that the HUD will not expose patients to an unreasonable or significant risk of illness or injury and the probable benefit to health from use of the device outweighs the risk of injury or illness from its use while taking into account the probable risks and benefits of currently available devices or alternative forms of treatment.

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 an 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 an 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. The collection of safety and efficacy data about an HUD to support a pre-marketing approval application constitutes a clinical investigation subject to 21 CFR 50, 56.

4.3.1. If data can be collected in a clinical investigation for the HDE-approved indication no IDE is required. If data is being collected for a different indication than the HDE-approved indication, the clinical investigation requires an FDA-approved IDE.

4.4. The IRB HUD application will be submitted to the full Board for review (HRPP policy #2.2) and approval. Expedited review will not be used.

4.5. The IRB will review the use of the HUD following the review criteria in 21 CFR 56.111.

4.6. The IRB will review (1) a copy of the HDE approval order; (2) a description of the device; (3) the product labeling; (4) any patient information packet that may accompany the HUD; (5) the consent form for the use of the HUD; and (6) a summary of how the physician proposes to use the
device, including a description of any screening procedures, the HUD procedure, and any patient follow-up visits, tests or procedures.

4.7. The IRB will normally not review and approve individual patient uses of an HUD within the IRB-approved HUD Application. However, on a case-by-case basis, the IRB may decide to require such approval.

4.8. An HUD may be used in an emergency situation without prior IRB approval in accordance with the applicable sections of HRPP policy 6.4 (Emergency Use of a Test Article).

4.9. The UNMC IRB requires that written informed consent be obtained from patients who will be recipients of HUDs, except as described in section 4.8.

4.9.1. The Consent Form should include at least (1) an explanation that the HUD is designed to diagnose or treat the disease or condition described in the HDE labeling and that no comparable device is available to treat the disease or condition; (2) a statement that effectiveness of this device for this use has not been demonstrated; (3) a description of any ancillary procedures associated with the use of the HUD; (4) a description of the use of the HUD; (5) all known risks or discomforts; (6) and an explanation of the postulated mechanism of action of the HUD in relation to the disease or condition.

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.

4.10. Written informed consent is not required from patients who will be recipients of HUDs if all of the following conditions are met:

4.10.1. The patient is confronted by a life-threatening or severely debilitating situation necessitating the use of the test article.

4.10.2. Informed consent cannot be obtained from the patient because of an inability to communicate with, or obtain legally effective consent from the patient.

4.10.3. Time is not sufficient to obtain consent from the patient’s LAR.

4.10.4. 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.

4.11. The IRB HUD Continuing Review application will be reviewed via expedited review process (as per HRPP policy 2.3; Expedited Review).

ADMINISTRATIVE APPROVAL:
BRUCE G. GORDON, MD IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS
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POLICY AMENDED:
➢ REVISED FEBRUARY 12, 2018
➢ INITIAL JANUARY 12, 2016
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 IRB approval at a convened meeting.

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.

2.2. It is policy of the Organization 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.

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)].

   3.1.1. Life-threatening: Diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted.

   3.1.2. 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 General Considerations
4.1. Emergency Use of unapproved drugs or biologics does not constitute human subject research under HHS regulations. If the administration of the test article is subject to HHS regulations outcome of such care cannot be included in any report (for example, research article in a journal). However, Emergency use of unapproved drugs or biologics is considered a clinical investigation under FDA regulations, and data obtained during emergency use of the test article is subject to FDA inspection and may be required to be submitted to FDA in a marketing application.

4.2. 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.
4.3. 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 agent, 2) the treating physician obtains FDA approval of an expanded access submission, and 3) prospective IRB review and approval can and will be obtained.

See HRPP policy 6.1 (Research Involving Investigational and Marketed Drugs), section 7.1.

4.4. Emergency Use may be appropriate when an IND/IDE does not exist for the test article but there is reason to believe the patient would benefit, or when an IND/IDE exists and either there is no available clinical investigation, or the subject is not eligible for an available clinical investigation.

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:

5.1.1. The test article has not been used at the Organization to date under the FDA emergency use provisions. However, see section 7.9 below.

5.1.2. The patient is suffering from a life-threatening or severely debilitating condition.

5.1.3. 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.

5.1.4. When possible and/or required, the holder of the IND or IDE (sponsor or device developer) has authorized the emergency use.

5.1.5. 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.

5.1.6. 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.

7.0 Procedures for Emergency Use of a Test Article

7.1. The treating physician should contact the ORA (during normal work hours at 402-559-6463). An IRB Administrator will document the call, obtain pertinent information about the proposed
emergency use, notify the IRB Executive Chair, and instruct the treating physician to contact the IRB Executive Chair/designee to verbally justify the emergency use of the test article.

7.2. The treating physician should contact the IRB Executive Chair/designee directly after normal work (402 888-1125 or 402 680-0965) to verbally justify the emergency use of the test article. The Executive Chair/designee will subsequently contact the IRB Administrator during work hours.

7.3. The IRB Executive Chair/designee must verbally concur that the proposed emergency use has met all the requirements of 21 CFR 56.102(d), 21 CFR 56.104(c), and the criteria in section 5.0 above.

7.4. The IRB Executive Chair/designee will notify the IRB Administrator of his/her concurrence concerning the proposed emergency use and the IRB Administrator will issue an IRB acknowledgement of emergency use. The IRB database will be updated accordingly.

7.5. The IRB Executive Chair/designee will complete the Emergency Use Notification Report and forward it to the ORA promptly.

7.6. If a test article is an investigational drug or biologic, and there is sufficient time, the treating physician must:

   7.6.1. Contact the Chair of the P&T Committee/designee and obtain a P&T emergency use approval.

   7.6.2. Notify the Executive Director of the Pharmacy or Investigational Drug Pharmacist of the emergency use, and provide information concerning financial responsibility for the pharmacy costs of the test article.

7.7. The treating physician must complete and submit the Emergency Use of a Test Article Report to the IRB within five business days following initiation of the treatment. [21 CFR 56.104(c)].

7.8. The Emergency Use of a Test Article Report will be provided to the IRB as a notification at the next full IRB meeting.

7.9. Any subsequent use of the test article must have prospective IRB review and approval.

Note: 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”).

7.10. If the physician decides not to use the test article the IRB Administrator must be promptly notified.

8.0 Informed Consent

8.1. The treating physician should be prepared to obtain written informed consent from the patient or the patient’s legally authorized representative (LAR) unless conditions in section 8.4 below are met.

8.2. The Consent Form should be based on the standard IRB Emergency Use template available on the IRB website (https://www.unmc.edu/irb/forms/examples.html). Alternatively the sponsor’s ICF with an addendum containing local information can be used.

   8.2.1. The ICF must comply with the requirements of 21 CFR 50.25 (Basic and Additional Elements of Consent) and HRPP policy #5.1 (Obtaining Informed Consent from Research Subjects), section 4.1.

   8.2.2. The elements of informed consent should be worded to reflect the nature of the emergency situation (that is, 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).

8.2.3. The ICF must include HIPAA required information and a clear disclosure of the financial obligations of the patient.

8.3. If there is sufficient time, the ICF should be reviewed by the IRB Executive Chair/designee before consent is obtained.

8.4. Informed consent is not required if both the treating physician and a physician who is not otherwise participating in use of the agent certify in writing all of the following [21 CFR 50.23(a)]:

8.4.1. The subject is confronted by a life-threatening situation necessitating the use of the test article.

8.4.2. Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from, the subject.

8.4.3. Time is not sufficient to obtain consent from the subject's legal representative.

8.4.4. No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the subject'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.

8.5. 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.

ADMINISTRATIVE APPROVAL:
BRUCE G. GORDON, MD  IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS
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POLICY AMENDED:
➢ REVISED FEBRUARY 12, 2018
➢ INITIAL JANUARY 12, 2016
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. Subsequent use of stored HBM in research is addressed in HRPP policy 7.2 (Use of Human Biological Material in Research).

2.0 Policy
It is the policy of the Organization that excess or additional HBM may be collected for future unspecified research as part of an addendum study attached to another protocol, or as a free standing tissue banking protocol, 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: includes (but is not limited to) 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).

