CREIGHTON UNIVERSITY HUMAN RESEARCH PROTECTION PROGRAM POLICY MANUAL

Table of Contents

Section 1: General Human Research Protection Program Policies

1.1 Human Research Protection Program (HRPP)

1.0 Purpose

The purpose of this policy and procedures manual 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 defined:

3.1.1 Creighton University (CU), Omaha and Phoenix Campuses

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

3.3 All HRPP policies are made available to all investigators and research staff through the IRB website.

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

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.

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

4.2.1 Exercise oversight of research protection under the umbrella of the Institutional Review Board (IRB).

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

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

6.1.5 Applicable federal, state and local laws.
6.1.6 HRPP policies.

6.2 If a conflict arises between federal, state, and local law, the IRB will consult Creighton University's Office of the General Counsel or CU's Chief Compliance Office 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.

7.0 Federalwide Assurance (FWA)

7.1 The HRPP operates under the authority of its current Federal Wide Assurance: FWA00001078.

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, is the signatory of the FWA, and assumes the obligations specified in the FWA. The IO may delegate individual responsibilities but 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 and staff, applicable Research Compliance Office (RCO) 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, IRB staff, research personnel, and other members of the research community.

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

9.1.4 Appoint and oversee IRB members and Chairs.

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 Director and the Director of Research Compliance on a regular basis, and attend RCO 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 Director and the Director of Research Compliance 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 accessto 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 two fully constituted IRBs at Creighton University registered with DHHS OHRP 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 (IRB00000155) – Reviews Biomedical research involving human subjects.

9.2.1.2 IRB-02 (IRB00007137) - Reviews Social-Behavioral research involving human subjects.

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 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 (CU Ceding Review to an External Central IRB).

9.2.4 The IRB may serve as the IRB of record for external organizations in accordance with HRPP policy 1.3 (CU 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) Institutional Biosafety Committee (IBC), 2) Conflict of Interest Committee (CIRC), and 3) Radiation Safety Committee. The responsibilities of these committees are described in HRPP policy 1.10 (Other HRPP 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 Relationship Between Components

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

9.7.2 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 Research Compliance Committee (RCC) 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. The committee acts in an advisory capacity to the IO and Office of the Provost, 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 Institutional Review Board Office (IRB Office) is responsible for the day-to-day operations of the HRPP. All IRB Office 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 IRB Director reports to the Director for Research Compliance and has a close working relationship with the IRB Chairs and the committees specified above.

9.9.2 The IRB Office is located in the Criss I building of the Criss Health Sciences Complex on the Omaha Campus of Creighton University 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 the staff are found in their respective job descriptions on file with Human Resources and in the IRB Office. IRB staff are supervised on a daily basis by the IRB Director. 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 Ongoing Training

9.9.3.1.1 IRB Administrators are expected to become Certified IRB Professionals (CIP) as soon as they are eligible, and to 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 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 IRB Office Staff Ongoing Training

9.9.3.2.1 All IRB Office staff are encouraged to become Certified IRB Professionals (CIP) as soon as they are eligible, and to engage in on-going continuing education to enhance their knowledge and skill levels.

9.9.3.2.2 IRB Office staff must complete and keep current CITI certification.

9.9.4 Training Records

9.9.4.1 The IRB Office is responsible for maintaining all initial and continuing education training records for IRB Administrators and IRB Office staff. The IRB Office will monitor the status of CITI certification for all IRB administrators and staff and notify them when it is time for renewal.

1.2 Authorization Granted to the IRB by the Organization

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 ofthe

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 (CU 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 (CU 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, the expedited reviewer designated by the 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 Creighton University IRB before it is initiated in accordance with HRPP policy 2.6 (Exempt Research). The IRB will accept approval of exempt research by an external institution on a case-by-case basis.

2.5 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.

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

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

2.8 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.

2.9 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.

2.10 The IRB 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.

2.11 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.

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

2.11.2 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.

2.12 The IRB or the RCO may be periodically charged by the IO with review of other research activities. Charge by the IO constitutes authority to perform that review and requirement by faculty, students, staff, or other representatives of the Organization to abide by the findings of the IRB or RCO.

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.

1.3 CU IRB Serving as the Single IRB for Multisite Research

1.0 Purpose

The purpose of this policy and procedure is to describe the Organization's requirements for the CU IRB to serve as the Single IRB (sIRB) for multisite research.

2.0 Policy

2.1 It is the policy of the Organization that the CU IRB may serve as the SIRB for multisite research as permitted by HHS regulations at 45 CFR 46.114.

2.2 It is the policy of the Organization that the IRB Director has the sole authority to determine whether or not to allow the CU IRB to serve as the Single IRB for multisite research.

2.2.1 For all non-exempt federally-funded research, the Organization requires execution of a Reliance Agreement.

2.2.2 For exempt research and non-exempt research without federal funding, the Organization does not normally require execution of a Reliance Agreement.

2.3 It is the policy of the Organization that the CU IRB may serve as the IRB of record as permitted by HHS regulations at 45 CFR 46.114 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 It is the policy of the Organization that research conducted at external organizations where CU is the IRB of record must comply with HRPP policies of the relying institution, except as specified in this policy and/or in the Reliance agreement.

3.0 Definitions

3.1 Cede Review: An institution agrees to transfer IRB review and oversight authority for specified research to another institution's IRB (reviewing 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 the reviewing and relying IRBs.

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

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

3.6 Lead Principal Investigator (Lead PI): The study wide lead Principal Investigator with ultimate responsibility for the conduct and integrity of multisite research.

3.7 Reviewing IRB: The IRB which is responsible for conducting IRB review and approval as described in 45 CFR 46.109 for cooperative human subject research.

4.0 CU IRB, Relying Institution, and Lead PI Responsibilities

4.1 It is the responsibility of the CU IRB (as reviewing IRB) to:

4.1.1 Conduct 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).

4.1.1.1 Review any COI management plans from the relying institution to assure the plan is adequate in consideration of the nature of the conflict. The CU IRB as reviewing IRB may apply additional restrictions and/or limitations but may not override those required by the relying institution.

4.1.2 Obtain additional DHHS-required determinations when the research involves pregnant women, fetuses, and neonates; or children; or prisoners.

4.1.3 Determine 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 regulations).

4.1.4 Report 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

4.1.5 Report to the Relying Institution:

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

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 OHRP, sponsors, and CROs.

4.1.5.5 Any reports filed with the OHRP.

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

4.1.5.7 Any other communication from any governmental agency citing improper or inadequate research practices.

4.1.5 Notify the Investigator and the Relying Institution (when applicable) of the IRB's determinations.

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

4.1.8 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 IRB's determinations to the Relying Institution).

4.1.9 Ensure HRPP policies are readily accessible to Relying Institutions through the IRB website and there is a mechanism for communicating updates to the policies.

4.1.10 Maintain all research records for at least seven years after completion of the research and make available for inspection or copying by the HHS Office of Human Research Protection (OHRP) upon request in accordance with federal regulations.

4.1.11 Ensure compliance with CU's OHRP-approved FWA.

4.2 It is the responsibility of the Relying Institution to:

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

4.2.2 Advise the CU IRB of completion of all additional reviews required by the Institution, including but not limited to biosafety review, radiation safety review, recombinant DNA research review, and conflict of interest, and of any requirements resulting from the additional Institutional reviews.

4.2.3 Advise the CU IRB of any circumstances when the review must take into account additional regulatory or local HRPP requirements.

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

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

4.2.5 Advise the CU IRB of any allegations of noncompliance. The CU IRB, in conjunction with the participating site IRB, will determine how best to handle the allegation in consideration of the need to maintain due process and protect the whistleblower.

4.2.6 Advise the CU IRB of any complaint directly from subjects or others. The ResearchCompliance Auditor will assist in the resolution of the complaint as necessary.

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

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

4.2.9 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.

4.2.10 Maintain a copy of the signed informed consent document in accordance with relying institution policies, applicable HHS regulations, and ICH-GCP.

4.2.11 Maintain all research records in accordance with relying institution policies, applicable HHS regulations, ICH-GCP and HIPAA Privacy rule as appropriate.

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

4.2.13 Permit the CU IRB, or its authorized representatives, and OHRP to the extent permitted by law, to conduct the following:

4.2.13.1 Examine and inspect the Relying Institution facilities used for the performance of the studies, including storage and use of any investigational products.

4.2.13.2 Observe the conduct of the studies.

4.2.13.3 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.

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

4.3 It is the responsibility of the Lead (CU) PI to:

4.3.1 Serve as the primary contact with the CU IRB. The Lead PI assumes primary responsibility for notifying the relying sites of all CU 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 CU IRB approved template and include applicable site-specific required language provided by each relying institution.

4.3.5 Provide participating sites 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 CU determinations and communications, including initial review, continuing review, Requests for Modifications, and reportable events.

4.3.8 Ensure Site PIs submit in a timely manner the participating site (InfoEd) Continuing Review Application.

4.3.8.1 The Lead PI must notify the Site PI of any lapse in IRB approval of their site and any applicable corrective action plans.

4.3.8.2 Provide access, upon request, to all study records by audit by any Relying Institution, the CU 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 single IRB request form must be submitted for each research protocol to the CU IRB. The sIRB request form requests:

5.1.1 The identity of the research network (if applicable) and participating sites

5.1.2 Provides rationale for use of the CU IRB as the sIRB for the research.

5.1.3 Identifies any relevant deadlines or funding agency requirements.

5.2 The CU IO must agree to allow the CU IRB to serve as the sIRB.

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" electronic platform. However, if justifiable, an alternate form of the Reliance Agreement will be initiated between the Reviewing and the Relying Institutions/IRBs.

5.4 For federally-funded research, each Relying Institution IRB must agree to cede IRB review to the CU IRB for each specific research proposal by completion of a Reliance Agreement, or other agreed upon mechanism.

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

5.5 Once the Organization has agreed to serve as the sIRB, the Lead PI will complete the appropriate CU IRB application through InfoEd 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 CU 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 CU HRPP policies, such as those related to reporting adverse events, deviations, noncompliance, and compensation, as well as relevant participating site HRPP policies, such as those related to, advertisement, ethical access, recruitment, short form consent, process and documentation of consent, etc.

5.7 The CU-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 CU study team, modified with local context information by the participating site study team, and approved by the IRB Chair/IRB Administrator. These are available on the IRB website.

5.8 Each Site PI must complete and submit to the CU IRB the InfoEd Application for the research. This application provides local context information specifically related to the research proposal.

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 Modifications. The IRB has determined that addition of sites may be handled under expedited review (see HRPP Policy 2.3, as applicable).

1.4 CU IRB Ceding Review to an External Central IRB

1.0 Purpose

The purpose of this policy and procedure is to describe the Organization's requirements for the CU IRB to cede review to an external IRB.

2.0 Policy

2.1 It is the policy of the Organization that all non-exempt research under the authority of the CU IRB and conducted, supported, or otherwise subject to regulation by any Federal department or agency which has adopted the Common Rule will rely on upon approval by a single IRB for that portion of the research that is conducted in the United States, in accordance with 45 CFR 46.114, unless excluded from this requirement under 45 CFR 46.114(b)(2).

2.2 It is the policy of the Organization that all NIH-funded research will rely on upon approval by a single IRB, in accordance with the NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research (NOT-OD-16-094), unless excluded from this requirement under NIH policy (NOT-OD-18-003).

2.3 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 commercially sponsored clinical trials, with the exceptions specified under Section 2.5 below.

2.4 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 Clinical Trials Network (NCTN) as permitted by HHS regulations at 45 CFR 46.114 and FDA regulations at 21 CFR 56.114.

2.5. 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 2.6 below, provided the following conditions are met:

2.5.1 For research which constitutes greater than minimal risk, the external IRB is part of a qualified HRPP or has completed the OHRP QA Self Assessment

2.5.1.1 A qualified IRB is defined as an accredited HRPP or an HRPP belonging to a partner organization of CU.

2.5.2 For research which constitutes no more than minimal risk, the external IRB reviews the research appropriately, in compliance with all federal, state, and local regulations, and the review criteria utilized by the external IRB are in compliance with the Organization's ethical standards and with applicable laws and regulations, and with the specific approval of the IO, in consultation with the IRB Director and Director of Research Compliance as appropriate.

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

2.6 It is the policy of the Organization that, unless use of a single IRB subject is required by 45 CFR 46.114, or required by NIH policy, the use of an external IRB is not permitted for:

2.6.1 Research involving prisoners as subjects.

2.7 It is the policy of the Organization that the IO, in consultation with the IRB Director and Director of Research Compliance as appropriate, has the sole authority to determine whether or not to allow the CU IRB to cede review of research described in 2.5 to an external IRB.

2.8 It is the policy of the Organization that the IO, in consultation with the IRB Director and Director of Research Compliance as appropriate, has the sole authority to allow exceptions to the exclusions in 2.6 above.

2.9 It is the policy of the Organization that it will accept the review and approval of an external IRB for human subject research exempt under 45 CFR 46.104; however, the Organization will not require the execution of a Reliance Agreement.

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

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

commercial IRB, for all non-exempt federally funded research; however the IO has the authority to allow exceptions to this policy.

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

2.13 It is the policy of the Organization that research conducted under the purview of an external IRB will be subject to all relevant policies of the external (reviewing) IRB, and investigators of the Organization must comply with those policies.

2.14 It is the policy of the Organization that investigators must comply with Organization policies.

2.15 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).

3.0 Definitions

3.1 Cede Review: The Organization has agreed to transfer IRB review and oversight authority for specified research to another institution's IRB (reviewing or external 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 between the reviewing and relying IRBs.

3.3 Relying Institution: A participating Institution that cedes IRB review to the IRB of record (reviewing IRB) designated under a Reliance Agreement.

3.4 Reviewing IRB (or External IRB): The IRB which is responsible for conducting IRB review and approval as described in 45 CFR 46.109 for cooperative human subject research. For the purpose of this policy, reviewing IRB and external IRB are the same.

4.0 External IRB, CU IRB, and PI Responsibilities

4.1. It is the responsibility of the external IRB (as reviewing IRB) to:

4.1.1 Conduct review of the research in full accordance with applicable federal and state regulations, and all relevant policies of the external IRB (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).

4.1.2 Obtain 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 Report 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 Report to the CU IRB:

4.1.4.1 Any unanticipated problems involving risk to the subject or others associated with subjects enrolled at the institution.

