1.1 Human Research Protection Program (HRPP)

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 ensure the rights and welfare of human subjects are protected, will evaluate and continually improve the protection of human research subjects, and will 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), including Children's Physician practice offices.
  - 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 and the online application system – Research Support System (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. When these policies provide a regulatory citations this refers to the Revised Rule (except when both rules are noted, in which case citations which are based on the Revised Rule will be noted with the prefix "rev").
        - 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.
    - 6.1.2 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. Research conducted at Children's Hospital and Medical Center, or any of its wholly owned Children's Physician's Practice offices, operates under the authority of the FWA held by that legal entity.

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 IRBs listed in section 7.0 above, 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 Institutional Official (IO). The IO is an official with sufficient standing, authority, and independence to ensure implementation and maintenance of the program. The IO is legally authorized to represent the Organization, and 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 six fully constituted IRBs registered with DHHS OHRP and the FDA which are responsible for review and approval of 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, as described in HRPP Policy 1.2 (Authority Granted to the IRB by the Organization).
        - 9.2.1.1. IRB-01 (IRB00000670) - primarily reviews research involving adult subjects.
        - 9.2.1.2. IRB-02 (IRB00000671) - primarily reviews research involving adult subjects.
        - 9.2.1.3. 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).
        - 9.2.1.4. IRB-04 (Joint Pediatric IRB) (IRB00007222) - primarily reviews research involving pediatric subjects.
        - 9.2.1.5. IRB-05 (SIRB) (IRB00012770) – primarily reviews research where the Organization acts as the reviewing IRB for multi-site projects.
        - 9.2.1.6. IRB-06 (IRB00013435) - primarily reviews research funded or conducted by the Department of Defense.

      Note: In all of the HRPP policies hereafter, "the IRB" will refer to all boards unless otherwise indicated.
    - 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 but are not limited to: 1) Fred & Pamela Buffett Cancer Center Scientific Review Committee (SRC), 2) Pharmacy & Therapeutics Committee (P&TC), 3) Investigational Device Committee, 4) Institutional Biosafety Committee (IBC), 5) the Radioactive Drug Research Committee (RDRC), and 6) Conflict of Interest Committee (COIC). The responsibilities of these committees are described in HRPP policy 1.10 (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 Pharmacy & Therapeutics Department (including Investigational Drug Service):
      - 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 or other representative of the CHMC Pharmacy 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 Analysts 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. IRB Staff are supervised on a daily basis by an IRB Analyst and/or the Assistant Vice-Chancellor for Regulatory Affairs. The performance of all Analysts 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 Analyst Ongoing Training
      - 9.9.3.1.1. IRB Analysts 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 Analysts must complete, and keep current CITI certification. IRB Analysts are expected to stay informed of new regulations and guidance issued by relevant authorities by attending IRB conferences and/or webinars, and by reviewing articles or other published works related to human subject protection.
    - 9.9.3.2. ORA Staff Ongoing Training
      - 9.9.3.2.1. 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.
      - 9.9.3.2.2. 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 for IRB Analysts and ORA staff. The ORA will monitor the status of CITI certification for all IRB analysts and staff and notify them when it is time for renewal.

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Revised: 5/3/2021 - Added IRB-05 (SIRB) (IRB00012770) in section 7.2.5; revised sections 6.1.1.3 and 6.1.1.6 to delete and clarify references to transition to Revised Common Rule; cClarified that section 9.6.1 does not represent a complete list of ancillary committees; clarified that the Pharmacy Manager or other representative of the CHMC Pharmacy is a member of the Joint Pediatric IRB (section 9.7.3.2.2); deleted specifics of job requirements for IRB Administrators and ORA Staff (redundant to job descriptions); simplified and clarified training requirements for IRB Administrators and ORA Staff. Notification: not documented

Revised: 1/16/2023 - Added IRB-06; specified Children's Hospital & Medical Center (CHMC) includes Children's Physician practice offices; clarified that Children's Hospital and Medical Center and it's wholly owned Children's Physician's Practice offices operates under the authority of the FWA held by that legal entity; deleted comment that IO is the Associate Vice-Chancellor for Clinical Research; specified that the IO is an official with sufficient standing, authority, and independence to ensure implementation and maintenance of the program; replaced "Administrator" with "Analyst"; minor stylistic changes. {Approved Chris Kratochvil (Institutional Official), Bruce Gordon (Assistant Vice Chancellor for Regulatory Affairs, Executive Chair)}

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