3.2. Excess HBM refers to HBM that is leftover after research or clinically indicated tests are conducted, and would otherwise be discarded.

3.3. Additional HBM refers to HBM that is collected for the purposes of the research, and would not otherwise have been collected had the subject not been participating; or HBM that is collected solely for banking.

3.4. Identifiable HBM refers to HBM for which the identity of the subject is or may readily be ascertained by the investigator or associated with the HBM, as per 45 CFR 46.102(e)(6).

Note: Per Federal regulations, what constitutes “identifiable” will be re-examined on regular occasions; therefore, HBM currently considered not identifiable may become identifiable in the future as technologies and techniques change.

3.5. Human Biological Material (HBM) Bank (also referred to as biobank or biorepository) is a collection of human biological materials that are stored for future use in research. Samples may be obtained from specific IRB-approved trials (involving only that group of subjects participating in the associated trial), or may be collected as part of an IRB approved banking protocol involving subjects with a particular disease or condition, or involving random groups of subjects without regard to disease or condition, or normal healthy persons. Biobanks may also be composed of already existing HBM collected during the course of routine clinical care (for example, leftover clinical material in a Pathology department).

3.5.1. HBM bank may be non-local, usually associated with a cooperative group, another academic or research institution, or a research sponsor or commercial entity. The IRB recognizes that the investigators at UNMC will not have control over what studies are performed utilizing HBM obtained through these banks.

3.5.2. HBM Bank may be located within the Organization or operated entirely, or in part, by an investigator affiliated with the Organization.
4.0 IRB Review and Consent Requirements

4.1. The collection of identifiable HBM into an bank, whether as an addendum to another (clinical) protocol, or as a free standing HBM banking protocol, constitutes human subject research, and will be reviewed in accordance with all applicable federal regulations and HRPP policies.

4.2. The collection of HBM into an HBM bank may qualify for expedited review (under categories 2, 3 or 5), as per HRPP policy 2.3 (Expedited Review).

4.3. The collection of existing HBM into an HBM bank may be exempt as follows:
   4.3.1. Prior to the effective date of the Revised Rule, the collection of HBM into an HBM bank may be exempt under 45 CFR 46.101(b)(4).
   4.3.2. Following the effective date of the Revised Rule, the collection of HBM into an HBM bank may be exempt under rev 45 CFR 46.104(d)(4). The Organization does not utilize the exemption under 45 CFR 46.104(d)(7).

4.4. The collection of identifiable HBM into a bank requires informed consent of the person from whom the tissue is obtained.
   4.4.1. If the HBM to be banked will be collected as an addendum to another (clinical) protocol, separate informed consent must be obtained from the subject.
   4.4.2. Collection of HBM for banking cannot be a requirement for participation in another study for which there is the potential of direct subject benefit.
   4.4.3. Excess HBM obtained from persons who refuse to consent to HBM banking may not be de-identified and banked.

4.5. If HBM is identifiable, the informed consent must include basic and additional elements of consent related to biospecimens as per 45 CFR 46.116.

4.6. The banking of excess discarded de-identified HBM obtained solely for clinical purposes does not constitute human subject research subject to 45 CFR 46. However, where the donor of the HBM is known and reasonably accessible, consent of the donor is respectful.

5.0 Commercialization of Banked Human Biological Material

5.1. It is reasonable to expect that the possibility exists that banked HBM may be used for commercial profit at some time in the future. Therefore, the consent form must include a statement that the subject’s HBM (even if identifiers are removed) may be used for commercial profit and must state whether the subject will or will not share in this commercial profit. This statement must not contain any exculpatory language.

5.2. If the bank will be housed within the Organization, the consent form must contain the standard statement indicating that the donated HBM is the property of the Organization.

5.3. If the bank will be housed outside the Organization, the consent form must address the issue of who owns the HBM based on the agreement with the owner of the bank.

5.4. The ICF is not meant to serve as a commercial contract where subject compensation is presented. Commercial compensation as negotiated by the researcher, representatives of the Organization, the subject, and their legal counsel is presented in a document separate from the ICF.
ADMINISTRATIVE APPROVAL:
BRUCE G. GORDON, MD  IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS
CHRISTOPHER KRATOVIL, MD  INSTITUTIONAL OFFICIAL

POLICY AMENDED:
- REVISED JANUARY 25, 2018
- INITIAL JANUARY 14, 2016
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 be used in research in accordance to 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 (but is not limited to) 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).

3.2. Identifiable HBM refers to HBM for which the identity of the subject is or may readily be ascertained by the investigator or associated with the HBM.

   3.2.1. At a minimum, HBM is identifiable when it is associated with any of the 18 HIPAA identifiers.

   Note: Following the effective date for the Revised Rule, what constitutes “identifiable” will be re-examined on regular occasions; therefore, HBM currently considered not identifiable may become identifiable in the future as technologies and techniques change.

3.3. Coded HBM refers to HBM which is associated with a code which can be used to indirectly identify the donor of the HBM.

   3.3.1. Coded HBM is considered identifiable for the purposes of this and other HRPP policies unless:

       3.3.1.1. Specimens were not collected specifically for the research AND

       3.3.1.2. The investigators cannot readily ascertain the identity of the individuals.

4.0 IRB Review and Consent Requirements

4.1. The use of identifiable HBM previously stored in an HBM bank or pathology archive constitutes human subject research, and will be reviewed in accordance with all applicable federal regulations and HRPP policies.

4.2. The use of identifiable HBM previously stored in an HBM bank or pathology archive requires informed consent of the donor, unless:

   4.2.1. Consent can be waived under 45 CFR 46.116(d) (or rev 45 CFR 46.116(f)).

   4.2.2. Consent obtained at the time the HBM was obtained and banked was sufficiently detailed with regard to the future use of the HBM that a reasonable person would expect that the consent would permit the types of research conducted.
4.3. The use of non-identifiable HBM previously stored in an HBM bank does not constitute human subject research subject to 45 CFR 46; therefore, no IRB review is required and no informed consent is needed.

4.3.1. Under FDA regulations, clinical investigations using human specimens (even those that are non-identifiable) conducted in support of premarket submissions to FDA are considered human subject investigations, and therefore subject to the informed consent requirements of 21 CFR 50.20. However, FDA intends to exercise enforcement discretion as to the informed consent requirements for clinical investigators, sponsors, and IRBs if an in vitro diagnostic device investigation is performed and the requirements in section 4 of FDA Guidance “Informed Consent for In Vitro Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable” (April 25, 2006) are met.

4.4. The use of coded HBM previously stored in an HBM bank or pathology archive constitutes human subject research, and requires IRB review, unless (1) the HBM was not collected specifically for the proposed research AND (2) the investigator cannot readily ascertain the identity of the donors of the HBM. If both these conditions are met, the HBM is considered non-identifiable, and no IRB review is required.

4.5. If the coded HBM is identifiable (as above), informed consent is required unless:

4.5.1. Consent can be waived under 45 CFR 46.116(d) (or rev 45 CFR 46.116(f)).

4.5.2. Consent obtained at the time the HBM was obtained and banked was sufficiently detailed with regard to the future use of the HBM that a reasonable person would expect that the consent would permit the types of research conducted.

4.6. The use of HBM previously stored in an HBM bank may qualify for expedited review (under category 5), as per HRPP policy 2.3 (Expedited Review).

4.7. The use of HBM previously stored in an HBM bank may be exempt under 45 CFR 46.101(b)(4) (prior to the effective date of the Revised Rule), or rev 45 CFR 46.104(d)(4) (following the effective date of the Revised Rule). The Organization does not utilize the exemption under rev 45 CFR 46.104(d)(8).

**ADMINISTRATIVE APPROVAL:**
BRUCE G. GORDON, MD  IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS
CHRISTOPHER KRATOCHVIL, MD  INSTITUTIONAL OFFICIAL

**POLICY AMENDED:**
- **REVISED JANUARY 25, 2018**
- **INITIAL JANUARY 14, 2016**
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, and for research use of data from a registry.

2.0 Policy
2.1. It is the policy of the Organization that internal registries, as defined in section 3.1 below, utilized, either wholly or in part, for human subject research must be reviewed and approved by the IRB. All IRB approved registries must comply with the following requirements.