4.1.4.2 Any serious or continuing noncompliance.

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

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

4.1.4.5 Any reports filed with the FDA or OHRP.

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

4.1.4.7 Any other communication from FDA or other governmental agency citing improper or inadequate research practices.

4.1.5 Notify the Investigator and the Institution (when applicable) of the IRB's determinations.

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

4.1.7 Upon written request, provide CU 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 IRB's determinations).

4.2 It is the responsibility of the CU IRB and HRPP (on behalf of the relying institution) to:

4.2.1 Advise the external IRB of any applicable state or local laws governing research conducted at this Organization.

4.2.2 Advise the external IRB of completion of all additional reviews required by the Institution, including but not limited to biosafety review, radiation safety review, conflict of interest, and of any requirements resulting from the additional Institutional reviews.

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

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

4.2.4.1 Notify the external IRB of the termination, suspension, or modification of any clinical privileges of the Organization's Staff who are participating in the studies authorized by the external IRB.

4.2.5 Advise the external IRB of any allegations of noncompliance which are received by the RCO and which are found to be serious or continuing, or which represent an unanticipated problem involving risk. The external IRB, in conjunction with the RCO, will determine how best to handle the allegation in consideration of the need to maintain due process and protect the whistleblower.

4.2.6 Advise the external IRB of any complaint directly from subjects or others. The Research Compliance Office Auditor will assist in the resolution of the complaint as necessary.

4.2.7 Advise the external IRB of any contact by the FDA, HHS, or any other persons or entities regarding the research within three business days of contact.

4.2.8 Notify the external IRB within three business days, in the event that the FDA or other governmental agency issues the relying 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 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.

4.2.10 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.

4.2.11 Notify the reviewing IRB when local policies that impact IRB review are updated.

4.3 It is the responsibility of the CU PI to:

4.3.1 Complete all requirements for submission to the external IRB.

4.3.2 Comply with all relevant CU HRPP policies, such as, but not limited to, those related to compensation, advertisement, ethical access, short form consent, process and documentation of consent.

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.

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

Note: The external IRB may impose additional safeguards; however, the external IRB may not be less stringent than what is required by the CU COI management plan.

4.3.6.3 Incidents of noncompliance. Copies of all reports to the federal government (e.g., OHRP, FDA, federal sponsor or funding agency) must also be provided to the RCO.

4.3.6.4 Protocol deviations.

4.3.6.5 Any complaints from subjects or others. The RCO Auditor will assist in the resolution of the complaint as necessary.

4.3.6.6 Data Safety Monitoring Reports

4.3.6.7 Internal adverse events and other events which qualify as an unanticipated problem involving risk to the subject.

4.3.7 Promptly report to the CU IRB

4.3.7.1 Any new or modified conflicts of interest of responsible personnel (per HRPP policy 1.25 Financial Conflicts of Interest), and any new or modified management plans.

4.3.7.2 Additional requirements by the external IRB to the CU COI management plan.

4.3.7.3 Incidents of non-compliance

4.3.7.4 Copies of all reports to OHRP and/or FDA.

4.3.7.5 Reports of internal adverse events

4.3.7.6 Changes in study personnel

4.3.8 Ensure all investigators and research staff have the appropriate qualifications and expertise to conduct the research.

4.3.9 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.

4.3.10. Conduct monitoring in addition to, or in cooperation with, the external IRB and the RCO.

4.3.11. Notify the IRB when a study is completed.

4.4 There may be additional external IRB, CU 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 For all non-exempt, federally funded human subject research, the PI must request from CU IRB or the IO permission to rely on an external IRB. The request, via email, must be accompanied by the following documents:

5.1.1 Full protocol

5.1.2 Sponsor's template consent forms and/or information sheets

5.2 The IRB Director must determine that the request to utilize an external IRB satisfies the requirements of Section 2 above. The Director, in consultation with the Director of Research Compliance, as appropriate, will then present to the IO the request to allow the CU IRB to cede IRB review to the external IRB.

5.3 If the IO approves the request, the CU IRB Director will review the request to rely on an external IRB to determine that:

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

5.3.1.1 HRPP policies as described in addendum 2.

5.3.1.2 Review and approval by other components of the HRPP.

5.3.1.3 Contract review by Sponsored Programs Administration.

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 CU IRB and external IRB.

5.3.3 The CU IRB Director will issue a conditional acceptance letter to the investigator, with conditions based on Organizational requirements.

5.3.4 The following items are available to investigators and may be provided to the external IRB:

5.3.4.1 CU Consent Form letterhead (use recommended but not required).

5.3.4.2 The CU required consent form language.

5.3.4.3 Any COI management plan including 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.

5.3.5 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 Director will provide the PI with an acceptance letter granting acceptance of IRB oversight by the external IRB.

5.3.6 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 4.3.7 above. CU 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 CU IRB will not review or provide an approval stamp on any consent forms or information sheets approved by an external IRB.

5.4 For research exempt under 45 CFR 46.104 and for non-exempt research that is not federally funded, no documentation is required to be provided to the CU IRB.

5.5. 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 RCO, 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.

1.5 Requirements for Research Conducted with International Sites

1.0 Purpose

The purpose of this policy is to describe the Organization's requirements for research conducted with international sites. For the purposes of this policy, "Research conducted with International Sites" (international research) is defined as (1) research conducted by a faculty member, staff, student, or other representative of the Organization at an international site, or (2) research conducted by external investigators under the direction of a faculty member, staff, student, or other representative of the Organization, or (3) research where an investigator receives identifiable private information or identifiable biospecimens from an international site.

2.0 Policy

It is the policy of the Organization that:

2.1 The PI assumes 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 CU HRPP policies.

2.2 Non-exempt research conducted with an international site by the Organization's faculty, staff, students, or other representative of the Organization, must be reviewed and approved by both the CU 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 Chair.

2.3 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 CU IRB, 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 IRB Chair/designee.

2.4 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".

2.5 When conducting or participating in international research conducted entirely or in part in other countries, 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 Protections of human subjects at the international site must be at least equivalent to HHS regulations at 45 CFR 46

2.7 International research involving prisoners is not permitted.

3.0 Investigator Responsibilities

3.1 Non-Exempt International Research

3.1.1 In order for the Organization's faculty, students, staff, or other representatives to conduct non-exempt research with an international site, the following must be submitted to the IRB for review:

3.1.1.1 The appropriate IRB application.

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

3.1.1.3 A copy of the ICF approved by the local IRB which has been translated into English (as applicable).

3.1.1.4 A copy of the ICF approved by the local IRB in the native language (as applicable).

3.1.1.5 An agreement between the international site and the investigator and/or institution which specifies the responsibilities of the local IRB/REB which includes, but is not limited to, the following:

3.1.1.5.1 The frequency of continuing review, if any.

3.1.1.5.2 Post approval monitoring as appropriate will be conducted at the site.

3.1.1.5.3 Reports of complaints, serious or continuing noncompliance, protocol deviations, and unanticipated problems involving risk to the subject or others will be forwarded to the CU IRB.

3.1.1.5.4 Reports of other serious problems in the conduct of the research will be forwarded to the CU IRB.

3.2. Exempt International Research

3.2.1 In order for the Organization's faculty, staff, students, staff, and other representatives to conduct exempt research with an international site, the following must be submitted to the IRB for review:

3.2.1.1 The appropriate IRB application.

3.2.1.2 A copy of the approval letter from the local IRB or authorized official.

3.2.1.3 A copy of the ICF approved by the local IRB (if a consent form is required) which has been translated into English.

3.2.1.4 A copy of the ICF approved by the local IRB (if a consent form is required) in the native language.

3.3 When any international research involves the shipment of human biological materials, hazardous materials, or dangerous goods, the PI must comply with the instructions of the CU Biosafety Officer.

3.4. The PI is responsible for ensuring all appropriate host country permissions to conduct research are in place (including as appropriate, institutional, governmental or ministerial, IRB or EC, local or tribal).

4.0 IRB Responsibilities

4.1. Non-Exempt International Research

4.1.1 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 at the international site.

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

4.1.4 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, provided that the research presents no more than minimal risk of harm to subjects and there is an appropriate alternative mechanism for documenting 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 and OHRP as necessary.

4.2 Exempt International Research

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

4.2.2 As appropriate, the IRB will consider whether:

4.2.2.1 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 If informed consent is required, 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 complaints, noncompliance, protocol deviations, and unanticipated problems involving risk to subject or others.

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.

4.3 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.

1.6 IRB Composition, Leadership, Qualifications, and Responsibilities

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 satisfy requirements of 45 CFR 46.107, and will include an appropriately diverse mixture of backgrounds, gender, and race/ethnicity.

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 The IRBs will include one or more members who are knowledgeable about or and experienced in working with children, pregnant women and fetuses, and decisionally impaired individuals.

3.5 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.

3.6 The IRB shall not consist entirely of members of one profession.

3.7 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.

3.8 Each IRB will include at least one member that is not affiliated with the Institution.

3.8.1 The unaffiliated member should be able to represent the general perspective of research subjects and/or of the community. These members should be particularly cognizant of the need to protect subjects vulnerable to coercion and undue influence.

3.8.2 The unaffiliated member must not have any professional relationship with the Institution as an employee, consultant, faculty (including voluntary faculty), or student, or have an immediate family member who has such a professional relationship with the Institution.

3.8.3 It is required that at least one unaffiliated member will be present at each meeting of each IRB.

3.9 When reviewing community-based participatory research, as necessary, a consultant (or a knowledgeable board member) will supply the IRB with information about the community and how it will be served by the research.

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

3.11 In situations where prisoners will be or 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.

3.12 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).

3.13 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:

3.13.1 Either before or during review of a protocol, the IRB Chair/designee, assigned IRB reviewer, or the IRB itself may determine there is a need for appointment of one or more expert consultants, as per 45 CFR 46.107(f) (or rev 45 CFR 46.107(e)).

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

3.13.3 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).

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

3.13.5 Consultants may participate in the IRB's discussion of the protocol but they may not vote and will leave the meeting before a vote is taken.

3.14 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.

3.15 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.

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

3.17 A full listing of IRB members will be maintained by the CU IRB. This list will include for each IRB member name earned degrees, scientific status (that is, scientist or non-scientist), representative capacity (for example, children, pregnant women, prisoners), indications of experience (that is, brief descriptors of relevant experiences that describe each member's chief anticipated contributions to IRB), relationship to the organization, affiliation status, office (for example, chair or vice chair), membership status (member, alternate member, or non-voting), and, as applicable, alternate member for and list the members or class of members for whom the alternate member can substitute.

3.17.1 Roster will be updated as necessary with the addition or removal of board members.

3.18 The IRB 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 Chairs

4.1.1 The IRB Chair(s) is appointed by the IO, in consultation with the IRB Director and Director of Research Compliance. The Chair must:

4.1.1.1 Have at least four years of IRB experience.

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

4.1.1.3 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, and participates in the development of policies, procedures, IRB forms and checklists.

4.2.3 As needed, the IRB Chair may carry out the duties of an IRB member, as noted in section 4.5.4 below.

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 the IRB Director and Director of Research Compliance on an on-going basis, about performance and competence of the IRB Vice-Chair(s), IRB members and IRB 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 must satisfy continuing education requirements per HRPP policy 1.24 (HRPP Training Requirements for IRB Members).

4.2.9 The IRB Chair 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 IRB Vice Chairs

4.3.1 The IRB Vice-Chair(s) is appointed by the IO, in consultation with the IRB Director and Director of Research Compliance. 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) will serve in the capacity as IRB Chair when the Chair is unavailable (or recused).

4.3.3 As needed, the IRB Vice-Chair may carry out the duties of an IRB member, as noted in section 4.5.4 below.

4.3.4 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).

4.3.5 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.

4.4 IRB Executive Committee

4.4.1 The IRB Executive Committee is comprised of the IRB Chairs, the IRB Director, and the Director of Research Compliance.

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 on a rotating basis.

4.4.4 The purpose of the IRB Executive Committee is to:

4.4.4.1 Facilitate effective and timely communication between the IRB Office, IRB Chairs, and Research Compliance Office.

4.4.4.2 Perform ongoing assessment of the IRBs.

4.4.4.3 Assist in the development of HRPP policies and procedures.

4.4.4.4 Assist in the development of IRB forms.

4.4.4.5 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 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 Chair(s), IRB Vice-Chairs, and Director of Research Compliance. However, unsolicited nominations may be submitted to the IRB Chair or the IO at any time.

4.5.2 Prior to appointment to the board, the prospective member will be interviewed by the IRB 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 Director of Research Compliance and IRB Director.

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 with full voting privileges.

4.5.4.2 Serve as a reviewer for new protocols.

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

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

4.5.4.7 Serve as a reviewer for incidents of noncompliance.

4.5.5 IRB members are expected to attend the majority of scheduled meetings to which they are assigned 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 IRB Office 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) and are required to maintain all disclosures and documentation required by the IRB SOP on Training, Documentation, and Disclosure Requirements for IRB Members.

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 An IRB Administrator may serve as a member of the IRB for purposes of performing expedited review. Administrators are appointed as IRB members or alternate members by the IO, in consultation with the IRB Director and IRB Chairs, as noted above.

4.5.8.1 IRB administrators will be classified as scientist or non-scientist based on specific degree, education, or experience.

4.5.8.2 IRB administrators must have at least 1 year of experience with the CU IRB or another IRB, and must be approved by the IRB Chairs, before they can act as an expedited reviewer.

4.5.8.3 An IRB administrator serving as an alternate member of the IRB will have the same responsibilities and requirements as noted in section 4.5.4 above.

4.5.8.4 The term of appointment for an IRB administrator serving as an alternate member of the IRB will be indefinite.

4.6. IRB Alternate Members

4.6.1 The appointment, responsibilities, training, evaluation and re-appointment 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 IRB roster identifies the regular members(s) for whom each alternate member may substitute.

4.6.4 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.

4.6.5 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.

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

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

4.7 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.

1.7 IRB Member, Consultant, Staff, and Guest Conflict of Interest Identification and Management

1.0 Purpose
The purpose of this policy is to describe the Organization's requirements for the identification and management of IRB member, consultant, staff, and guest potential conflicts of interest.

2.0 Policy
It is the policy of the Organization that:

2.1 All financial and non-financial interests which may represent a conflict of interest for an IRB member, consultant, staff, or guest 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 review process.

2.2 Any financial interest of any monetary value by an IRB member, consultant, staff or guest at the meeting is considered a conflict of interest for the purposes of this policy.

2.3 Disclosure of the specifics of the conflict to the convened IRB at which the IRB member, consultant, staff, or guest is attending is not required. It is sufficient for the convened Board to understand that a conflict exists and to be familiar with the requirements of the management plan.