2.1.1. The purpose and goals of the registry are clearly justified.
2.1.2. The registry complies with all applicable requirements of HHS regulations at 45 CFR 46.
2.1.3. The minimum amount of PHI necessary to accomplish the purpose and goals of the registry is entered into the registry.
2.1.4. There is acceptable security to safeguard the confidentiality and integrity of data in the registry, and which satisfies the requirements of Organizational policies regarding data and PHI security.
2.1.5. There are procedures in place for release of PHI from the registry that comply with Organization privacy policies.
2.1.6. As necessary, a Data Use Agreement (DUA), Data Transfer Agreement (DTA), or a Business Associate Agreement (BAA) is in place before any data is released.

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.

3.0 Definitions
3.1. Internal Data Registry is a repository of clinical or other patient 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; or d) other non-research purposes.

3.2. External Data Registry is a repository of clinical or other patient 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; or d) other non-research purposes.

3.3. 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 that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (for example, a medical record).

3.4. Identifiable Private Information refers to private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information, as per 45 CFR 46.102(e)(5).
Note: Per Federal regulations, what constitutes “identifiable” will be re-examined on regular occasions; therefore, HBM currently considered not identifiable may become identifiable in the future as technologies and techniques change.

4.0 IRB Review and Consent Requirements for Internal Data Registries

4.1. The creation of a registry that is utilized, either wholly or in part, for human subject research is subject to IRB review, and healthcare professionals who develop and maintain the registry must submit a Data Registry Application. If the registry will also include collection of human biological material (HBM) the Human Biological Material Banking Application must be completed instead.

4.2. The collection of identifiable private information into a registry that is utilized, either wholly or in part, for human subject research constitutes human subject research, and will be reviewed in accordance with all applicable federal regulations and HRPP policies. Specifically, the IRB must find that

4.2.1. The registry complies with all applicable requirements of HHS regulations at 45 CFR 46.
4.2.2. The purpose and goals of the registry are clearly justified.
4.2.3. The minimum amount of PHI necessary to accomplish the purpose and goals of the registry is entered into the registry.
4.2.4. There is acceptable security to safeguard the confidentiality and integrity of data in the registry, and which satisfies the requirements of Organizational policies regarding data and PHI security.
4.2.5. There are procedures in place for release of PHI from the registry that comply with Organization privacy policies.
4.2.6. As necessary, a Data Use Agreement (DUA), Data Transfer Agreement (DTA), or a Business Associate Agreement (BAA) is in place before any data is released.

4.3. The collection of identifiable private information into a data registry that is utilized, either wholly or in part, for human subject research may qualify for expedited review (as per HRPP policy 2.3) or may be exempt (as per HRPP policy 2.6).

4.4. The collection of identifiable private information into a registry that is utilized, either wholly or in part, for human subject research requires informed consent of the person from whom the data is obtained.

4.4.1. If the data to be entered into the registry will be collected as an addendum to another (clinical) protocol, separate informed consent must be obtained from the subject.
4.4.2. Collection of data for a registry cannot be a requirement for participation in another study for which there is the potential of direct subject benefit.

4.5. The informed consent must include basic and additional elements of consent related to identifiable private information as per 45 CFR 46.116.

5.0 ORA Review and Consent Requirements for External Data Registries

5.1. Submission of clinical data with or without identifiers that has been collected solely for clinical purposes to an external data registry (that is utilized, either wholly or in part, for human subject research) does not constitute engagement in human subject research. It is therefore not subject to UNMC IRB approval, provided the healthcare professional submitting the data (1) is not involved
with the research (aside from submitting the clinical data), and (2) will not, in the future, use data in
the external registry for research in which he/she is participating.

5.1.1. Healthcare professionals who submit clinical data to external data registries as
described above must submit the Data Registry Application to the ORA. The information will
be entered into the IRB database for tracking purposes.

5.1.2. If the clinical data contains PHI, authorization for disclosure of the PHI to the External
Data Registry must be obtained in accordance with 45 CFR 164.508(c), or authorization must
be waived by the UNMC IRB or the Privacy Board associated with the External Data Registry
in accordance with 45 CFR 164.512(i).

5.1.3. 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, Assistant Vice-Chancellor for Regulatory Affairs, in
consultation with the IO, may require submission of additional information regarding
administration of the registry, data security, and processes for release of data.

5.2. If the healthcare professional submitting the data is involved with the research (for example,
will be an author on manuscripts, or plans to subsequently use data in the registry for different
research purposes) then the Organization is engaged, and the submission of identifiable private
information constitutes research. It is therefore subject to UNMC IRB approval (per section 4.2
above) and the requirement for informed consent (per sections 4.5 and 4.6 above).

5.3. The appropriate agreements (Data Use Agreement, Data Transfer Agreement) must be fully
executed prior to final release of the Data Registry or Medical Records Research.

6.0 Research Use of Data from a Registry

6.1. The Data Registry Application must be submitted in accordance with HRPP policy 2.1
(Submission of Items for Review by the IRB).

6.2. Applications which require review by the full IRB will be processed and reviewed in
accordance with HRPP policy 2.2.

6.3. Applications that are eligible for review by the expedited method will be processed and
reviewed in accordance with HRPP policy #2.3.

6.4. Applications which appear to be eligible for exemption will be processed and reviewed in
accordance with HRPP policy #2.6.

6.5. The use of identifiable private information previously stored in a data registry requires informed
consent of the donor, unless:

6.5.1. Consent can be waived under 45 CFR 46.116(d) (or rev 45 CFR 46.116(f)), and, if
PHI is involved, authorization is waived under 45 CFR 164.512(i).

6.5.2. Consent obtained at the time the data was placed into the registry was sufficiently
detailed with regard to the future use of the data that a reasonable person would expect that
the consent would permit the types of research conducted.

ADMINISTRATIVE APPROVAL:
BRUCE G. GORDON, MD  IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS
CHRISTOPHER KRATOCHVIL, MD  INSTITUTIONAL OFFICIAL

POLICY AMENDED:
➢ REVISED MARCH 2, 2018
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements for reviewing and approving research involving the use of fetal tissue (FT) and human embryonic stem cells (hESC).

2.0 Policy
2.1. It is the policy of the Organization that all research, including human embryonic stem cells (hESCs), will be conducted in accordance with Federal and Nebraska state law, and University of Nebraska Board of Regents policies.

2.2. It is the policy of the Organization that all research involving human embryonic stem cells, including fetal tissue research, will be reviewed and approved by the UNMC Scientific Research Oversight Committee (SROC) and, if approved, by the Institutional Review Board prior to any conduct of research.

3.0 General Requirements for Research Involving Human Embryonic Stem Cells (hESCs)
3.1. Research involving the use of hESCs, regardless of the source of funding, is limited to cell lines from the NIH Human Embryonic Stem Cell Registry.

3.2. The NIH Registration Number for the hESC line must be cited in the application to the SROC.

3.3. All research involving hESCs will be reviewed and approved by the SROC, and subsequently by the Institutional Review Board prior to the research being conducted.

4.0 General Requirements for Research Involving Fetal Tissue
4.1. Research involving the use of fetal tissue, regardless of the source of funding, is limited to tissues obtained from the NIH funded University of Washington fetal tissue bank. Requests from other sources of fetal tissue must be approved and will be considered on a case by case basis after review of their procedures and sources of acquisition as determined by the chancellor or his/her designee.

4.2. Tissue must be accompanied by a copy of the approval letter from the IRB which has jurisdiction over the tissue bank.

4.3. The Tissue Bank provider can only be compensated for the costs of preparing the tissue for shipping and transport to UNMC.

4.4. Investigators conducting research involving fetal tissue must demonstrate how they evaluated other non-fetal tissue sources, and these efforts must be documented at the time of initial and continuing review.
5.0 Scientific Research Oversight Committee (SROC)

5.1. The purpose of the SROC is to provide oversight of all issues related to use of hESC lines and fetal tissues for research, and to facilitate education of investigators involved in hESC and fetal tissue research.

5.2. The SROC is composed of a chair, vice-chair and no less than 6 additional members, with expertise in topics likely to be reviewed by the committee (for example, developmental biology, stem cell research, molecular biology, assisted reproduction and ethical and legal issues in hESC research), and includes one or more independent representatives of the lay public.