3.0 Definitions

3.1 Covered Persons: Covered persons are IRB members, consultants, IRB staff, or guests at an IRB meeting, and the 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 Conflicts of Interest: a situation in which financial or non-financial interest may compromise, or have the appearance of compromising, a covered person's professional judgment or objectivity in reviewing or evaluating research involving human subjects.

3.3 Financial Interest: includes any of the following: 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 (excluding mutual funds); or 3) a position as director, officer, partner, trustee, or any other significant position in the company sponsoring the research or such position in the past twelve months; or 4) 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; or 5) 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.

3.4 Non-financial interest: a personal or professional circumstance that includes (but is not limited to) 1) serving as an investigator, participating personnel, or coordinator for the protocol, or serving as a faculty advisor for a student as PI; or 2) having a personal relationship, or a conflict, with any research personnel listed on the IRB application which would compromise, or have the appearance of compromising, a covered person's professional judgment or objectivity in reviewing or evaluating research.

Note: In general, the covered person is not considered to have a conflict of interest if 1) the individual serves on the sponsor's scientific advisory board for an area unrelated to the research under review; or 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.

3.5 Guests: persons attending the IRB meeting who are neither members, non-voting alternates, or IRB staff. Guests may be organizational officials (for example, Chief Compliance officer, or Privacy Officer), legal counsel, representatives of other components of the HRPP (for example, the FPBCC Scientific Review Committee) or other persons specifically invited to attend.

4.0 Procedures for identification and management of conflict of interest by members and consultants

4.1 IRB members (including IRB administrators serving as IRB members) must notify the IRB Office if they have a conflict related to any protocol being reviewed by the board at a which they are attending. If the member is assigned to review any action related to a protocol for which they have a conflict, they must notify the IRB Office in advance of the meeting so the protocol can be re-assigned to a non-conflicted member.

4.2 Consultants will be provided with this policy and must certify in writing that they do not have a conflict of interest. They will be excluded from serving as a consultant if a conflict exists.

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 An IRB member with a conflict of interest (other than serving as participating personnel; see below) must be absent from the meeting room or teleconference 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. 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 An IRB member whose only conflict is that he/she is participating personnel on a protocol may participate in the discussion regarding the protocol and remain in the meeting room/on the teleconference during the vote but will abstain from voting.

4.4.2 If the conflicted member is attending the meeting by videoconference, "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 participating personnel or other study personnel, that individual may participate in the Board's discussion but is required to abstain from voting.

4.6 The IRB meeting minutes will specifically record that COI is the reason any IRB member is out of the room/absent from the teleconference and did not vote.

4.7 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 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 a conflict are excluded from serving as the primary 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 primary IRB administrator assigned to process the study; however, he/she may not be the sole expedited reviewer for any non-compliance, AEs or UAPs in which he/she was directly involved during his/her tenure as study personnel.

5.3 IRB staff 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 which they have a conflict.

6.0 Procedures for identification and management of conflict of interest by guests at the IRB meeting

6.1 Guests 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 which they have a conflict.

1.8 Investigational Activities Requiring IRB Review and Approval

1.0 Purpose
The purpose of this policy is to describe the investigational activities that require IRB approval.

2.0 Policy
It is the policy of the Organization that:

2.1 IRB review and approval is required for research involving human subjects 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 CU 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 CU Ceding Review to an External IRB).

2.2 The IRB does not routinely review activities which do not meet the definition of human subject research, unless a non-research designation is requested from the IRB for publication or presentation purposes.

2.2.1 Nothing in this policy prevents the establishment of alternate review methods for non-human subjects research within the Organization.

2.3 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” (45 CFR 46.102(l)). 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.”

3.1.1.2 Systematic investigation means an activity described in a protocol which includes a set of scientific aims or objectives, procedures to pursue the objectives (for example, interventions or interactions), analysis of the data, and conclusions drawn based upon the analysis.

3.1.1.3 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).”

3.1.1.4 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 and UC Berkeley HRPP).

3.1.1.5 Certain activities described in section 6.0 are deemed not to be research, as per 45 CFR 46.102(l)

3.1.2 Human Subject is defined as “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” (45 CFR 46.102(e))

3.1.2.1 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.

3.1.2.2 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.

3.1.2.3 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).

3.1.2.4 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.

3.1.2.5 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 Human subject research means research activities which involve human subjects.

3.1.4 Engagement in Human Subject Research. The CU 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:

3.1.4.1 Data about the subjects of the research through intervention or interaction with them; or

3.1.4.2 Identifiable private information about the subjects of the research; or

3.1.4.3 Informed consent of the human subjects of the research.

3.2 FDA Regulations

3.2.1 The Creighton University IRB does not provide review or oversight to FDA regulated research, but instead relies upon qualified external IRBs for review and oversight of this research as permitted by HRPP Policy 1.4.

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 “Therapeutic” research characterized as research which involves a drug, medical device, technique or other intervention or strategy (including non-physical means, like diet, cognitive therapy, etc.) to diagnose, treat, prevent or otherwise study a particular condition or disease.

4.1.2 “Non-therapeutic" research characterized as 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; 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 the case is limited solely to a description of the clinical features and/or outcome of individual patients.

Note: When a physician or other health care professional authors a case history that is not research, ethical guidelines should, nevertheless, be taken into consideration; specifically, Informed consent should be obtained from the patient; and 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 a limited number of other invited guests. This does not include presentation in a student research fair or forum, where the public are invited or have easy access.

Note: Undergraduate students may present the results of a classroom project without meeting the definition of human subjects research if the presentation is also a classroom assignment.

Note: 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: An investigation conducted to meet educational requirements with no intent to present the results of the investigation outside of the organization but is then re-analyzed in order to prove or disprove a hypothesis does constitute human subject research.

5.7 Pilot Testing: small investigations characterized as "pilot testing" prior to conduct of research are not considered human subject research provided the procedures meet the following conditions:

5.7.1 Pilot testing is limited to interventions intended to test the equipment or the methodology, or to refine the parameters of the protocol, or to train the student to use the equipment.

5.7.2 The pilot testing is not explicitly named as one of the aims of the research.

5.7.3 The data generated from the pilot testing is not retained after the completion of the specific goals of the pilot testing (as per 5.7.1 above)

5.7.4 The data generated from the pilot testing is not presented in any public format (abstract, poster, or publication) nor used as background material for a grant application or similar purpose.

5.7.5 The pilot testing will only involve healthy volunteers (preferably research staff) as participants.

5.7.6 The pilot testing procedures constitute no greater than minimal risk to participants.

5.8 Secondary research involving non-identifiable newborn screening blood spots.

6.0. Other Activities Deemed Not Research

Other activities specifically defined in 45 CFR 46.102(l) are deemed "not research." These activities include:

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 IRB for guidance in determining whether or not a proposed activity constitutes human subjects research. An IRB Administrator, in consultation with the IRB Chair/designee as necessary, will determine whether or not the planned activities constitute human subject research,

using the OHRP Human Subject Decision Charts, the criteria in sections 4, 5 and 6 of this policy, and if necessary consultation with OHRP.

7.2 Once a determination is made, the investigator will be so informed.

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 IRB staff in accordance with HRPP policy 2.6.

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

1.9 Resources Necessary to Protect Human Subjects

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.

3.0 PI and Certifier Obligation

3.1 The PI is required to sign an assurance (that is part of the IRB application in InfoEd) 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 others.

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 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.

1.10 Other HRPP Committee Review of Research

1.0 Purpose

The purpose of this policy and procedure is to describe the Organization's requirements for 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) conducted under the jurisdiction of the CU IRB.

2.0 Policy

2.1 Human subject research under the jurisdiction and oversight of the CU IRB will also be reviewed by other component committees of the HRPP, as appropriate.

3.0 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:

3.3.1 Conflict of Interest Review Committee (CIRC)

3.3.2. Radiation Safety Committee

None of these committees has the authority to approve human subject research to begin that has not yet been approved, or has been disapproved, by the IRB, as per HRPP policy 1.2 (Authority Granted to the IRB by the Organization).

1.11 HRPP Access to Legal Counsel

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 RCO 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 CU Chief Compliance Officer

3.1.2 CU Associate General Counsel/Privacy Officer

3.1.3 CU Director, Intellectual Resources Management

3.1.4 CU General Counsel

3.2 A representative from the Office of General Counsel attends CU IRB meetings and is available to address legal issues which arise during the meetings.

3.4 The IRB Director and the Office of General Counsel 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.

1.12 Sponsored Research

1.0 Purpose
The purpose of this policy is to describe the Organization's requirements for research sponsored by an external funding agency or commercial sponsor.

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.

3.0 Definitions

3.1 Sponsor is defined as the company (pharmaceutical, device or biotechnology), other non-federal agencies, non-profit foundations, or individual donors providing financial or other support for a research study. Where applicable, the term sponsor also includes agents of sponsors (for example, contract research organizations).

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

3.3 A Federal Awarding Agency is defined as a Federal agency that provides a Federal award directly to the Organization.

3.4 A Notice of Award is the legal document issued to a non-Federal entity (which would include the Organization) for a Federal Awarding Agency that an award has been made to support the study or project at the non-Federal entity.

3.5 A Subaward is an award of financial assistance made under a Notice of Award by a non-Federal entity to the Organization to carry out part of the scope of work or study.

3.6 A Subcontract is an agreement made under a contract between a commercial, non-federal agency, or foundation to another entity, which that entity is passing down financial assistance and the terms and conditions of that contract to the Organization.

4.0. Investigator Responsibilities

4.1 The investigator is responsible for assuring that all appropriate approvals are obtained from Sponsored Programs and the IRB prior to initiating any research interventions, including screening of potential subjects.

4.2 The investigator is responsible for assuring all charges for research activities are billed appropriately to the cost center or work order associated with the Contract, Notice of Award, Subaward or Subcontract.

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

4.2.1.1 An exception to this policy can be made by the IRB on a case by case basis.

4.3 The investigator is responsible for promptly reporting to the IRB if they are advised by the sponsor of (1) any findings that could affect the safety of subjects or the willingness of subjects to continue participation in the study (for example, serious adverse events), or (2) any findings that could influence the conduct of the study, or (3) any noncompliance, or (4) any other information important to the IRB's continued approval of the study.

4.4 The investigator is responsible for promptly reporting to the IRB if they are advised by the sponsor of any results of on-site monitoring conducted by the Sponsor at CU or other sites under the jurisdiction of the CU IRB.

4.5 The investigator is responsible for promptly initiating any corrective action required by the sponsor.

4.6 The investigator will notify subjects if they are advised by the sponsor after completion of the study of any findings that may directly affect the safety or medical care of subjects.

5.0 Sponsor Responsibilities

5.1 The Sponsor must promptly (no longer than 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.

5.2 The Sponsor must 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.

5.3 The Sponsor must report to the Organization and/or PI any results of on-site monitoring conducted by the Sponsor at CU or other sites under the jurisdiction of the CU IRB.

5.4 The Sponsor must have a plan in place to notify the Organization and/or PI of the results upon completion of the study when the findings may directly affect the safety or medical care of subjects.

6.0 Organization Responsibilities

6.1 All Contracts, Subcontracts, and Subawards are reviewed by CU Sponsored Programs.

6.2 In negotiating contracts with commercial sponsors, Sponsored Programs will utilize template language which is consistent with requirements in Addendum I (Contract or Funding Arrangement) below, and with AAHRPP accreditation standards.

6.2.1 If a sponsor is unwilling to utilize approved template language, the IRB and Sponsored Programs, in consultation with the Research Compliance Office, and appropriate legal counsel as needed, will determine whether the substitute language is consistent with requirements in Addendum I below, and with AAHRPP accreditation standards.

6.3 The Organization will not enter into a contract or other funding arrangement that does not obligate the sponsor (and/or the investigator) to fulfill its responsibilities as detailed in this policy, or that does not satisfy the requirements of Addendum I (Contract or Funding Arrangement) below.

6.4 When the Notice of Award or Contract agreement includes human research activities that will be conducted by investigators who are not employees or agents of the Organization, a Subcontract/Subaward must be executed between the Organization and the collaborating institution.

6.4.1 The Subcontract/Subaward 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.

6.4.2 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.

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

1.13 Compliance with ICH GCP Guidelines

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 the Organization does not provide review oroversight to research subject to ICH GCP Guidelines.

2.2 Research subject to ICH GCP Guidelines conducted by individuals affiliated with the Organization will be reviewed and approval maintained by a external IRB according to the requirements set out by HRPP Policy 1.4.

1.14 Research Subject to Department of Defense Regulatory Requirements

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 32 CFR 219, Department of Defense Regulations, "Protection of Human Subjects" (DoD adoption of the "Common Rule").

2.2.3 Title 45 Code of Federal Regulations Part 46, (45 CFR 46) Department of Health and Human Services Regulations, "Protection of Human Subjects," Subparts B, C, and D as made applicable by DoD Instruction (DoDI) 3216.02, 15 April 2020.

2.2.4 Title 21 Code of Federal Regulations 50, 56, 312, and 812, Food and Drug Administration (FDA) Regulations.

2.2.5 DoDI 3216.02, “Protection of Human Subjects and Adherence to Ethical Standards in DoD-Conducted and -Supported Research” April 15, 2020, Change 1, June 29, 2022.

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 DoDI 1100.13, “DoD Surveys”, March 31, 2017.

2.2.10 When conducting research supported by the Department of the Navy.

2.2.10.1 SECNAVINST 3900.39E of 29 May 2018.

2.2.10.2 OPNAVINST 5300.8C of 24 April 2008.

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

2.3.1 Education and Training Requirements In addition to investigator and research staff training requirements as described in HRPP policy 1.23 (HRPP Training Requirements and Opportunities for Research Personnel), it is the Principal Investigator’s responsibility to ensure that research staff has completed all appropriate educational requirements as mandated by DoD policy. (per DoDI 3216.02, 15 April 2020, or later; http://www.onr.navy.mil/About-ONR/compliance-protections/Research-Protections/Research-Protection-Training-References.aspx.)

2.3.2 Additional Protections for Pregnant Women, Prisoners, and Children {Subparts B, C and D) of 45 CFR 46) DoDD 3216.02, section 3.9}. In addition to protections described in HRPP policies 4.2 (Research Involving Pregnant Women, Human Fetuses, and Neonates), 4.3 (Research Involving Prisoners), 4.4 (Research Involving Children), and other policies as applicable, the following additional protections apply:

2.3.2.1 Regarding Research Involving Pregnant Women and Human Fetuses:
Research involving pregnant women, fetuses, or neonates as human subjects must comply with 45 CFR 46 subpart B except as below:

(1) For purposes of applying this section, the phrase "biomedical knowledge" is replaced with "generalizable knowledge."

(2) The applicability of 45 CFR 46 subpart B is limited to research involving pregnant women as human subjects involved in HSR that is greater than minimal risk, and includes interventions, as defined in 32 CFR 219, or invasive procedures involving: (a) The woman or the fetus; or (b) Fetuses or neonates as human subjects.

2.3.2.2 Regarding Research Involving Prisoners
Research involving prisoners as human subjects must comply with 45 CFR 46 subpart C except as below:

2.3.2.2.1 In addition to the categories of permissible HSR involving prisoners identified in 45 CFR 46 subpart C two additional categories are permissible:

(a) Epidemiological research that meets the waiver criteria in accordance with Federal Register 68: 36929-36931, may be approved in accordance with the applicable requirements of 45 CFR 46 subpart C, DoDI 3612.02 and other applicable requirements.

(b) HSR that would otherwise meet exemption criteria may be conducted but must first be approved by an IRB and must meet the requirements in 45 CFR 46 subpart C, DoDI 3612.02, and other applicable requirements.

2.3.2.2.2 When a previously enrolled human subject becomes a prisoner, and the protocol has not been reviewed and approved by the IRB in accordance with 45 CFR 46 subpart C, the PI must promptly notify the IRB and the Organization must notify the Human Research Protection Official (HRPO).

2.3.2.2.2.1 All research interactions and interventions with the prisoner-subject (including obtaining identifiable private information) must cease until and unless:

The IRB Chair or designee determines that it is in the best interest of the prisoner-participant to continue to participate in the research while a prisoner. In this case, 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

The convened IRB review and approves the protocol in accordance with 45 CFR 46 subpart C, DoDI 3612.02, and HRPP policy 4.3 (Research Involving Prisoners).

2.3.2.2.3 Research may not involve detainees unless the research involves an investigational drug or device when the same product would be offered to members of the US military in the same location for the same medical condition.

2.3.2.2.4 Research may not involve Prisoners of War.

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

2.3.2.3 Regarding Research Involving Children: Research involving children as human subjects must comply with 45 CFR 45 subpart D. The DoD considers all active-duty service members and all reserve component members in a Federal duty status to be adults; and therefore not subject to the protections of 45 CFR 46 subpart D. 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.

2.3.3 Additional Safeguards for Research Conducted with International Populations
In addition to the requirements described in HRPP policy 1.5 (Requirements for Research Conducted at International Sites) the following apply:

2.3.3.1 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.

2.3.3.2 The institution shall confirm that all applicable national laws and requirements of the foreign country have been met. The IRB shall also consider the cultural sensitivities in the setting where the research will take place (SECNAVINST 3900.39E, section 3d).

2.3.4 Limitation of Waivers and Exceptions from Informed Consent

2.3.4.1 Sections 219.116(e) and (f) of Title 32, CFR, identify conditions where an IRB may waive informed consent for DoD-conducted and DoD-supported HSR.

2.3.4.2 Section 980 of Title 10, U.S.C. (1) Imposes limitations on waiving informed consent when DoD appropriated funds are used to finance the research; (2) Is applicable only to DoD-conducted and DoD-supported research when involving a human being as an experimental subject as defined in this issuance. Research involving a human being as an experimental subject, governed by Section 980 of Title 10, U.S.C., is a subset of research involving human subjects, regulated by Title 32, CFR; and (3) Is not applicable to exempt HSR.

2.3.4.3 For research involving a human being as an experimental subject to which Section 980 of Title 10, U.S.C., applies, informed consent must be obtained in advance from the experimental subject or the subject's legal representative (consistent with Part 219 of Title 32, CFR, if the subject cannot consent). If consent is obtained from the subject's legal representative, the intention of the key investigator must be for the research to be beneficial to the subject.

2.3.4.4 For research governed by Section 980 of Title 10, U.S.C., that involves no more than minimal risk, as defined by Part 219 of Title 32, CFR, an IRB may alter or waive other required elements of informed consent pursuant to Part 219 of Title 32, CFR, so long as it still preserves informed consent of the subject (i.e., the consent indicates the subject's participation in the research is completely voluntary and includes the requirement that the subject is informed of research risks).

2.3.4.5 The advance informed consent requirement pursuant to Section 980 of Title 10, U.S.C., may be waived by the DOHRP or its delegate, if the following conditions are met: (1) The research is to advance the development of a medical product necessary to the DoD; (2) The research may directly benefit the individual experimental subject; and (3) The research is conducted in compliance with all other applicable laws and regulations.

2.3.5 Limitations on Compensation for U.S. Military Personnel

2.3.5.1 Federal employees while on duty (including military personnel) may be compensated for blood draws for research for up to $50 for each blood draw. Compensation is not allowed for general research participation.

2.3.5.2 Federal employees while off-duty (including military personnel) may be compensated for blood draws for research for up to $50 for each blood draw. Compensation is allowed for general research participation, as approved by the IRB; however, payment may not come directly from a federal source.

2.3.5.3 Non-Federal personnel may be compensated for blood draws for research for up to $50 for each blood draw. Compensation is allowed for general research participation, as approved by the IRB; payment may come from any federal or non-federal source.

2.3.6 Requirements for Informed Consent Forms
In addition to requirements described in HRPP policy 5.1 (Obtaining Informed Consent From Research Subjects) the following apply:

2.3.6.1 If the research includes any risks to the fitness for duty for DoD personnel (e.g., health, availability to perform job, data breach), the informed consent documentmust

inform DoD-affiliated personnel about these risks and that they should seek command or Component guidance before participating.

2.3.6.2 The informed consent document must include, if applicable, potential risks for the revocation of clearance, credentials, or other privileged access or duty

2.3.6.3 The informed consent document must include a statement that the DoD or a DoD organization is funding the study, and a statement that representatives of the DoD are authorized to review research records.

2.3.7 Classified Research

2.3.7.1 Classified research must receive prior approval from the DoD Office for Human Research Protections.

2.3.7.2 Classified research will be conducted following the requirements of DoD Instruction 3216.02 section 3.13.

2.3.7.3 Classified research is not eligible for review under expedited review procedures, or for a waiver of consent.

2.3.8 Undue Influence [DoDD 3216.02, para.4.4.4]

2.3.8.1 Superiors are prohibited from influencing the decisions of their subordinates regarding participation as subjects in research involving human subjects and shall not be present at any human subject recruitment sessions or during the consent process.

2.3.8.2 For research involving service members as human subjects that has been determined to be greater than minimal risk and when recruitment occurs in a group setting, the IRB shall appoint an ombudsman. The ombudsman shall not be associated in any way to the research and shall be present during the recruitment in order to monitor that the voluntary involvement or recruitment of the Service members is clearly and adequately stressed, and that the information provided about the research is clear, adequate, and accurate.

2.3.8.3 For research involving service members as human subjects, that has been determined to be NO greater than minimal risk and when recruitment occurs in a group setting, and for research involving DoD civilians, the IRB shall determine when it is appropriate to appoint an ombudsman for the purposes described above. The decision to require the appointment of an ombudsman should be based in part on the human subject population, the consent process, and the recruitment strategy.

2.3.9 Requirements for Research Related Injury

2.3.9.1 Consent for DoD-supported research that is greater than minimal risk must include information about available compensation or medical treatments if a research-related injury occurs.

2.3.9.2 For research subject to Department of the Navy (DON) requirements, every project involving greater than minimal risk shall include an arrangement for emergency treatment and necessary follow-up of any research-related injury. The IRB will determine whether research involving minimal risk also might include a similar arrangement for research-related injury.

2.3.10 Requirements for Reporting

2.3.10.1 When participating in DoD supported non-exempt human subject research, the organization must provide to the HRPO (1) documentation that the DoD-supported HSR has been reviewed and approved by an IRB, including scientific merit, amendments, and additional reviews; (2) documentation of key investigators' human research protection training; (3) IRB-approved protocol documents; and (4) current FWA and IRB registration numbers.

2.3.10.2 When participating in DoD supported exempt human subject research, the organization must submit institutional documentation of the determination that the research is exempt HSR to the HRPO, to include all protocol documents.

2.3.10.3 When participating in DoD supported non-exempt human subject research the Organization must promptly notify the HRPO of the following:

2.3.10.3.1 IRB-approved changes to HSR that involve changes to key investigators or institutions; decreased benefit or increased risk to subjects in greater than minimal risk research as defined in 32 CFR 219; addition of vulnerable populations, or DoD-affiliated personnel as subjects.

2.3.10.3.2 Transfer of HSR oversight to a different IRB.

2.3.10.3.3 Notification by any federal body, State agency, official governing body of a Native American or Alaskan native tribe, other entity, or foreign government that the non-DoD institution's DoD-supported HSR is under investigation.

2.3.10.3.4 Any problems involving risks to subjects or others, suspension or termination of IRB approval, or any serious or continuing noncompliance pertaining to DoD-supported HSR.

2.3.10.3.5 The results of the IRB's continuing review, if required.

2.3.10.3.6 Change in status when a previously enrolled human subject becomes pregnant, or when the researcher learns that a previously enrolled human subject is pregnant, and the protocol was not reviewed and approved by the IRB in accordance with 45 CFR 46 subpart B.

2.3.10.3.7 Change in status when a previously enrolled human subject becomes a prisoner, and the protocol was not reviewed and approved by the IRB in accordance with 45 CFR 46 subpart C.

2.3.10.3.8 A DoD-supported study's closure.

2.3.10.4 When participating in DoD supported non-exempt human subject research the Organization must make records that document compliance or noncompliance with DoDI 3612.02 accessible for inspection and copying, as determined by DoD Human Research Protection Program personnel, by authorized DoD representatives.

2.3.10.5 When participating in Department of the Navy (DoN) supported non-exempt human subject research, the organization must inform the DoN HRPP Office (within 30 days of the incident) of any of the following:

2.3.10.5.1 The initiation and results of investigations into allegations of noncompliance.

2.3.10.5.2 Serious adverse events; or audits, investigations, or inspections of research.

2.3.10.5.3 Audits, investigations, or inspections of the Organization HRPP conducted by outside entities.

2.3.10.5.4 Significant communication between institutions conducting research and other federal departments and agencies regarding compliance and oversight.

2.3.10.5.5 All restrictions, suspensions, or terminations of the Organization assurances.

2.3.11 Requirements for a Medical Monitor:
For DoD-supported research, prior to April 15, 2020, a named independent research monitor was required for greater than minimal risk research and was optional for minimal risk research. As of April 15, 2020, a research monitor is no longer required by the DoD for DoD-supported research, regardless of risk level.

2.3.12 Requirements for Survey Research:

The Principal Investigator for any DoD-supported research involving surveys is responsible for arranging for the review of the survey by the appropriate DoD component. This review is in addition to review by the IRB. For DoN funded survey research, a Privacy Act Statement must be displayed prominently on all Navy personnel surveys. 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 (OPNAVINST 5300.8C).

2.3.13 Requirements for DoD Oversight:
The HRPP will support the oversight by the sponsoring DoD component, including communicating to the sponsoring DoD component about:

2.3.13.1 information needed to assure that the approval of the initial submission is in compliance with all applicable requirements; and

2.3.13.2 IRB-approved substantive changes, including a notification that the Principal Investigator is informed that the changes cannot be implemented prior to acceptance by the sponsoring DoD component; and

2.3.13.3 the results of the continuing review; and

2.3.13.4 other information reported as required by section 2.3.11 (Requirements for Reporting) above.

2.3.14 Research involving Chemical or Biological Agents

2.3.14.1 The organization does not permit research involving chemical or biological agents.

2.3.15 Confidentiality of Research Data

2.3.15.1 Data or information acquired by the DoD component under a pledge of confidentiality for exclusively statistical purposes must be used exclusively for statistical purposes and may not be disclosed in identifiable form for any other purpose, except with the informed consent of the respondent (per DoDI 3216.02 June 29, 2022).

2.3.15.2 All studies involving large scale genomic data collected on/from DoD-affiliated personnel will apply an DHHS Certificate of Confidentiality (per DoDI 3216.02 June 29, 2022).

3.0 Definitions

3.1 For DoD supported research, the following definitions apply (and supersede definitions in other HRPP policies)

3.1.1 Research Involving a Human Being as an Experimental Subject - An activity, for research purposes, where there is an intervention or interaction with a living individual for the primary purpose of obtaining data regarding the effect of the intervention or interaction. Research involving a human being as an experimental subject is a subset of research involving human subjects. This definition relates only to the application of Section 980 of Title 10, U.S.C.; it does not affect the application of Part 219 of Title 32, CFR.

3.1.2 Minimal Risk - 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 (32 CFR 219). This definition does not include does not include the inherent occupational risks that certain subjects face in their everyday life, such as those (1) encountered by Service members, law enforcement, or first responders while on duty; (2) resulting from or associated with high-risk behaviors or pursuits; (3) experienced by individuals whose medical conditions involve frequent tests or constant pain (DoDI 3216.02 section 3.8b).

3.1.3 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 Instructions (DoDI) 3216.02. These entities include the Office of the Secretary of Defense (OSD), the Military Departments, the Office of the Chairman of the Joint Chiefs of Staff and the Joint Staff, the Combatant Commands, the Office of the Inspector General of the Department of Defense, the Defense Agencies, the DoD Field Activities, and allother organizational entities within the DoD.

3.1.4 Support of a Study - funds or assistance that are provided by the DoD to non-DoD institutions for HSR through a grant, contract, or similar arrangement subject to the DFARS or other applicable DoD regulations, such as the DoD Grant and Agreement Regulations. Included in this definition is the DoD's provision of assistance to non-DoD institutions, whether or not through collaboration between DoD and non-DoD institutions, such as facilities, equipment, personnel (investigators or other personnel performing tasks identified in the research protocol), access to or information about DoD-affiliated personnel for recruitment, or data or specimens.

3.1.5 Detainee - any individual captured by, or transferred to the custody or control of, DoD personnel pursuant to the law of war. This does not include persons being held solely for law enforcement purposes, except where the United States is the occupying power.Detainees who are U.S. citizens or U.S. resident aliens will continue to enjoy all applicable rights and privileges under U.S. law and DoD regulations (DoDD 2310.01E).

3.1.6 DoD Personnel - Service members, Reserve Service members, National Guard members,DoD civilians, and DoD contractors. (DoDI 3216.02).

3.1.7 Service Members - Individuals appointed, enlisted, or inducted for military service under the authority of the DoD. The Military Services are the Army; the Navy, including the Coast Guard under circumstances involving the declaration of war; the Air Force; the Marine Corps; and the Reserve Components. Members of the Reserve Components are included when in a duty status.