5.3. The SROC must have suitable scientific, medical and ethical expertise to conduct its own review and should have the resources needed to coordinate the management of various other reviews required for a particular protocol (for example, animal use, recombinant DNA, human subject research).

5.4. The SROC is not a subcommittee of the IRB.

5.5. The SROC shall be scheduled to meet every month or as needed to review proposals submitted, as determined by the Chair. If there are no items to review on any given month the meeting may be cancelled.

5.6. The SROC will conduct a review of 1) initial proposals to use hESCs, fetal cells and fetal tissue and/or their derivatives, 2) amendments to approved protocols and 3) continuing review of approved protocols.

5.7. The SROC shall have the authority to approve, approve with required modifications, table, or disapprove research involving hESC or fetal tissue.

5.8. The SROC will also discuss areas of research that may have ethical implications prior to any proposals being submitted and propose new policies for UNMC based on national policies or regulations as they are developed.

6.0 Procedures for Review of Research

6.1. Investigators must complete the SROC Application.

6.2. The SROC will review initial research proposals and requests for changes in existing protocols, and conduct continuing review (CR) at a Full Committee Review (FCR) meeting when a quorum of the committee is present including at least one non-affiliated member. Real time electronic communication is permitted.

6.3. The SROC Administrator will conduct a pre-review of the submission before the FCR meeting.

6.4. To approve the research the SROC must find and document that

6.4.1. The PI and other involved research personnel have the knowledge and expertise to carry out the research described in the protocol in order to obtain scientifically valid data.

6.4.2. The PI has sufficient resources, funding, and personnel to conduct the research.

6.4.3. The research design is scientifically sound and has scientific merit.

6.4.4. There are no other scientifically equivalent alternatives to the use of hESCs or fetal tissue (as applicable), which can be used to pursue the scientific objectives.

6.4.5. The use of hESCs or fetal tissue, as applicable, in the research is otherwise in compliance with Federal and Nebraska state law, and Board of Regents and University policies.
6.4.6. For research involving hESC lines, the research uses only NIH approved hESC lines in compliance with the University of Nebraska and Board of Regents policy and any applicable state laws.

6.4.7. For research involving fetal tissue, the tissue has been obtained from the University of Washington NIH funded fetal tissue bank, or other source as specified in section 4.1 above.

6.5. Approval requires a vote of the majority of the members present.

6.6. Research approved by the SROC must subsequently be reviewed by the UNMC IRB at a full board meeting, in accordance with all standard IRB policies for review (HRPP policies 2.2- Full IRB Review, or 2.3-Expedited Review). The IRB will review (a) the SROC research application, (b) all pertinent SROC correspondence, and (c) all other relevant documents.

6.7. The IRB must find and document the criteria listed above in section 6.3; in addition the IRB must find that the SROC has certified its approval that the research complies with the foregoing criteria.

6.8. All approved research will undergo continuing review no less often than annually, unless more frequent review is required by the SROC or the IRB, or there is any change in federal, state, or Board of Regents policy relevant to this research. The SROC will conduct CR at a FCR meeting. The UNMC IRB will conduct CR at a full board meeting after the SROC has re-approved the protocol.

6.9. The SROC will review amendments which require a change in human biological material, procedures, and/or study objectives by FCR. Amendments must also be reviewed and approved by the UNMC IRB. Other minor amendments, such as change in personnel, will be reviewed by expedited review which only requires approval by the chair/designee.

6.10. If the SROC disapproves a protocol or amendment the PI has the right to appeal to the committee who is authorized to make the final decision.

6.11. The SROC will inform the UNMC Chancellor of all initial protocols, amendments and continuing reviews which have been approved or disapproved on a quarterly basis or at his/her request.

**Administrative Approval:**

JENNIFER LARSEN, MD   VICE CHANCELLOR FOR RESEARCH
CHRISTOPHER KRATOCHVIL, MD   INSTITUTIONAL OFFICIAL
BRUCE G. GORDON, MD   IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS

**Policy Amended:**

- Initial September 11, 2017
- Revised January 15, 2018
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.

This policy does not make a differentiation between medical and non-medical AEs.

AEs occurring in the context of an FDA regulated clinical investigation are defined as any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug related (21 CFR 312.32(a)).

3.1.1. Unexpected AE: An AE in which the specificity, severity, or frequency is not consistent with (a) the IRB application and detailed protocol; (b) Risk information in the ICF; (c) the current investigator’s brochure; or (d) Investigational plan or protocol

3.1.2. Related AE: An AE which there is clear causality, or a strong temporal relationship with the research intervention or procedure.

3.1.3. Possibly Related AE: An AE which may have been caused by the research intervention or procedure, but there is insufficient information attribute clear causality. Am attribution as “possibly related” requires less certainty than “related”; however, there must still be evidence suggesting such a causal relationship (for example, temporal relationship to the intervention, known pharmacological property of drug, exclusion of other causes).

3.1.4. Serious AE: An AE which results in any of the following outcomes:

3.1.4.1. Death
3.1.4.2. A serious injury, or otherwise seriously impacts on the health, safety or welfare of subjects
3.1.4.3. Inpatient hospitalization or prolongation of existing hospitalization
3.1.4.4. Required intervention to prevent permanent impairment or damage
3.1.4.5. Persistent or significant disability or incapacity
3.1.4.6. Congenital anomaly or birth defect
3.1.4.7. Other serious important medical events
3.1.4.8. Any event that requires treatment to prevent one of the outcomes listed above

Note: Under FDA IND regulations 21 CFR 312.32(a)) a serious AE is one which results in any of the following outcomes: death, a life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or a congenital anomaly/birth defect; or one which requires medical or surgical intervention to prevent one of the outcomes listed.

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 (per 21 CFR 812.3(s)).

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). Significantly, an AE may be expected or unexpected, related or unrelated, or serious or not serious. An UADE is related (“caused by, or associated with”) and unexpected (“not previously identified”).

3.2.1. Serious UADE: An UADE which results in any of the outcomes listed in section 3.1.4 above, or one in which required intervention to prevent permanent impairment or damage

3.3. Internal AE or 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.

3.4. External AE or 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).

4.0 Procedures for Reporting AEs/UADEs

4.1. Internal AEs and UADEs

4.1.1. Internal AEs must be reported to the IRB if the PI determines that all of the following conditions are met:

4.1.1.1. The AE is unexpected.

4.1.1.2. The AE is related to, or possibly related to, the research intervention or procedures.

4.1.2. All internal AEs/UADEs that meet the conditions listed above must be reported promptly to the IRB (in no case later than two 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.

4.1.3. Internal AEs occurring more than 90 days after the subject has completed study interventions are generally considered “unrelated” and are therefore not reportable; exceptions include congenital anomalies or birth defects, and cancer.

4.1.4. Internal UADEs must be reported for as long as the device is classified as investigational.

4.1.5. Internal AEs/UADEs are reported to the IRB on-line through RSS (https://net.unmc.edu/rss).
4.2. External AEs

4.2.1. External AEs must be reported to the IRB if the PI determines that all of the following conditions are met:

4.2.1.1. The external AE is unexpected.

4.2.1.2. The external AE is related or possibly related to the research intervention or procedure.

4.2.1.3. The external AE is serious.

4.2.1.4. The external AE requires a change to the protocol and informed consent form and re-consent of subjects.

4.2.2. All external AEs that meet the conditions listed above must be reported promptly to the ORA (in no case later than five business days following PI notification that the event occurred)

4.2.2.1. The IRB will be notified of External AEs that meet the above criteria

4.2.2.2. It is expected that the submission of a report of an External AE which satisfies the criteria of section 4.2.1 will be followed by a Change Request, and the IRB will review the Change Request in accordance with HRPP policy 2.4 (IRB Review of Changes in Previously Approved Research).

4.2.3. 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.

4.2.4. 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.

4.2.5. 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

4.4. External UADEs which occur at other institutions must be reported to the UNMC IRB (in no case no later than five business days following PI notification from the sponsor that the event occurred) in accordance the requirements of 21 CFR 812.150(b)(1).