3.1.8 Human Research Protection Official (HRPO) - A federal employee designated by a DoD Component or institution to conduct administrative review of DoD-supported research and whose review of DoD-supported research is intended to ensure compliance with DoD HSR requirements.

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 consult the Research Subject to Department of Defense Research Regulatory Requirements Checklist to ensure compliance with all applicable DoD requirements, DoN requirements, and requirements of this and all other HRPP policies.

4.3 As appropriate and required (per section 2.3.9 above) the IRB will appoint an ombudsman to protect the rights of service members.

4.4 The IRB Administrator responsible for the protocol will assure that the PI has:

4.4.1 Notified appropriate DoD entities, as described above, and confirmed that the DoD component has conducted an administrative review as required by DoDI 3612.02 section 3.5b.

4.5 The IRB Administrator responsible for the protocol will:

4.5.1 Assure the Organization has a valid FWA as required by DoDI 3612.02 section 3.4a.

4.5.2 Assure that the requirements of this policy are met.

4.5.3 Assure that the informed consent form complies with provisions of section 2.3.6 (Requirements for Informed Consent Forms) above.

4.5.4 Make reports to the DoD (or have the PI make reports to the DoD) as described above.

1.15 Research Subject to Department of Justice Regulatory Requirements

1.0 Purpose

The purpose of this policy and procedure is to specify the Organizations 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 IRB Office.

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 CUCU 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) inorder 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 results 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 Creighton University 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 in the study.

4.2.7.1.6 Anticipated results of the study.

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 participant.

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 who 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.

4.2.9 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.

1.16 IRB Office Record Keeping Requirements

1.0 Purpose

The purpose of this policy is to describe the Organization's requirements for maintenance of documentation of IRB activities. Retention of records by the investigator is described in HRPP policy 1.17 (Retention of Research Records).

2.0 Policy

It is the policy of the Organization that the IRB will maintain documentation of all IRB activities in accordance with 45 CFR 46.115 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:

In accordance with 45 CFR 46.115, the IRB will maintain, in paper or electronic format:

3.1.1 Copies of all research proposals reviewed, scientific evaluations, if any, that accompany the proposals, approved sample consent forms, progress reports submitted by investigators, and reports of injuries to subjects.

3.1.2 Minutes of IRB meetings which shall be in sufficient detail to show attendance at the meetings; actions taken by the IRB; the vote on these actions including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution.

3.1.3 Records of continuing review activities, including the rationale for conducting continuing review of research that otherwise would not require continuing review as described in §46.109(f)(1).

3.1.4 Copies of all correspondence between the IRB and the investigators.

3.1.5 A list of IRB members in the same detail as described in §46.108(a)(2).

3.1.6 Written procedures for the IRB in the same detail as described in §46.108(a)(3) and (4).

3.1.7 Statements of significant new findings provided to subjects, as required by §46.116(c)(5).

3.1.8 The rationale for an expedited reviewer's determination under §46.110(b)(1)(i) that research appearing on the expedited review list described in §46.110(a) is more than minimal risk.

3.1.9 Documentation specifying the responsibilities that an institution and an organization operating an IRB each will undertake to ensure compliance with the requirements of this policy, as described in §46.103(e).

3.2 Records of protocol related activities submitted electronically through InfoEd are maintained indefinitely in InfoEd.

3.3 Records of protocol related activities submitted on paper are maintained in CU storage in either electronic or paper format. Files will be maintained by the IRB as described in HRPP 1.17 (Retention of Research Records).

3.4 Records of protocol related activities will be retained by the investigator as described in HRPP 1.17 (Retention of Research Records).

3.5 Copies of IRB agendas,minutes, IRB member Curriculum Vitae, and IRB membership rosters are maintained within InfoEd or as electronic or paper documents within the IRB Office.

3.6 Copies of all educational items given to the IRB members are maintained within InfoEd oras electronic or paper documents within the IRB Office.

3.7 Copies of HRPP policies are maintained on the CU website.

4.0 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.

1.17 Retention of Research Records

1.0 Purpose
The purpose of this policy is to describe the 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.

2.1 All records associated with non-exempt human subject must be retained securely, for at least seven years beyond the termination of the study or longer as required by sponsors. If records include subject identifiers, those identifiers must be retained with the research records.

2.2 All records associated with exempt human subject research must be retained securely for at least three years beyond the termination of the study.

3.0 Required Records

3.1 Research records include:

3.1.1 All applications, other forms, communications, reports and other documents created in, or stored in, InfoEd. For the purposes of this policy the presence of this information within InfoEd constitutes retention.

3.1.2 Subject files including original signed consent documents, case report forms, laboratory results and other applicable information.

3.1.3 All communications between the investigator and the sponsor or funder, or, for multisite studies, between the local investigator and other investigators or coordinating center(s).

3.2 For applications and reports generated within InfoEd (for example, the IRB Application, Request for Modifications, Continuing Review, etc.), a paper copy may be printed an retained as above, or the presence of the information within InfoEd 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 PI's department or college maintain the research records.

4.1.1 If the research is conducted by a student, the faculty advisor is responsible for assuring retention of records as above.

4.1.2 If the PI is volunteer faculty then the Dean or other person taking responsibility for assuring the PI fulfills his/her responsibilities (as described in HRPP 1.26 (PI Qualifications and Responsibilities)) must maintain the research records.

4.2 The PI may request a copy of the research records in accordance with applicable Organizational policies.

1.18 Review and Approval of HRPP Policies and Procedures

1.0 Purpose

The purpose of this policy is to describe the Organization's requirements for the review and approval of HRPP policies.

2.0 Policy

It is the policy of the Organization to continually assess the adequacy of existent policies 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

3.1 The IRB Administrators, IRB Director, Director of Research Compliance, IRB Chairs, and IO will review HRPP policies on a rolling basis, with a target of review of policies at least every three years. 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 which are regulatory in nature (that is, which are dictated by federal, state, and local laws, regulations, and guidance), or which solely describe IRB Office 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 which are extra-regulatory in nature will be reviewed and approved by the IRBs that have scheduled meetings (IRBs -01 and -02), the Director of Research Compliance, and in select cases, other Organizational officials.

4.0 Full IRB Review of Draft HRPP Policies

4.1 New and revised (draft) HRPP policies requiring review by the full IRB (per section 3.3 above) will either be (1) discussed at all 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 Chair for further discussion and revision before re-consideration.

4.3 Review by email

4.3.1 At the discretion of the IO or the IRB 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 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.

4.3.4 For the vote to be valid, a majority of the entire IRB membership must cast a vote. For the policy to be approved, a majority of those voting must be attained.

4.3.5 If the motion to approve a policy fails to pass, the draft policy may be referred to the IRB Chair for further discussion and revision before re-consideration.

5.0 Organizational Notification of Changes to HRPP Policies

5.1 Changes to HRPP policies will be communicated to the Organization's research community by email, notification on the IRB website, and/or other media as appropriate.

5.2 IRB Administrators and staff will be notified by email or at a staff meeting.

1.19 IRB Signature Authority

1.0 Purpose
The purpose of this policy is to describe the Organization's requirements for granting signature authority for the IRB Office and IRB correspondence.

2.0 Policy
It is the Organization's policy that the Director of Research Compliance, IRB Director, the IRB Chairs and Vice-Chairs and qualified IRB staff will have appropriate signature authority on behalf of the IRB Office and the IRB.

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

3.1 Director of Research Compliance and the IRB Director have the authority to sign: 1) HRPP policies in conjunction with the Institutional Official (IO), 2) IRB authorization agreements after review and approval by 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 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 3) other IRB correspondence as necessary. In exercising this authority, the IRB Administrators will consult the IRB Chair, vice-chair, or other IRB members as necessary and may refer IRB review letters or other correspondence to the IRB Chair for signature.

1.20 Community Involvement in Outreach Activities and Community Based Participatory Research (CBPR)

1.0 Purpose

The purpose of this policy is to describe the Organization's outreach activities to enhance the public's understanding of research, obtain feedback about any community concerns, disseminate results of research conducted by the Organization and encourage involvement of the community in the research process.

2.0 Policy

It is the policy of the Organization that:

2.1 Outreach activities will be undertaken through a variety of mechanisms and venues to enhance the understanding of research by both the communities the Organization serves, as well as the members of those communities.

2.2 Outreach activities will be undertaken to make the community aware of current and proposed research activities of the Organization, and to provide advice about the needs of the community.

2.3 As appropriate considering the nature of the research, the Organization will involve 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.

3.0 Outreach Activities for Education of the Community

3.1 The Organization utilizes the following established outreach activities for educational purposes, as well as the dissemination of research results:

3.1.1 Participation in CU Research Week activities.

3.1.2 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 greater Nebraska. Results from completed research may also be presented in community forums.

3.1.6 Websites: Websites maintained by components of the Organization are available containing information about the Organization and its research activities, including material pertinent to research.

4.0. Evaluation of Outreach Activities

4.1 The IRB Director, in conjunction with the IO, Director of Research Compliance, and IRB Chairs perform an ongoing evaluation of community outreach activities to identify the needs of the community and any concerns.

1.21 Post-Approval Monitoring of Research

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.

4.1.1.1.6 Minimal risk research.

4.1.1.1.7 Closed 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 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 or the Research Compliance Office (RCO) Auditor. 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 nine 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 or RCO Auditor. 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 or RCO Auditor 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 IRB 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 Chair or Director of Research Compliance.

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 or RCO Auditor 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 or RCO Auditor 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 or RCO Auditor 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 Chair, IRB Director, Director of Research Compliance, and the IO.

4.2.2.12 The designated IRB Administrator or RCO Auditor, in consultation with the IRB Director, Director of Research Compliance, IO and the IRB 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 or RCO Auditor. In some cases, the PI and/or other study personnel may be required to undergo specific training 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.

4.2.3.1 It is expected that "For Cause" Audits will be conducted by the Research Compliance Office Auditor. The RCO Auditor may request assistance or support from the IRB as needed or desired.

1.22 Assessment of the Effectiveness and Efficiency of the HRPP

1.0 Purpose

The purpose of this policy 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 Director of Research Compliance, IRB Director, IRB Chairs and IRB staff.

3.1.2 Organizational officials may bring problems, or suggestions for improvement, to the attention of the IO, Director of Research Compliance, IRB Director, or IRB Chairs for appropriate action.

3.1.3 The Director of Research Compliance, IRB Director, 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 RCO Office Meetings as well as at IRB team 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 each board will be randomly selected for audit quarterly (as available). 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).

3.1.5.1 Audits will be conducted by IRB Administrators with assistance from the RCO Auditor.

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 Chairs, IO, IRB staff, Director of Research Compliance, or IRB Director.

3.1.6.1 As appropriate, the IRB Director and IRB Administrators may schedule focus group discussions with Investigators from components of the Organization to discuss the effectiveness of the HRPP.

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 Director

3.2.1 The Director of Research Compliance will evaluate the performance of the IRB Director 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 Director of Research Compliance will obtain feedback from the IRB Members and IRB administrators regarding the performance of the IRB Director.

3.2.3 If the IRB Director's performance is judged to be deficient, the Director of Research Compliance will discuss his/her concerns with the IRB Director and seek a satisfactory resolution.

3.3 Evaluation of the Chairs and Vice-Chairs

3.3.1 The IO, in consultation with the Director of Research Compliance and the IRB Director, will review the performance of the IRB Chairs and Vice-Chairs on an annual basis considering, but not limited to, the following criteria:

3.3.1.1 Meeting leadership.

3.3.1.2 General regulatory knowledge.

3.3.1.3 Active participation in IRB Executive Committee (for IRB Chairs) and involvement in activities of the IRB Office.

3.3.1.4 Attendance at meetings.

3.3.1.5 Timeliness and completeness of IRB reviews, as assigned.

3.3.1.6 Participation in IRB discussions.

3.3.2 If an IRB Chair or Vice-Chair's performance is judged to be deficient, the IO will discuss his/her concerns with the Chair or Vice-Chair and seek a satisfactory resolution. Upon recommendation of the Director of Research Compliance and the IRB Director, 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 Director will convene a meeting with the IRB Administrators and staff to evaluate the IRB Members considering, but not limited to, the following:

3.4.1.1 Attendance at meetings for which they have been assigned review items.

3.4.1.2 Timeliness and completeness of IRB reviews, as assigned.

3.4.1.3 Participation in IRB discussions.

3.4.1.4 General regulatory knowledge.

3.4.2 IRB members will be provided feedback, by letter or in person, regarding their performance.

3.4.2.1 If an IRB member's service is judged to be satisfactory or exceptional, the IRB Director in consultation with the Director of Research Compliance, will so inform the member.

3.4.2.2 If an IRB member's service is judged to be significantly deficient, the IRB Director in consultation with the Director of Research Compliance, will discuss the concerns with the member and seek a satisfactory resolution.

3.4.3 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 Director of Research Compliance and the IRB Director.

3.4.4 Upon request of individual IRB members, the Director of Research Compliance 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 IRB Director will annually evaluate the performance of the IRB Administrators.

3.5.1.1 The IRB Director will provide feedback verbally to each IRB Administrator during the annual review process, as well as written comments using the CU Performance Evaluation System.

3.5.1.2 The IRB Director will also provide ongoing feedback about the performance of the IRB Administrators throughout the year.

3.6 Annual Evaluation of the HRPP

3.6.1 The evaluation of the HRPP will be conducted utilizing the HRPP Assessment Survey. Each component of the HRPP, IRB members, investigators, and other research personnel will be invited to participate and provide feedback. The survey will assess the interactions between the IRBs, investigators, and other components of the HRPP, as well as the overall effectiveness of the HRPP. The IO in conjunction with the Director of Research Compliance and the IRB Director and any other personnel deemed appropriate will review the Annual HRPP Assessment Form with the objective to:

3.6.1.1 Determine which items on the Annual HRPP Assessment Form are judged to be Excellent (E), Satisfactory (S) or Unsatisfactory (US).

3.6.1.2 All items judged to be unsatisfactory will require a corrective action plan with set goal(s) in a time frame based upon the seriousness of the deficiency.

3.6.1.3 At least one item rated satisfactory will be targeted for further improvement before the next evaluation, and to set specific goals dependent upon available staff and resources.

3.6.1.4 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.

1.23 HRPP Training Requirements for Research Personnel

1.0 Purpose

The purpose of this policy 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 CU 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 Required Training

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:

4.1.1.1 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.

4.1.1.2 Faculty Advisors of student investigators.

4.1.2 The CITI Training Program is accessible via http://www.citiprogram.org, or through a link on the CU IRB website.

4.1.3 The Biomedical and the Behavioral and Social Science courses consist of a series of Basic (core) modules which must be completed by users, and additional modules (primarily related to specific types of research or research subject populations). The GCP course consists of a series of required modules.

4.1.4 CITI training course requirements

4.1.4.1 The Biomedical course must be completed by personnel described in section 4.1.1 who conduct biomedical human subjects research (including medical records and human biological material within the Organization or at external sites where the CU IRB serves as the IRB of record.

4.1.4.2 The Behavioral and Social Science course must be completed by personnel described in section 4.1.1 who conduct Behavioral and Social Science human subjects research within the Organization or at external sites where the CU IRB serves as the IRB of record.

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

4.1.4.3.1 Personnel described in section 4.1.1 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).

4.1.4.3.2 Personnel described in section 4.1.1 who conduct research utilizing an FDA regulated drug, device or biologic.

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

4.1.5.1 Personnel described in section 4.1.1 must complete all Basic (core modules) appropriate for the type of research (as per 4.1.3.1 thru 4.1.3.3).

4.1.5.2 Personnel described in section 4.1.1 who are conducting research where the additional modules are relevant must attest that they have completed those additional modules before final release of the protocol by the IRB Office.

4.1.6 New research personnel added to IRB-approved research via a Request for Modifications or Application for Continuing Review must complete CITI training as described above prior to involvement in the research.

4.1.7 The Organization will accept CITI Training records from other institutions if the other institution utilized the CITI training courses specified above.

4.1.7.1 For all but greater than minimal risk research, the IRB will accept the attestation of an investigator from another institution that he/she is compliant with the CITI requirements of their home institution.

4.1.7.2 External investigators (other than those employed by CU's Pheonix partners) conducting greater than minimal risk research under the oversight of CU IRB must complete CU IRB's CITI training requirements.

4.1.8 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 has been completed in the previous three years. The IRB Director, in consultation with the IO as needed, will have the sole authority to accept such training.

4.1.9 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 CU IRB is the IRB of record. The PI must certify that all external research personnel have completed appropriate 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 4.1.1. However, personnel already listed on an active protocol whose CITI training expires may continue associated with that protocol.

4.2 Conflict of Interest Training
Conflict of Interest Training is required in accordance with CU Financial Conflict of Interest (CIRC) Policy 3.1.10 and HRPP policy 1.25 (Financial Conflicts of Interest).

5.0 Additional (Optional) Training

5.1 CU Websites

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

5.1.2 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.

5.1.3 The CU IRB Office will periodically post access to relevant presentations and other educational materials on the IRB website.

5.2 Individual Training

5.2.1 The IRB Administrators provide individualized training to any research personnel upon request. This training may be conducted in the IRB or at any requested location within the Organization.

5.2.2 Supervisors of new employees of the Organization may request IRB Introduction and Overview as mandatory training. This training is generally provided by an IRB Administrator.

5.3 CU 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.

5.4 Student Education: Didactic classroom presentations are offered to CU students on topics pertaining to human subject protection by request.

5.5 Webinars: The IRB Office facilitates access to webinars sponsored by external organizations on topics relevant to Human Subject Research.

5.6 UNMC HRPP 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 Creighton University and the Great Plains IDeA-CTR Network, brings together national and local speakers to explore cutting edge topics in human research subject protection. The conference has occurred annually since 2010, though postponed in 2020 due to the Coronavirus pandemic. The target audience is IRB administrators and staff, IRB members, investigators and research coordinators.

6.0 Procedures for Assessing Training Requirements

6.1 At regular intervals, the IRB Director, Director of Research Compliance, and IO will re-evaluate the content, specific requirements, and effectiveness of training for research personnel associated with the

Organization. This assessment will take into consideration current literature and evolving federal guidance regarding various aspects of research ethics and human subject protection, feedback from research personnel regarding their training needs, assessment of the quality and completeness of IRB submissions by IRB members and the IRB Administrators.

7.0 Procedures for Maintaining Training Records
The IRB 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.

1.24 HRPP Training Requirements for IRB Members

1.0 Purpose
The purpose of this policy 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.

4.0 Initial Training and Orientation

4.1 New IRB members, including alternate members, will meet with the IRB Director or designee, and appropriate IRB Administrators for orientation to cover the following items:

4.1.1 Overview of HHS 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 InfoEd.

4.2 New IRB members 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).

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

4.4 Full orientation must be completed before the new IRB members may serve as a reviewer or count as a voting member. Prior to completion of orientation, agenda will record new IRB members as "non-voting."

4.5 New IRB members are assigned an experienced IRB Administrator 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 RCO/IRB Office 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 RCO/IRB Office via email or at IRB meetings.

5.3 Completion of required continuing education will be assessed at the time of the annual evaluation of IRB members (see HRPP policy 1.22) in terms of general regulatory knowledge. Members who remain deficient after this review may have their appointment terminated.

1.25 Financial Conflicts of Interest

1.0 Purpose

The purpose of this policy 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
It is the policy of the Organization that:

2.1 All potential financial COIs of responsible personnel engaged in human subjects 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; and b) National Science Foundation (NSF) regulations.

2.2 The IRB will interact with the Conflict of Interest in Research Committee (CIRC), 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 Any changes in financial interest must be promptly disclosed and managed in accordance with Section 2.1 above.

2.4 The Research Compliance Office will ensure that the organization has adequate policies and procedures to ensure 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: any faculty, students, staff, or other representatives of the Organization who are responsible for the design, conduct, or reporting of research, or the development of proposals to conduct research. This includes: Principal Investigator, Co-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, 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).

3.3 Conflict of Interest (COI): 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 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 (1) anything of monetary value that exceeds $5,000 which the Covered Person has received in the past 12 months preceding the disclosure or intends to or had knowledge of earning during the reporting year; or (2) 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: 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: a situation when the Organization itself, or any of its component parts, or any of senior organizational officials, have a financial interest in the design, conduct, or outcome of human subject research. 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 Conflict of Interest in Research Committee (CIRC): 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.

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.

5.0 COI Management Plan

5.1 A COI Management plan will be developed for research where responsible personnel have a significant financial interest.

5.1.1 For multi-institution research where the CU IRB is the reviewing IRB, the COI Management plan may be generated by the relying institution, in accordance with the terms of the reliance agreement.

5.2 The COI management plan may include an appropriate disclosure of the presence of a financial COI of the Responsible Person(s) in the consent form, in any presentations, publications, or news articles regarding the research, and to all personnel involved in the research including students. Additional management strategies may include (but are not limited to) more frequent and/or independent monitoring of the research; modification of the research protocol to manage potential bias (for example, through blinding); monitoring of the consent process; divesting or appropriately reducing the financial interest giving rise to the COI; severing relationships existing between the Covered Person and the company or other entity that is the source of the COI; or disqualification of the Covered Person from participation in all or a portion of the research.

5.3 In addition to any features required by the CIRC and the IRB, the COI management plan will prohibit:

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 Review of COI Management Plans

6.1 Management plans for responsible personnel with non-significant financial interest will not be reviewed by the convened IRB. The IRB Office will be notified by the Director of Research Compliance of the management plan, and the investigator's agreement to abide by it.

6.2 Management plans for responsible personnel with significant financial interest will be reviewed by the convened IRB (for FB studies) or by an expedited reviewer (for minimal risk studies).

6.3 For management plans reviewed by the convened IRB the following apply:

6.3.1 The full IRB will be provided with the COI management plan approved by the CIRC.

6.3.2 The IRB chair or designee will verbally describe the nature of the financial interest, and the specifics of the management plan proposed by the CIRC.

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).

6.3.3 The full IRB must approve the COI Management Plan proposed by the CIRC 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 CIRC.

6.4 For management plans reviewed by an expedited reviewer, the reviewer may approve the plan, or may refer to the convened IRB if he/she believes that a more stringent COI management plan is required. The expedited reviewer may not adopt a less stringent plan than that approved by the CIRC.

6.5 Management plans for responsible personnel with significant financial interest who are participating in a study where the Organization relies on an external IRB will not be reviewed by the convened IRB. The IRB Office will acknowledge receipt of the plan and will instruct the PI to notify the IRB of record.

6.6 In all cases, the 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 of record.

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 RCO/IRB Office 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 RCO/IRB Office 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, or any senior organizational officials, have a financial interest in the design, conduct, or outcome of human subject research.

9.2 In accordance with the CU Financial Conflict of Interest in Research policy (3.1.10), CU 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 CIRC as soon as it is identified.

9.4 Organizational COI may be identified through:

9.4.1 The required disclosure of financial interest of the Responsible Personnel at the time the IRB application is submitted.

9.4.2 The required annual disclosure of financial interest of senior administrators when it relates to human subject research.

9.4.3 Review by technology transfer officials or other officials at organizational components.

9.5 If an Organizational COI is identified, the CIRC will review the potential Organizational COI and propose any required management plans for approval.

9.6 Initial review of non-exempt human subject research for which an organizational COI has been identified will be performed by the convened IRB.

9.7 The IRB Director will provide the full IRB with the FCOI committee's approved COI Management Plan.

9.8 The IRB Director, IRB Chair, or designee will describe the nature of the financial interest, and the specifics of the management plan proposed by the CIRC.

9.9 The IRB will review the management plan and if any concerns are identified, these will be conveyed to the CIRC for further consideration and action.

9.10 The IRB must be assured that any Organizational COI is appropriately managed in the interest of the safety and welfare of human subjects.

9.11 Organizational COI management plans approved by the IRB will be maintained in the RCO/IRB Office for no less than seven years following cessation of the activity.

1.26 PI Qualifications and Responsibilities

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 (as applicable) 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 Sub-Investigator (Sub-I).

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 CU HRPP policies.

3.3 Sub-Investigator (Sub-I) 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 CU 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 CU IRB is the IRB of record.

3.5 A researcher employed or otherwise representing another institution who is under the jurisdiction of another IRB which has a reliance agreement with CU and for which the CU is acting as a central or single IRB is not considered an XI (per HRPP policy 1.28; External Investigator Assurance).

3.6 Sponsor-Investigator is the individual, who initiates the research, assumes overall responsibility for the research as indicated in section 3.2 above.

4.0 Qualification Requirements for the PI

4.1 The PI must be an employee, faculty, or student of the Organization. Faculty shall include full- or part-time persons or emeritus faculty. Faculty include those with special faculty appointments, such as volunteer, adjunct, courtesy (without a CU faculty appointment) research or visiting faculty (collectively referred to as "volunteer faculty").

4.1.1 When a learner or trainee is the PI, a researcher sufficiently experienced in the area of the trainee's research interest and satisfying the requirements of Section 4.1 above must serve as a co-investigator for research and be jointly responsible for oversight of the research.

4.1.2 Undergraduate students and medical students may not serve as PI for a research study.

4.1.3 Graduate students, residents, and fellows may serve as PIs for minimal risk research only.

4.2 Individuals other than employee, faculty, or student of the Organization may serve as PI only upon the permission of the IO.

4.3 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 CU HRPP policies.

4.3.1 When a student or trainee is the PI, a researcher sufficiently experienced in the area of the trainee's research interest and satisfying the requirements of Section 4.1 above must serve as a co-investigator for research and be jointly responsible for oversight of the research.

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 or exemption 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 sub-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 sub-investigator(s) conducting the research and other study personnel (as appropriate) with a copy of the: a) CU 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 sub-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 collectedto 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) 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, 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 sub-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 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 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 CU 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, and the sponsor (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 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 CU IRB for oversight of research. The PI must assure:

6.8.1 Compliance with HRPP policy 1.3 (CU 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 CU IRB review.

6.8.4 The research records contain:

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 CU 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 fulfil all applicable requirements specified in HRPP policy 1.4 (CU IRB Ceding Review to an External IRB), and as described in the Reliance Agreement.

1.27 Research Personnel Qualifications and Responsibilities

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 CU 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)

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 Sub-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 CU 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 Sub-Investigator(s) (SI):

4.2.1 Sub-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, 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.

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 while 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.

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 RCO/IRB Office. 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 while 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 while 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).

1.28 ClinicalTrials.gov Reporting

1.0. Purpose

The purpose of this policy is to describe the requirements for registration and compliance with ClinicalTrials.gov.

2.0. Policy

It is the policy of the Organization that:

2.1 FDA regulated trials that meet the definition of an "applicable clinical trial" (ACT) will be registered and updated on ClinicalTrials.gov in compliance with HHS regulations at 42 CFR 11 (Final Rule for Clinical Trials Registration and Results Information Submission).

2.1.1 Investigators are required to 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.

2.2 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 All qualifying clinical trials which will render claims for items and services to the Center for Medicare and Medicaid Services (CMS) will be registered and updated on ClinicalTrials.gov as specified in the "Medicare National Coverage Determination (NCD) Manual," section 310.1.

2.4 If an investigator voluntarily registers a study on ClinicalTrials.gov even though registration is not required, all ClinicalTrials.gov requirements and CU HRPP policies related to ClinicalTrials.gov reporting apply.

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. The NIH definition of "clinical trial" is, however, broader than the term "applicable clinical trial" as defined in 42 CFR 11 (below).

3.1.2.2 The NIH definition of a clinical trial includes “Basic Experimental Studies involving Humans” (BESH) that meet both the definition of basic research and the NIH definition of a clinical trial. BESH are subject to NIH clinical trials policies such as registration and results reporting.

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).

3.3.1.1 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, and has authority and control, is considered to be the Responsible Party.

3.3.2 The sponsor of the clinical trial may designate the PI to be the Responsible Party, if the PI satisfies the requirements of 42 CFR 11.4(c)(2).

3.3.3 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.

3.4 Record Owner: ClinicalTrials.gov Protocol Registration and Results System (PRS) account holder who creates a study record in PRS and is authorized by the Responsible Party to enter information into the PRS.

4.0. Investigator Responsibilities

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 PI is responsible only for assuring the IRB Application correctly reflects that the research study is registered with clinicaltrials.gov and that the NCT number is accurate. Otherwise, this section does not apply.

4.1 The PI must ensure the following trials are registered in the ClinicalTrials.gov PRS system:

4.1.1 All NIH-funded clinical trials

4.1.1.1 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 clinical trials studying interventions not regulated by the FDA, such as behavioral interventions are covered by this policy.

4.1.2.2 The investigator is responsible for submitting to Sponsored Programs a copy of the award letter or other documentation from the NIH which specifies whether the trial constitutes a clinical trial subject to NIH Policy NOT-OD-16-149.