4.5. The PI should submit the report received from the sponsor along with any required Change Request.

4.6. 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 report will be reviewed by the IRB Executive Chair/designee to determine if the AE satisfies the criteria in section 4.1.1 (unexpected, and related to, or possibly related to, the research) or the event is a UADE (related and unexpected).

5.2. The IRB Executive Chair/designee will take all actions necessary to protect human subjects including, if warranted, immediate halting of the study (per HRPP policy 8.6: Study Hold, Suspension, and Termination).
5.3. Upon completion of the IRB Executive Chair/designee review, all internal AEs which satisfy section 4.1.1, and all internal or external UADEs will be reviewed by the convened IRB.

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 (Full IRB Review).

6.2. To approve the AE report, the IRB must ensure the following criteria are met:

6.2.1. The risk/benefit relationship of the research remains acceptable.

6.2.2. No additional changes in protocol are necessary to further minimize risk.

6.2.3. No additional monitoring of data is necessary to ensure the safety of subjects.

6.2.4. The consent document(s) as written/revised are acceptable.

6.2.5. 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).

6.3. The IRB must determine whether

6.3.1. Re-consent must be obtained from currently enrolled subjects, and, if so, how soon such re-consent must occur.

6.3.2. Currently enrolled subjects may continue on study.

6.3.3. Further subject accrual is permitted.

6.3.4. Additional information must be provided to past participants

6.3.5. The current continuing review schedule is appropriate.

6.4. The IRB must determine if the AE/UADE is a UP and that the action plan is appropriate in accordance with HRPP policy 8.3 (IRB Review of Unanticipated Problems Involving Risk to the Subject or Others).

7.0 Reporting AEs/UADEs that are UPs to Institutional Officials, OHRP, FDA, and Department or Agency Heads

7.1. All required reports will be submitted in accordance with HRPP policy 8.7 (Reporting Incidents to Institutional Officials and Federal Agencies).

Administrative Approval:

BRUCE G. GORDON, MD  IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS

CHRISTOPHER KRATOVIL, MD  INSTITUTIONAL OFFICIAL

Policy Amended:

➢ NOVEMBER 27, 2017

➢ INITIAL JANUARY 18, 2016
1.0 Purpose
The purpose of this policy and procedure is to describe the procedures for reporting complaints to the IRB and the process for review of complaints.

2.0 Policy
2.1. It is policy of the Organization that complaints involving the human research protection program be promptly reported to the IRB and appropriate Organizational officials, and be investigated and resolved as appropriate. For the purposes of this policy “complaints” includes problems, concerns, or questions raised by current, prospective, or post-research participants or their designated representatives.

2.2. It is the policy of the Organization that 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 HRPP policy 8.7 (Reporting Incidents to Institutional Officials and Federal Agencies).

3.0 Reporting Complaints to the ORA
3.1. Complaints may be received by the Principal Investigator, other investigators, study staff, IRB members, IRB staff, the Research Subject Advocate, or any other Organizational officials.

3.2. Complaints may also be received through the IRB website (http://www.unmc.edu/irb), utilizing the “Report a Problem or Complaint” tab, or University of Nebraska’s ethics hotline (EthicsPoint) at www.nebraska.ethicspoint.com

3.3. Any complaint that is received by the investigator or study staff that involves risk to participants or others, or changes the risk-potential benefit profile of the study, or which cannot be resolved by the investigator must be promptly reported to the IRB.

3.4. Any complaint that is received by the investigator or study staff that does not involve risk to participants or others, or does not change the risk-potential benefit profile of the study, and that is resolved by the investigator should be submitted in a summary format to the IRB for consideration at continuing review.

4.0 ORA Procedures for Reviewing Complaints
4.1. Complaints received by the IRB, or reported to the IRB by the investigators will be reviewed by the appropriate IRB Administrator. Additional information will be obtained from the complainant, the study documents, the investigator or research staff, or from other sources as appropriate.

4.2. Based on this initial review, in consultation with the Executive Chair or designee, the IRB Administrator will determine:

4.2.1. Whether the complaint represents an allegation of non-compliance, an adverse event, or an unanticipated problem involving risk. If so, the complaint will be handled in accordance with HRPP policy 8.1 (IRB Review of Adverse Events or Adverse Device Effects), 8.3 (IRB Review of Unanticipated Problems Involving Risk to the Subject or Others), or 8.4 (Review of Noncompliance Involving the PI and Study Personnel).
4.2.2. Whether the complaint involves risk to participants or others, or changes the risk-potential benefit profile of the study. If so, the complaint will be reported and reviewed by the full IRB at a convened meeting (HRPP policy 2.2: Full IRB Review).

4.2.3. Whether additional actions need to be taken immediately to protect the rights and welfare of human subjects, in accordance with HRPP policy 8.6 (Study Hold, Suspension, and Termination) or section 5.2 below.

4.3. The IO will be notified of all complaints which involve risk to participants or others, or which change the risk-potential benefit profile of the study.

4.4. 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.

5.0 IRB Review of Complaints

5.1. Complaints that do not involve risk to participants or others, or do not change the risk-potential benefit profile of the study are reported in aggregate at continuing review, and will be considered by the IRB in determining whether the research continues to satisfy the criteria for approval.

5.2. Complaints that involve risk to participants or others, or change the risk-potential benefit profile of the study, or which cannot be resolved by the investigator will be reviewed by the full IRB at a convened meeting. The IRB will determine:

5.2.1. Whether the complaint constitutes noncompliance per HRPP policy 8.4 (Review of Noncompliance Involving the PI and Study Personnel).

5.2.2. Whether the complaint constitutes an unanticipated problem involving risk per HRPP policy 8.3 (IRB Review of Unanticipated Problems Involving Risk to the Subject or Others).

5.2.3. Whether the research continues to satisfy the criteria for approval under 45 CFR 46.111, 21 CFR 56.111, and HRPP policy 2.5 (Criteria for IRB Approval).

5.2.4. Whether further actions are necessary to protect the rights and welfare of human subjects. Such actions may include (but are not limited to):

5.2.4.1. Requiring modification of the research protocol or the consent form

5.2.4.2. Notification of current participants if such information may relate to participants’ willingness to continue to take part in the research, with or without requiring re-consent.

5.2.4.3. Requiring additional information be provided to past participants.

5.2.4.4. Modification of the continuing review schedule.

5.2.4.5. Monitoring of the research or the consent process.

5.2.4.6. Study hold, suspension or termination.

5.2.4.7. Referral to other organizational entities.
ADMINISTRATIVE APPROVAL:
BRUCE G. GORDON, MD  IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS
CHRISTOPHER KRATOCHVIL, MD  INSTITUTIONAL OFFICIAL

POLICY AMENDED:
- **Revised January 19, 2018**
- **Initial January 20, 2016**
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. It is the policy of the Organization that 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. It is the policy of the Organization that the full IRB is responsible for determining whether the event, incident, outcome, or complaint meets the criteria for classification as a UP.

3.0 Definitions

3.1. Unanticipated Problems Involving Risk to Subjects or Others (UP):

3.1.1. Any event (incident, experience, or outcome) which meets all of the criteria specified below:

3.1.1.1. The event is unexpected in terms of specificity, severity, or frequency, considering the nature of the research, the characteristics of the subject population, and the information contained in the protocol, protocol-related documents, and the ICF. In addition, the event is not consistent with the expected natural progression of any underlying disease, disorder, or condition of the subject.

3.1.1.2. 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 that the event may have been caused by procedures involved in the research or resulted from participation in the research by the subject.

3.1.1.3. 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.

3.1.2. Though not a required criterion for definition of an event as a UP, 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: 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.
Note: 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 3.1.1 to be met.

Note: UPs may occur in research other than clinical trials, for example social and behavioral research (for example, a stolen laptop or thumb drive containing identifiable information), and may involve risks other than physical harm (for example, 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 8.1 (IRB Review of Adverse Events and Adverse Device Effects).

4.2. Reports of complaints are submitted in accordance with HRPP policy 8.2 (IRB Review of Study Related Complaints).

4.3. Reports of noncompliance are submitted in accordance with HRPP policy 8.4 (Review of Noncompliance Involving the PI and Study Personnel).

4.4. IND safety reports, DSMB reports, or other outcome information on risk are submitted in accordance with HRPP policy 3.2 (Data and Safety Monitoring).

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) must be promptly reported to the IRB via letter or email.

4.5.1. The report must include appropriate identifying information for the research protocol, such as the title, investigator's name, and the IRB project number; a detailed description of the adverse event, incident, experience, or outcome; an explanation of the basis for determining that the adverse event, incident, experience, or outcome represents an unanticipated problem; and a description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the unanticipated problem.

5.0 IRB Review of Potential UPs

5.1. The IRB will review reports under Section 4.1 - 4.5 above in accordance with the criteria specified in HRPP policies 2.2 (Full IRB Review), 8.1 (IRB Review of Adverse Events and Adverse Device Effects), 8.2 (IRB Review of Study Related Complaints), and 8.4 (Review of Noncompliance Involving the PI and Study Personnel), and will make determinations as described in those policies.

5.2. The IRB will determine whether or not the event is a UP in accordance with Section 3.1 of this policy.

5.3. 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.

5.4. In addition to the required actions specified in HRPP policy 2.2 (Full IRB Review), the IRB may consider the following possible actions:

5.4.1. Modification of the protocol.

5.4.2. Modification of the information disclosed during the consent process.

5.4.3. Notification of current participants when such information might relate to participants' willingness to continue to take part in the research.
5.4.4. Providing additional information to past participants.
5.4.5. Requiring current participants to re-consent to participation.
5.4.6. Modification of the continuing review schedule.
5.4.7. Monitoring of the research.
5.4.8. Monitoring of the consent process.
5.4.9. Referral to other organizational entities.

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 8.7 (Reporting Incidents to Institutional Officials and Federal Agencies).

**Administrative Approval:**

Bruce G. Gordon, MD  
IRB Executive Chair & Assistant Vice Chancellor for Regulatory Affairs

Christopher Kratochvil, MD  
Institutional Official

**Policy Amended:**

- Revised November 27, 2018
- Initial April 4, 2016
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

2.1. It is the policy of the Organization that any allegations or reports of noncompliance with Federal Regulations related to the protection of human subjects of research, HRPP policies, or the requirements or determinations of the IRB, must be promptly reported to the IRB and the IO.

2.2. It is the policy of the Organization that 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.

2.3. It is the policy of the Organization that allegations or incidents of noncompliance will be promptly addressed by the ORA/IRB and appropriate action taken in order to ensure protection of the rights and welfare of research subjects.

2.4. It is the policy of the Organization that 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 46.108(a)(4)(i), and 21 CFR 56.108(b)(2) as specified in HRPP policy #8.7 (Reporting Incidents to Institutional Officials and Federal Agencies).

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 # 8.3 (IRB Review of Unanticipated Problems Involving Risk to the Subject or Others).

3.1.1. 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.

3.1.2. Non-serious noncompliance is defined as an incident that does not satisfy the definition of serious noncompliance in Section 3.2 of this policy.

3.1.3. Continuing noncompliance is defined as repeated incidents of the same or substantially similar noncompliance despite appropriate retraining and/or specific corrective
action as directed by the IRB, or of such a nature that an investigator should have reasonably been expected to know that such an action was noncompliance.

3.2. **Allegation of noncompliance** is defined as an unproved assertion of noncompliance.

3.3. **Incident of noncompliance** is defined as a proven noncompliance.

4.0 **Reporting an Allegation of Noncompliance**

4.1. Allegations of noncompliance may be received by the Principal Investigator, other investigators, study staff, IRB members, IRB staff, the Research Subject Advocate, or any other Organizational officials.

4.2. Allegations of noncompliance may also be received through the IRB website (http://www.unmc.edu/irb), utilizing the “Report a Problem or Complaint” tab, or through other electronic reporting systems sponsored by the Organization.

4.3. Lists of deviations from protocol are often provided after a review of CRFs and other materials by a sponsor, CRO or Audit committee. If these deviations are submitted to the ORA they will be reviewed administratively. Violations which represent non-serious noncompliance as defined here do not need to be formally reported to the IRB.

5.0 **ORA Procedures for Reviewing Allegations of Noncompliance**

5.1. Allegations of noncompliance received by the ORA will be reviewed by the appropriate IRB Administrator. Additional information will be obtained from the reporter, the study documents, the investigator or research staff, or from other sources as appropriate.

5.2. Based on this initial review, in consultation with the Executive Chair or designee as necessary, IRB Administrator will determine:

5.2.1. Whether the allegation of noncompliance has a basis in fact.

5.2.1.1. If the IRB Administrator, in consultation with the Executive Chair or designee determines that the episode of noncompliance may represent serious or continuing noncompliance, it will be referred for review by the full IRB at a convened meeting *(HRPP policy 2.2: Full IRB Review)*.

5.2.1.2. If the IRB Administrator, in consultation with the Executive Chair or designee determines that the episode of noncompliance does not represent serious or continuing noncompliance, it will be reported to the full IRB as a notification item *(HRPP policy 2.2: Full IRB Review)*.

5.2.2. Whether the allegation of noncompliance merits further investigation by an IRB Compliance Subcommittee. This determination is made based on the seriousness of the allegation, and the available information regarding the allegation’s basis in fact. If this determination is made, the IO and UNMC Chief Compliance Officer will be informed, and the full IRB will be notified at the next convened meeting that an investigation is ongoing.

5.2.3. Whether additional actions need to be taken immediately to protect the rights and welfare of human subjects, in accordance with *HRPP policy 8.6 (Study Hold, Suspension, and Termination)*.

5.2.4. If the allegation of noncompliance comes from someone other than the investigator then the IRB Administrator or Executive Chair will notify the PI (and other involved individuals)
that there has been an allegation, and the investigator will be provided an opportunity to provide any relevant information and/or records that should be considered.

5.2.5. The PI (and other involved individuals) will be afforded due process, and Whistleblower protection will be provided in accordance with UNMC Policy 8003.

6.0 Procedures for IRB Compliance Subcommittee Investigations

6.1. If the allegation of noncompliance merits further investigation by an IRB Compliance Subcommittee, the subcommittee will be assembled by the IRB Administrator. The subcommittee will consist of the IRB Executive Chair/designee, the Institutional Compliance Officer (UNMC, UNO CHMC or BMC as appropriate), IRB Administrator(s), other IRB members as necessary, and internal consultants as necessary.

6.1.1. A written record of the on-going investigation will be maintained.

6.1.2. As necessary, the subcommittee will obtain additional information from the reporter, the study documents, the investigator or research staff, or from other sources as appropriate.

6.1.3. During the investigation, or at the conclusion of the investigation, the subcommittee will determine whether additional actions need to be taken immediately to protect the rights and welfare of human subjects, in accordance with HRPP policy 8.6 (Study Hold, Suspension, and Termination).

6.1.4. Upon conclusion of an investigation of noncompliance the IRB Administrator will prepare a written report of the results of the investigation.

6.1.4.1. If the Subcommittee finds that the allegation is substantiated, the report will be provided to the full IRB at a convened meeting (HRPP policy 2.2: Full IRB Review), and further action taken by the IRB as per section 7.2 below.

6.1.4.1.1. The report will be provided to the IO, the Institutional Compliance Officer, and the investigator.

6.1.4.1.2. The investigator will be instructed to complete a Noncompliance Report via RSS (https://net.unmc.edu/rss), including a corrective action plan.

6.1.4.2. If the Subcommittee finds that the allegation is not substantiated, the report will be provided to the full IRB as a notification item.

7.0 IRB Procedures for Reviewing Episodes of Noncompliance

7.1. The full IRB will determine:

7.1.1. Whether the episode represents serious and/or continuing noncompliance.

7.1.2. Whether the non-compliance is an unanticipated problem involving risk.

7.1.3. Whether the corrective action plan is adequate.

7.1.4. Whether the research continues to satisfy the approval criteria at 45 CFR 46.111 or 21 CFR 56.111.

7.1.5. Whether subject accrual should be allowed to continue.

7.1.6. Whether currently enrolled subjects should be notified of information related to the noncompliance.
7.1.7. Whether previously enrolled subjects who have completed participation in the study should be notified of information related to the noncompliance.