4.1.3 All Qualifying clinical trials which will render claims for items and services to the Center for Medicare and Medicaid Services (CMS) will be registered and updated on ClinicalTrials.gov as specified in the "Medicare National Coverage Determination (NCD) Manual," Section 310.1.

4.1.4 Though not a requirement of the Organization, investigators should be aware that the International Committee of Medical Journal Editors (ICMJE) requires and recommends that all clinical trials be registered in a public registry at or before the time of first participant enrollment as a condition of consideration for publication. ICJME accepts registration in any registry that is a primary register of the WHO International Clinical Trials Registry Platform (ICTRP), including ClinicalTrials.gov. A listing of non-ICJME journals that follow ICJME's recommendations is available on the ICJME website.

4.1.5 Though not a requirement by the Organization, investigators should be aware that funding sources, such as international non-governmental organizations (NGOs) or private funders, may require registration and compliance with a publicly available registry.

4.2 The PI is responsible for assuring that the IRB Application correctly reflects that a research study is registered with clinicaltrials.gov and that the NCT number is accurate. If registration is done after initial approval, a Modifications Request will be required.

4.3 If a research study which does not require registration is voluntarily registered with clinicaltrials.gov, then the responsible party is obligated to satisfy all requirements noted in this policy.

4.4 If the clinical trial is not registered with ClinicalTrials.gov the PI must provide justification why the trial is not registered.

4.5 The PI must update the ClinicalTrials.gov record in accordance with Section 801 of FDAAA (https://clinicaltrials.gov/ct2/manage-recs/fdaaa) and 42 CFR 11.64. This may apply to some changes, study status, and annual update.

4.6 The PI is responsible for uploading required documents in accordance with 42 CFR 11.48(a)(5).

4.7 The PI is responsible for ensuring the submission of all appropriate study results as defined in 42 CFR 48 at the conclusion of the study, in accordance with in 42 CFR 11.42.

4.8 Should the PI leave the Organization, the PI is responsible for assuring that the record is transferred to a new Responsible Party, the record is resolved (completed, terminated, or withdrawn) with all applicable information entered, or the record is transferred to the PI's new Institution (applicable only to on-going studies).

4.9 If a study subject to this policy is completed (that is, when the investigator files a completion report), the IRB protocol must remain open and active until the ClinicalTrials.gov record is resolved.

5.0 IRB Office Responsibilities

The following describes the responsibilities of the RCO/IRB Office where faculty, student or employee of the Organization is the Responsible Party for a record on ClinicalTrials.gov; otherwise, the CU HRPP Policies do not apply.

5.1 For studies where registration on ClinicalTrials.gov is required, IRB Office will not issue full approval of any protocol where the Responsible Party is part of the Organization until the trial is registered and NCT number is issued.

5.1.1 Under certain limitedcircumstances, full approval may be granted before issuance of the NCT number, provided registration has been completed (for example, if a Letter of Award or grant

funding is dependent on IRB approval). In those circumstances, a letter of IRB approval will be provided, but subject enrollment may not begin, and funds may not be spent, until the NCT number is provided as a Modifications Request in protocol.

5.2 Approval of any subsequent IRB submissions will not be issued until the ClinicalTrials.gov record is in compliance. The IRB Administrator will communicate the problems with the Responsible Party and Record Owner, and ensure the problems are resolved appropriately.

5.3 The PRS Administrator will routinely review the Organization's ClinicalTrials.gov records for problems and will notify the Responsible Party and Record Owner, and ensure the problems are resolved appropriately.

5.4 The PRS Administrator will review the ClinicalTrials.gov record when a protocol amendment is submitted and will ensure that applicable changes are appropriately updated on the record.

5.5 Investigators who are non-compliant with ClinicalTrials.gov requirements or this HRPP Policy may be subject to disciplinary actions as per HRPP policy 8.4 (Review of Noncompliance Involving the PI and Study Personnel), and per the IO.

1.29 Special and Emergency IRB Meetings

1.0 Purpose

The purpose of this policy and procedure is to describe the criteria for use of, and the procedures for emergency review by CU IRBs.

2.0 Policy

2.1 It is the policy of the Organization that emergency IRB meetings 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.

3.0 Constitution

3.1 Emergency meetings are subject to the membership requirements set out by HRPP policy 1.6 (IRB Composition, Leadership, Qualifications, & Responsibilities).

4.0 Criteria for Use

4.1 An emergency meeting may be called by the IO or IRB Chair for rapid review of new protocols, previously tabled protocols, requests for modfications in approved research or continuing reviews of approved research.

4.1.1 In order for the IRB to review a previously tabled protocol, one member of the convened emergency meeting 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 emergency meeting as a non-voting observer.

4.2 Activation is at the discretion of the IRB Chair, in consultation, if necessary, with the IO. In general, emergency meetings 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 the CU IRBs.

4.3.2 The research is not eligible for expedited review, per HRPP policy 2.3 (Expedited Review).

4.4 In general, the CU IRBs 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.

5.3 The 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 IRB Chair.

5.4.1 The investigator, IRB Administrator, and the IRB Chair may discuss issues related to the protocol, IRB application and ICF 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 ICFs as they become available prior to the meeting; they will be supplied with any revisions of these documents as they are available. All IRB members will be supplied with the agenda, complete IRB application, full protocol, and ICFs at the time of the meeting.

5.4.3 CU IRB review will occur concurrent with review by other committees (for example, 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 IRB. The investigator will then leave the room allowing the IRB adequate time for more discussion, and the vote.

5.4.5 The IRB Administrator(s) assigned to the emergency meeting will make modifications to the IRB Application and the ICF based on discussion with the investigator during the IRB meeting, and the investigator's responses to IRB directed comments following the meeting.

5.4.6 IRB Administrator(s), in consultation with the IRB Chair (as appropriate), will review the investigator's written responses, and revised application and ICFs, and are authorized to grant final approval if the conditions placed by the full IRB have been satisfied.

1.30 Observers at IRB Meetings

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 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 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 IRB 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 investigators 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.

1.31 Confidentiality of the Review Process

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 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 RCO.

2.2 It is the policy of the Organization that findings and decisions 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 or the expedited reviewer, is cause for action against that IRB member, RCO 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 IRB Office.

3.2 IRB Office Staff will sign a Confidentiality Agreement at the time they are hired. The signed agreement will be retained by the IRB Office.

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 IRB Office.

3.4 Consultants to the IRB will sign a Confidentiality Agreement prior to attending the meeting. The signed agreement will be retained by the IRB Office.

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 “noncompliance” 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 RCO/IRB Office 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.

1.32 Posting of Clinical Trial Consent Forms

1.0 Purpose

The purpose of this policy and procedure is to describe the Organization’s requirements for posting of clinical trial consent forms, per requirements of 45 CFR 46.116(h).

2.0 Policy

2.1. It is the policy of the Organization that, for clinical trials conducted or supported by a Common Rule department or agency, the awardee of a grant will post one IRB approved informed consent form used to enroll subjects on a publicly available Federal Web site that will be established as a repository for such informed consent forms. Posting shall occur after the clinical trial is closed to recruitment, and no later than 60 days after the last study visit by any subject, as required by the protocol.

3.0 Definitions

3.1 Clinical Trial (for the purpose of this Policy) means 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.”

4.0 Investigator Responsibilities

4.1 If a CU investigator is the awardee of the grant from a Common Rule agency or department or is the principal investigator of a clinical trial conducted by a Common Rule agency or department, then he/she is responsible for posting the consent form as described in this policy.

4.2 The PI must notify the IRB Office when the clinical trial is closed to recruitment.

4.3 The PI must post one IRB approved unsigned consent form to ClinicalTrials.gov (or other website as designated by OHRP) after the clinical trial is closed to recruitment, and no later than 60 days after the last study visit by any subject, as required by the protocol (per 45 CFR 46.116(h)). In practice, the IRB Office requires that the consent form be posted within 30 days of enrollment of the last subject.

4.3.1 The consent form need not be the current version.

4.3.2 If there are multiple consent forms, only one must be posted. That is, if there are different consent forms for different classes of subjects (for example, for adults and for minors), or for different phases of the research (for example, screening and intervention) or for different interventions in different groups (for example, for an investigational group and a control group) only one needs to be posted.

4.3.3 If the Federal department or agency supporting or conducting the clinical trial determines that certain information should not be made publicly available on a Federal Web site (for example, confidential commercial information), such Federal department or agency may permit or require redactions to the information posted. Without such permission or requirement, the consent form must be posted as it had been approved.

4.4 The PI must notify the IRB Office when the consent form has been posted.

5.0 IRB Procedures

5.1 At the time the IRB Office is notified that the clinical trial is closed to recruitment, the administrator will log the date into InfoEd, and the IRB Office will notify the investigator of the requirements and advise that consent form must be posted within 30 days.

5.2 After 30 days, the IRB Office will query the investigator to verify that the consent form has been posted. In addition, the IRB Office may choose to review CT.gov to determine if consent form has been posted.

5.3 Failure to report relevant events (per section 4.2 and 4.4), or to respond the IRB Office queries, constitute noncompliance subject to disciplinary actions as per HRPP policy 8.5.

5.4 Failure to post consentforms as per section 4.3 constitutes serious noncompliance subject to disciplinary actions as per HRPP policy 8.5, and per the Office of the IO.

1.33 Emergency Preparedness for the Research Compliance Office and IRBs

1.0 Purpose
The purpose of this policy is to describe the Emergency Preparedness and Continuity of Operations Plan (EP/COOP) for the HRPP. This policy and accompanying documents focus on the IRB. The Organization maintains plans for other components of the HRPP.

2.0 Policy
It is the policy of the Organization that:

2.1 The HRPP has an Emergency Preparedness and Continuity of Operations Plan, appropriate to the size and complexity of the HRPP, that addresses how continuity of operations will be maintained to ensure human participant protections during an emergency.

2.2 The HRPP Emergency Preparedness and Continuity of Operations Plan is periodically evaluated and, when necessary, adjusted to ensure continuity of operations.

2.3 Education about the HRPP Emergency Preparedness and Continuity of Operations Plan will be provided to IRB members and staff, researchers and research staff, and other persons in the HRPP as appropriate.

3.0 General Comments

3.1 The purpose of the attached Emergency Preparedness /Continuity of Operations Plan (EP/COOP) is to provide the framework for restoring essential functions to the IRB Office and the CU IRBs as components of the HRPP in the event of an emergency that affects its operations. It is a supporting document to the CU Emergency Operations Plan (EOP).

The attached document establishes the EP/COOP procedures for any perational disruption, including but not limited to:

- Loss of access to a facility (such as damage to the building),
- Loss of service due to a reduced workforce (such as due to pandemic virus), and
- Loss of service due to protracted equipment or systems failure (such as IT systems failure).

The intent of this HRPP EP/COOP is to lay out procedures to allow the RCO and IRBs, as components of the HRPP in the event of an emergency, to implement actions to promptly begin continuity operations and to maintain essential functions until full operative capacity can be resumed.

3.2 Depending on the nature of the risk and the potential impact to the HRPP and the Director of Research Compliance in consultation with the IO, the IRB Director, IRB Chairs, and representatives from components of the HRPP as appropriate, will determine which actions need to be undertaken to minimize the impact on research activities and mitigate risk to research participants, study team members, and the institution.

3.3 The CRO and IRBs, as components of the HRPP, will work with the appropriate Institutional personnel (Emergency Manager, Department of Public Safety) to coordinate activities as appropriate with Institutional plans already in place to address the event.

3.3.1 If the emergency only affects the RCO or IRBs, the Director of Research Compliance will assure that appropriate Institutional personnel (Emergency Manager, Department of Public Safety) are informed.

4.0 Specific Responsibilities in the Event of an Emergency

4.1 Specific responsibilities are described in the attached EP/COOP document.

5.0 Specific Actions by the RCO and/or IRBs in the Event of an Emergency

- 5.1 Specific actions are described in the attached EP/COOP document.

6.0 EP/COOP Maintenance

6.1 The IO will periodically review (at least biennially) and update the CU HRPP EP/COOP based on legislative changes, CU guidance, departmental or personnel changes, and procedural changes based on lessons learned from exercises and actual events.

7.0. Training and Education

The RCO/IRB Office will provide targeted communications and education/training regarding the CU HRPP EP/COOP to researchers and research staff, IRB Chairs and IRB members, study team members and PIs. As appropriate, the RCO/IRB Office, in collaboration with the Department of Public Safety will conduct periodic exercises to assure validity and operability of the plan.

Section 2: Process of Review

2.1 Submission for Items for Review by the IRB

1.0 Purpose
The purpose of this policy is to describe Organization's requirements for submission and pre-review of all applications and research related forms and reports.

2.0 Policy
It is the policy of the Organization that all submissions will be processed efficiently by the IRB Office for review in accordance with applicable HRPP policies.

3.0 Submission Requirements

3.1 All applications and research related forms and reports will be submitted using the online IRB management system – InfoEd Global – except as below:

3.1.1 Documentation of research activities involving CU learners taking place at our partner institutions in Phoenix, AZ may be submitted in report form via email.

3.1.1.1 The forgoing does not apply to non-exempt federally funded research for which a reliance agreement would be required.

4.0 Deadlines for Submission

4.1 The deadline for submission of any materials requiring review by the CU IRB is 10 working days prior to each meeting. The IRB meeting dates are published on the CU IRB website.

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 IRB Office workload.

4.1.2 Exceptions to the above deadline may be made on a case-by-case basis by the IRB Chair or his/her designee.

4.1.3 Items that qualify for expedited review in accordance with HRPP policy 2.3 (Expedited Review) have no deadlines for submission.

4.1.4 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 10 protocols (new submissions and previously tabled protocols) at each full meeting. Assignments to the IRB meeting are made on a first-come, first-served basis. Protocols in excess of 10 will be assigned to the following IRB meeting.

5.2 The IRB will review reports of Prompt Reporting Events, Modification Request, Incident Reports, and Special Review Items requiring full Board review 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 InfoEd will be triaged to the appropriate IRB Administrator and processed in accordance with RCO/IRB Office SOPs.

6.2 The IRB Administrator, in consultation as necessary with the IRB Director or IRB 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).

2.2 Full IRB Review

1.0 Purpose
The purpose of this policy 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:

2.1 IRB review will be conducted in accordance with HHS regulations at 45 CFR 46.109 and will satisfy the criteria for IRB approval described in HRPP policy 2.5 (Criteria for Approval) and in 45 CFR 46.111 as applicable.

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 that will apply 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).