7.2. After making the determinations above, the IRB may act in accordance with its authority as per §.108 and §.109, and HRPP policies to:

7.2.1. Require modification of protocol or consent forms, require notification and/or re-consent of enrolled subjects, institute monitoring of the research and/or the consent process, require more frequent continuing review.

7.2.2. Audit the research, or any of the investigator’s active or completed studies.

7.2.3. Require additional investigator or study staff education and training.

7.2.4. Suspend or terminate the research.

7.2.5. Notify other components of the Organization, including senior Organizational Officials, Nebraska Medicine or CHMC Risk Management or QA/QI, General Counsel, or Research Integrity Officer (RIO).

7.2.6. Make recommendations to the IO regarding restrictions on, or termination of, other protocols submitted by the investigator.

7.2.7. Make recommendations to the IO regarding other sanctions against the investigator or staff, withdrawal or modification of pending or published manuscripts and/or destruction of research data or biological materials.

8.0 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 (Reporting Incidents to Institutional Officials and Federal Agencies).

ADMINISTRATIVE APPROVAL:
BRUCE G. GORDON, MD  IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS
CHRISTOPHER KRATOCHVIL, MD  INSTITUTIONAL OFFICIAL

POLICY AMENDED:
➢ REVISED JANUARY 19, 2018
➢ INITIAL JANUARY 20, 2016
Title: Noncompliance by the IRB or Other Components of the HRPP

1.0 Purpose
The purpose of this policy and procedure is to describe: 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. Allegations or reports of noncompliance by members of the IRB, ORA staff, or others involved in the HRPP with Federal Regulations related to the protection of human subjects of research, or 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 reviewed 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) and 21 CFR 56.108(b)(2) as required, in accordance with HRPP policy 8.7 (Reporting Incidents to Institutional Officials and Federal Agencies).

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 8.4 (Review of Noncompliance Involving the PI and Study Personnel).

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 8.3 (IRB Review of Unanticipated Problems Involving Risk to the Subject or Others).

3.1.1. 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.

3.1.2. Non-serious noncompliance is defined as an incident that does not satisfy the definition of serious noncompliance in section 3.2 of this policy.
3.1.3. **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, or HRPP policies.

*Note: In general, to represent continuing noncompliance, the events must have recurred after appropriate retaining and/or specific corrective action plan, or must be of such a nature that an individual should have reasonably been expected to know that such an action was noncompliance.*

3.2. **Allegation of noncompliance** is defined as an accusation or unproved assertion of noncompliance.

3.3. **Incident of noncompliance** is defined as a proven noncompliance.

4.0 **Reporting an Allegation of Noncompliance**

4.1. Allegations of noncompliance may be received by, or made by, an investigator, study staff, IRB members, IRB staff, the Research Subject Advocate, any other Organizational officials, or by FDA, OHRP or other federal agency.

4.2. Allegations of noncompliance can be received through the UNMC IRB website ([http://www.unmc.edu/irb](http://www.unmc.edu/irb)), utilizing the “Report a Problem or Complaint” tab, or though other electronic reporting systems sponsored by the Organization.

5.0 **Procedures for Reviewing Noncompliance**

5.1. Allegations or incidents of noncompliance are reviewed by the UNMC Chief Compliance Officer. Additional information will be obtained from the reporter, ORA or HRPP records, or from other sources as appropriate.

5.2. Based on this initial review, the UNMC Chief Compliance Officer will determine:

5.2.1. Whether the allegation has a basis in fact, or

5.2.2. Whether the allegation merits further investigation.

5.3. The UNMC Chief Compliance Officer will promptly initiate all necessary action(s) to ensure that human subjects are fully protected, and the interests of the Organization are appropriately considered. These actions could include, but are not limited to, any or all of the following:

5.3.1. Requesting that the Executive Chair convene an emergency meeting of the IRB ([HRPP policy 2.2: Full IRB Review](#)).

5.3.2. Recommend the IO and/or the IRB Executive Chair immediately suspend IRB approval of some or all research activities in accordance with [HRPP policy 8.6: Study Hold, Suspension, and Termination](#).

5.3.3. Refer the allegation or incident of noncompliance for investigation by a specially appointed ad hoc Subcommittee.

5.4. A record of the actions taken under this policy by the Chief Compliance Officer will be maintained on file.

5.5. All involved individuals will be afforded due process, and Whistleblower protection will be provided in accordance with [UNMC Policy 8003](#).
5.6. Upon conclusion of an investigation of noncompliance the UNMC Chief Compliance Officer will report of the results of the investigation to the IO, other Organizational officials, and to the IRB as appropriate.

5.7. The UNMC Chief Compliance Officer may recommend to the IO actions which are appropriate for the circumstances of noncompliance. These actions could include, but are not limited to, any or all of the following:

5.7.1. Make modifications to HRPP policies and/or procedures.

5.7.2. Inform the Organization’s general counsel of the noncompliance.

5.7.3. Refer the noncompliance to Nebraska Medicine or CHMC Risk Management for further action.

5.7.4. Take other actions against the involved parties.

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 (Reporting Incidents to Institutional Officials and Federal Agencies).

Administrative Approval:
Bruce G. Gordon, MD  IRB Executive Chair & Assistant Vice Chancellor for Regulatory Affairs
Christopher Kratochvil, MD  Institutional Official

Policy Amended:
- Revised January 11, 2018
- Initial January 20, 2016
1.0 Purpose
The purpose of this policy and procedure is to describe the IRB’s authority to: a) accept a study hold; b) impose a study hold; c) suspend IRB approval of research; d) terminate IRB approval of research, and e) implement an Organizational directed termination of IRB approval of research.

2.0 Policy
2.1. It is the policy of the Organization that the IRB has the authority to:
   2.1.1. Accept a study hold imposed by the PI, sponsor, DSMB, FDA or other funding agency.
   2.1.2. Suspend or terminate IRB approval of research.
   2.1.3. Implement institutional directed suspension or termination of IRB approval of research.

3.0 Definitions
3.1. **Study Hold:** A unplanned temporary halt to subject accrual and/or research activities, that is imposed by the PI, sponsor, DSMB, or FDA or other funding agency. A study hold may be full (affecting accrual and all study activities), or partial (affecting only accrual, or only some study activities).

   Note: A study hold as described above in Section 3.1 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.

3.2. **Suspension of IRB Approval:** A directive of the IRB at a convened meeting, or a directive of the IRB Executive Chair (in consultation with the IO as appropriate), that all, or some, research activities in one or more protocols must be temporarily suspended. Study suspension usually (but not exclusively) results from concerns regarding the safety, rights, or welfare of human research subjects, investigators, research staff, or others, or due to noncompliance concerns.

   Note: interruptions in human research resulting solely from the expiration of the IRB approval period does not constitute suspension of IRB-approval of research under 45 CFR 46.113; 21 CFR 56.113.

3.3. **Termination of IRB Approval:** A directive by the IRB at a convened meeting that all research activities must permanently cease in one or more protocols. Study termination usually (but not exclusively) results from concerns regarding the safety, rights, or welfare of human research subjects, investigators, research staff, or others, which cannot be otherwise resolved, or due to serious or continuing noncompliance with the applicable federal regulations and HRPP policies.

3.4. **Organization Directed Termination of IRB Approval:** A directive by the Institutional Official (IO) that an IRB approved study be terminated.
4.0 Procedures for Study Holds by PI, Sponsor, DSMB, FDA or Other Funding Agency

4.1. The PI, sponsor, DSMB, FDA or other funding agency may place a study hold by contacting the ORA by email or letter. When the ORA acknowledges the study hold subject accrual and/or research activities will cease in accordance with the conditions of the study hold.

4.2. The IRB will take appropriate action(s) to protect the rights and welfare of currently enrolled subjects.

4.3. 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.

4.4. The IRB will be notified at the next convened meeting that a study hold was placed on the protocol.

4.5. The PI, sponsor, DSMB, FDA or other funding agency may request a release of the study hold by contacting the ORA by email or letter.
   
   4.5.1. If the study hold was initiated for subject safety concerns only the full IRB (HRPP policy #2.2: Full IRB Review) may release the hold.
   
   4.5.2. If the study hold was initiated for other non-safety concerns, the IRB Executive Chair/designee may release the study hold.

5.0 Suspension of IRB Approval

5.1. The full IRB, or the IRB Executive Chair, may suspend IRB approval of research if such action is warranted due to concerns regarding the safety, rights, or welfare of human research subjects, investigators, research staff, or others, or due to noncompliance concerns, or other similar circumstances.
   
   5.1.1. The IRB Executive chair may exercise his/her authority to suspend research when, in his/her judgement, such action is necessary the protect the safety, rights, or welfare of human research subjects, investigators, research staff, or others before the next convened IRB meeting.

5.2. The IRB will take appropriate action(s) to protect the rights and welfare of currently enrolled subjects.

5.3. The PI will be responsible for notifying all study personnel that the study has been suspended and that all, or some, research activities are suspended.

5.4. The PI must report to the IRB any adverse events or outcomes associated with the suspension.

5.5. 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.

5.6. The IRB, or the Executive Chair, has the authority to permit subjects currently on study to continue if it is in their best medical interest to do so.

5.7. If the study was suspended by the Executive Chair, the IRB will be notified at the next convened meeting of the suspension.

5.8. The PI may file a written appeal of the suspension to the IRB. The IRB is granted the final authority to act on any appeals and the decision of the Board cannot be overturned.

5.9. The full IRB has the sole authority to release a study suspension.
6.0 Termination of IRB Approval

6.1. The full IRB may terminate IRB approval of research if such action is warranted due to concerns regarding the safety, rights, or welfare of human research subjects, investigators, research staff, or others, which cannot be otherwise resolved, or due to serious or continuing noncompliance with the applicable federal regulations and HRPP policies, or due to other similar circumstances.

6.2. The IRB will provide the PI with written justification for termination of IRB approval of the research.

6.3. The IRB will promptly notify the IO and other appropriate Organization officials of the termination of IRB approval of research.

6.4. The IRB will take appropriate action(s) to protect the rights and welfare of currently enrolled subjects.

6.5. The PI will be responsible for notifying all study personnel that the study has been terminated and that all research activities must cease.

6.6. The PI must report to the IRB any adverse events or outcomes associated with the termination.

6.7. The PI must notify research subjects currently on study of termination of the study. Subjects should be advised of any follow-up necessary for safety reasons.

6.8. The PI may file a written appeal of the suspension to the IRB within 30 days of the termination. 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. The IRB is granted the final authority to act on any appeals and the decision of the Board cannot be overturned.

7.0 Organization Directed Termination of IRB Approval

7.1. In consultation with appropriate Organization officials the IO may direct that one or more of an investigator’s IRB approved studies be terminated.

7.2. The IO will provide the PI with written justification for termination of the research.

7.3. The IO will notify appropriate the IRB Executive Chair, and Organization officials of the termination of the research.

7.4. The IRB will take appropriate action(s) to protect the rights and welfare of currently enrolled subjects.

7.5. The PI will be responsible for notifying all study personnel that the study has been terminated and that all research activities must cease.

7.6. The PI must report to the IRB any adverse events or outcomes associated with the termination.

7.7. The PI must notify research subjects currently on study of termination of the study. Subjects should be advised of any follow-up necessary for safety reasons.

7.8. The PI may file a written appeal of the suspension to the IO within 30 days of the termination. 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. The PI will be afforded due process and may be offered the opportunity to meet with the IO and/or the Appeals Panel. The investigator may bring legal counsel who will be restricted to observation only. The decision of the IO with regard to any appeal is final.
8.0 Reporting Suspensions and Terminations to OHRP, Department and Agency Heads, and FDA

Suspensions and terminations are reported in accordance with HRPP policy 8.7 (Reporting Incidents to Institutional Officials and Federal Agencies).

**Administrative Approval:**

BRUCE G. GORDON, MD  IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS
CHRISTOPHER KRATOCHVIL, MD  INSTITUTIONAL OFFICIAL

**Policy Amended:**

- Revised February 2, 2018
- Initial April 4, 2016
1.0 Purpose
The purpose of this policy and procedure is to describe the Organization’s requirements to ensure prompt reporting to Institutional Officials and Federal Agencies (including OHRP and FDA) unanticipated problems involving risk to the subject or others, serious or continuing noncompliance, suspensions of IRB approval, and terminations of IRB approval.

2.0 Policy
2.1. It is the policy of the Organization that unanticipated problems involving risk to the subject or others (UPs), serious or continuing noncompliance, suspensions of IRB approval, and terminations of IRB approval will be promptly reported to the Institutional Official (IO).

2.2. It is the policy of the Organization that unanticipated problems involving risk to the subject or others (UPs), serious or continuing noncompliance, suspensions of IRB approval, and terminations of IRB approval be reported to OHRP, FDA, and other Common Rule Department or Agencies, in accordance with federal requirements and the terms of the Organization’s Federalwide assurance.

3.0 Definitions
3.1. Unanticipated Problems Involving Risk to the Subject or Others: as per HRPP policy 8.3 (IRB Review of Unanticipated Problems Involving Risk to the Subject or Others).

3.2. Serious Noncompliance: as per HRPP policies 8.4 (Noncompliance Involving the PI and Study Personnel) and 8.5 (Noncompliance by the IRB or Other Components of the HRPP).

3.3. Continuing Noncompliance: as per HRPP policies 8.4 (Noncompliance Involving the PI and Study Personnel) and 8.5 (Noncompliance by the IRB or Other Components of the HRPP).

3.4. Suspension of IRB Approval of Research: as per HRPP policy 8.6 (Study Hold, Suspension, and Termination).

3.5. Termination of IRB approval of research: as per HRPP policy 8.6 (Study Hold, Suspension, and Termination).

4.0 Procedures
4.1. The IRB Executive Chair/designee will submit all required written reports to the IO promptly (as appropriate in consideration of the nature of the event but no longer than 30 days following determination that the event is a reportable incident). Follow-up reports will be provided as necessary in conjunction with ongoing investigations.

4.2. For Federally funded research subject to the Common Rule, the IO will submit all required written reports to OHRP and Department or Agency heads as appropriate promptly (as appropriate in consideration of the nature of the event but no longer than 30 days following determination that the event is a reportable incident). Follow-up reports will be provided as necessary in conjunction with ongoing investigations.

4.3. For research subject to FDA regulations, the IO will submit written reports to FDA promptly (as appropriate in consideration of the nature of the event but no longer than 30 days following...
determination that the event is a reportable incident). Follow-up reports will be provided as necessary in conjunction with ongoing investigations.

4.4. For non-Federally funded or FDA regulated research, reports of unanticipated problems involving risks to participants or others will not be reported to OHRP and/or FDA. However, the IO retains the right to submit written reports to OHRP and Department or Agency heads as appropriate if, in consultation with the IRB Executive Chair and Organizational officials, the IO determines that the seriousness of the incident justifies such reporting.

4.5. Copies of the report and any necessary supporting documents will be provided to the PI.

4.6. For Federally funded research, it is the responsibility of the PI to notify the federal department 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.

4.7. For commercially sponsored research, it is the responsibility of the PI to notify the sponsor and the Contract Research Organization (as applicable) and provide verification of this notification to the IRB.

4.8. Reporting events which occur at institutions not under the jurisdiction of the UNMC IRB are the responsibility of the external institution.

5.0 Contents of Reports

5.1. Reports to the IO, OHRP, FDA and Common Rule Department or Agencies must include the information described in OHRP document “Guidance on Reporting Incidents to OHRP (2011)” (https://www.hhs.gov/ohrp/compliance-and-reporting/guidance-on-reporting-incident/index.html), or any succeeding guidance.

5.2. Reports to FDA must also include IND or IDE number, if applicable.

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).

ADMINISTRATIVE APPROVAL:
BRUCE G. GORDON, MD  IRB EXECUTIVE CHAIR & ASSISTANT VICE CHANCELLOR FOR REGULATORY AFFAIRS
CHRISTOPHER KRATOCHVIL, MD  INSTITUTIONAL OFFICIAL

POLICY AMENDED:
- REVISED FEBRUARY 2, 2018
- INITIAL JANUARY 20, 2016