3.0 Definitions

3.1 Controverted issues are issues that cause controversy and dispute among the IRB membership during a convened meeting. Controverted issues that arise during the convened meeting may be the result of opposition to some aspect of the proposed research or may regard applicability or interpretation of ethics or regulation.

4.0 Procedures

4.1 All IRB applications are submitted to the RCO/IRB Office and processed in accordance with HRPP policy 2.1 (Submission of Items for Review by the IRB).

4.2 IRB Meeting Schedule

4.2.1 The schedule of IRB meeting dates is posted on the IRB website.

4.3 Quorum

4.3.1 A full IRB meeting cannot be convened without the presence of a quorum. Quorum is defined under this policy as a minimum of five members of the IRB, at least one of which is a member whose primary concerns are in scientific areas, at least one of which whose primary concerns are in nonscientific areas, and at least one who is a community member who is not otherwise affiliated with the institution.

4.3.2 IRB meetings may be conducted in person, or via video conferencing, as appropriate. Members will have access to all relevant materials prior to the meeting and will be able to participate actively and equally in all discussions.

4.3.3 When the IRB reviews any research involving children or cognitively impaired persons, an IRB member who is knowledgeable about and/or experienced in working with that specific population will be present in accordance with HRPP policy 1.6 (IRB Composition, Leadership, Qualifications, & Responsibilities).

4.3.4 When the IRB reviews any research involving other vulnerable populations, an IRB member who is knowledgeable about and/or 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).

4.3.5 When the IRB reviews any research involving prisoners, a prisoner representative must be present in accordance with HRPP policy 4.3 (Research Involving Prisoners).

4.3.6 Any IRB member who abstains from voting for reasons other than a COI (as defined in HRPP policy 1.7) is included in the quorum. This is recorded as an abstention in the minutes.

4.3.7 Any IRB member who has a COI will be recused in accordance with HRPP policy 1.7 (IRB Member, Consultant, Staff COI Identification & Management). This is recorded in the minutes as "recused due to conflict of interest" and the quorum is decreased accordingly. The name of the individual recused will be recorded in the minutes.

4.3.8 A designated IRB staff person 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.

4.3.9 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.

4.4 Assignment of Reviewers and Creation of the Agenda

4.4.1 Reviewers will be assigned by the IRB Administrators with advice from the IRB Director or IRB Chair as necessary.

4.4.2 For new IRB Applications and tabled IRB Applications, at least a regulatory and scientific reviewer will be assigned. The scientific reviewer shall have medical or other expertise in order to perform an in-depth review of the protocol.

4.4.3 For applications for continuing review, one reviewer will be assigned, unless it is determined by the IRB Chair/designee that more than one reviewer is necessary.

4.4.3.1 Continuing review of protocols in which subjects are in standard follow-up (all research interventions are completed) may be assigned to a non-scientist, provided there is a scientist present during the meeting with relevant scientific, medical, or other expertise.

4.4.4 For requests for modifications in protocol and/or ICF, reviews of internal Adverse Event reports, incident reports (including potential Unanticipated Problems involving risk to the subject or others, or noncompliance or complaints), or other special review items, one reviewer will be assigned, unless it is determined by the IRB Chair/designee that more than one reviewer is necessary.

4.4.5 If during the pre-review process, the IRB Administrator or reviewer determines that the Board will require additional expertise, the services of an expert consultant will be obtained prior to the meeting, as described in HRPP policy 1.6 (IRB Composition, Leadership, Qualifications, & Responsibilities).

4.4.6 All IRB members will receive a detailed agenda by email. This agenda contains: 1) education, policy, and informational items; 2) a categorized list of review items; 3) 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), 4) IRB approval criteria, and 5) description of IRB actions.

4.5 Review Materials Distributed to IRB Members

4.5.1 All members and alternates scheduled to attend an IRB meeting (in person or by videoconference) will have access through InfoEd to all submitted items described in HRPP policy 2.1 (Submission for Items for Review by the IRB), as well as all previously submitted materials, correspondence and IRB determinations related to protocols under consideration by the board.

4.5.2 Materials will be available at least 5 business days prior to the meeting with the following exceptions:

4.5.2.1 Materials pertaining to late additions to the agenda will be provided to the Board for review as soon as practicable. In all cases, the primary reviewer of these items (usually the IRB Director or a Senior IRB Administrator) will have had access to these items in advance of the meeting.

4.5.3. At least two days prior to each meeting, all members and alternates of all Boards will have access through RSS to the following:

4.5.3.1. IRB minutes of the last meeting of that Board.

4.5.3.2. Education, Policy and Information items.

4.5.3.3. Full agenda for that meeting.

4.6. IRB Member Review Procedures

4.6.1. 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 and HRPP policy 2.5 (Criteria for IRB Approval).

4.6.1.1. IRB members must be satisfied that they have the appropriate expertise to review the protocol. If they do not, then the reviewer or any IRB member may request that the review be deferred and a consultant with appropriate expertise be obtaining, in accordance with HRPP 1.6 (IRB Composition, Leadership, Qualifications, and Responsibilities) section 3.1.3.

4.6.2. IRB members are expected to consult the IRB study files in InfoEd (including but not limited to the IRB application, full protocol, investigator's brochure, questionnaires and surveys, recruitment and other subject facing materials, and consent documents), applicable regulations, and HRPP policies, as necessary during their review of the protocol.

4.6.3. IRB members are expected to submit written reviews, as early as possible, to the IRB Office using the InfoEd system.

4.6.4. 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, to the Reviewer Template, or to the Criteria for Approval at 45 CFR 46.111.

4.6.5. Deficiencies, errors, inadequate explanations, and excessively high readability level should be described sequentially according to the section of the ICF.

4.7. IRB Meeting Procedures

4.7.1. When a quorum of the Board is present, the IRB meeting is called to order by the IRB Chair, Vice Chair, or designee (subsequently referred to as "Chair" in this policy) and each item on the agenda is acted upon.

4.7.2. The Regulatory Reviewer will present the review followed by the other assigned reviewers (secondary reviewer, Jesuit reviewer, pharmacy reviewer, prisoner representative) 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.

4.7.2.1 Where the PI for an initial application, modification, or prompt reporting event attends the meeting, presentations by the regulatory and scientific reviewers may take place after the PI has concluded his/her/their presentation and left the meeting.

4.7.3. When appropriate, IRB staff will present submitted materials from InfoEd or information from other sources (including applicable federal, state, and local regulations, and HRPP policies) to assist IRB members in their deliberation.

4.7.4. Relevant regulatory information, including criteria for IRB approval, Subpart B, C, and D determinations, will be available to members, as part of the agenda, or when meeting in person, as placemats or other physical items, to assist IRB members.

4.7.5. 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.

4.8. Voting Requirements

4.8.1. The Regulatory Reviewer will recommend an action which must be seconded by another IRB member, normally the Scientific Reviewer.

4.8.2. 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.

4.8.3. 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.

4.8.4. 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.

4.8.5. Only those members physically in the room or attending by videoconference may vote. Absentee voting is not permitted.

4.8.6. 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 returned to the PI for whatever edits or revisions are requested by the Board in order to resolve the Board's concerns.

4.9. Criteria for IRB Approval and Other Determinations

4.9.1. During all reviews, the IRB must determine whether the criteria for IRB approval have been (or continue to be) met, per HRPP policy 2.5 (Criteria for IRB Approval).

4.9.2. As appropriate and as relevant to specific board reviews (such as review of new protocols, continuing reviews, review of requests for modificaitons in protocol or ICF or other types of IRB reviews as described previously) the IRB must also determine:

4.9.2.1. Whether the research requires continuing review more often than annually, as required at 45 CFR 46.108(a)(3)(ii) as appropriate to the degree of risk. In making this determination the IRB may consider factors including but not limited to: the nature of the risks associated with the research; the degree of uncertainty regarding the risks involved; the vulnerability of the

participants; the experience of the investigator in conducting the research; the IRB's previous experience with that researcher or sponsor; the projected rate of enrollment.

4.9.2.2. 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).

4.9.2.3. Whether the research needs verification from sources other than the PI that no material changes have occurred since the previous IRB review, as required at 45 CFR 46.108(a)(3)(ii).

4.9.2.4. Whether the current consent form is still accurate and complete.

4.9.2.5. 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).

4.9.2.6. 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.

4.9.2.7. 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.

4.9.3. 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, or are unacceptable. In this case, the IRB may choose to approve or conditionally approve those components that satisfy the IRB approval criteria. For those components that do not meet the IRB approval criteria the IRB may table or disapprove that component (as per IRB actions described below).

4.10. IRB Actions

4.10.1. Approval; initiation of the research is authorized (when institutional requirements are satisfied).

4.10.1.1. All of the criteria for IRB approval are satisfied and no changes are required.

4.10.2. Conditional approval; final IRB approval contingent upon IRB Chair/designee review and acceptance of specified modifications and/or submission of additional documents.

4.10.2.1. 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.

4.10.3. Tabled, full IRB re-review required.

4.10.3.1. 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.

4.10.3.2. If the protocol and application are revised by the investigator in response to the IRB's comments, the protocol will be returned to the full convened IRB for re-review.

4.10.4. Disapproved

4.10.4.1. Applications may be disapproved if, after thoughtful deliberation, including discussions with the investigator, the IRB (1) finds serious design flaws that either make obtainment of generalizable knowledge highly unlikely or places subjects at undue risk, or (2) the risk/benefit relationship is unfavorable, or (3) the protocol does not meet regulatory criteria for approval or institutional policy or requirements, and the investigator is unable or unwilling to make modifications to remedy these situations.

4.10.4.2. The investigator shall have an opportunity to appeal before the Board; however, the IRB has the final authority to act on any appeals and the decision of the Board cannot be overturned.

4.10.5. Suspension of IRB approval

4.10.5.1. 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.

4.10.6. Termination of the research

4.10.6.1. 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.

4.11. IRB Review Letters

4.11.1. IRB review letters, which reflect the deliberations and decisions of the Board, are developed by the IRB Administrators, in consultation with the IRB Director, Chair, or designee and reviewers as appropriate.

4.11.2. 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.

4.11.3. The IRB review letters will clearly document the following:

4.11.3.1. The decision to approve, require modifications, table, or disapprove.

4.11.3.2. A list of any modifications or clarifications required by the Board.

4.11.3.3. If the IRB disapproves the action, a statement providing the rationale for the disapproval, and an invitation for the investigator to appeal.

4.12. IRB Meeting Minutes

4.12.1. Basic Information

4.12.1.1. 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 Director, Chair, or designee.

4.12.1.2. Copies of the IRB minutes and addenda are available on InfoEd to IRB members (including alternates) and the Institutional Official before the next meeting of the board.

4.12.1.3. IRB members for each board have the opportunity to review and correct minutes for the previous convened meeting of that board.

4.12.1.4. 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.

4.12.2. The minutes will contain the following information, as appropriate:

4.12.2.1. 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 consultant did not vote on any actions.

4.12.2.2. Identification of IRB members classified as non-scientists.

4.12.2.3. If the meeting was conducted in-person, the minutes will note by name any IRB members, non-voting IRB member alternates and consultants who attended videoconferencing. If the entire meeting was conducted via teleconferencing, the minutes will so note.

4.12.2.4. Identification of alternate IRB members and the IRB member for whom they are substituting.

4.12.2.5. The names of IRB members who have a COI and are recused at the time of the discussion and vote on each board action.

4.12.2.6. 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.

4.12.2.7. IRB special agenda items per IRB minutes template.

4.12.2.8. Documentation of quorum for each separate vote count for all board actions (in favor, opposed, and abstentions).

4.12.2.9. 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.

4.12.2.10. Verification that all IRB members who attended through videoconferencing were able to actively participate in all discussions and votes.

4.12.2.11. A written summary of the discussion and resolution of controverted issues.

4.12.2.12. 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.

4.12.2.13. The reason(s) for disapproval of research.

4.12.2.14. A determination of when continuing review is required more often than annually.

4.12.2.15. A determination of which projects need verification from sources other than the PI that no material changes have occurred since the previous IRB review.

4.12.2.16. A determination of which projects should have a third party observe the consent process.

4.12.2.17. A determination of which projects require an audit of research records.

4.12.2.18. Rationale for conducting continuing review on research that otherwise would not require continuing review.

4.12.2.19. Rationale for an expedited reviewer's determination that research appearing on the expedited reviewer list is more than minimal risk.

5.0 Deadlines for PI Responses

5.1. The PI is given 90 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 90-day period, or by the expiration of an extension provided granted by the IRB Chair/designee) the study may be withdrawn or closed.

6.0 Review of PI Responses

6.1. 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 Chair/designee or IRB reviewers as necessary.

6.2. If, on consultation with the Chair, the Administrator determines that the investigator's response to the IRB review is inadequate or incomplete they may correspond with the investigator to resolve those issues or may refer the submission for review by the full convened IRB.

6.3. If, on consultation with the Chair, the Administrator determines that the investigator's response to the IRB review contains significant changes not initially reviewed by the IRB, they will refer the submission for review by the full convened IRB.

6.4. 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 regulatory and scientific reviewers.

7.0 IRB Approval Periods

7.1. 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.

8.0 Final IRB Approval Letter

8.1. Once all modifications or clarifications required by the Board (as per section 4.11) have been satisfied, and all outstanding Institutional Requirements have been met (section 9.) the IRB Office will inform the PI that the research may commence.

8.2. The final approval letter from the IRB Office will document the following determinations:

8.2.1. Pertinent dates:

8.2.1.1. Date of full Board review.

8.2.1.2. Date all conditions set by the IRB were determined to be met and the study was granted IRB approval.

8.2.1.3. Expiration Date for which continuing review is required (per section 7.1 above).

8.2.2. Compliance with applicable HHS regulations, HRPP policies and Institutional Requirements.

8.2.3. Documentation of the level of risk (minimal risk or greater than minimal risk).

8.2.4. 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.

8.2.5. 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.

8.2.6. 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.

8.2.7. Documentation that the IRB considered protocol specific findings for research involving decisionally impaired subjects, as per HRPP policy 4.6 (Review of Research Involving Subjects with Impaired Decision-Making Capacity).

8.2.8. 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).

8.2.9. 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).

8.2.10. 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).

8.3. The Final approval letter from the IRB Office will note that the determinations were made by the convened IRB.

9.0 Review by Other Organizational Committees

9.1. Before the IRB Office will grant final approval and release, the IRB Office must receive verification of approval or completion of review by components of the HRPP as described in HRPP Policy 1.10 (Other HRPP Committee Review of Research) and as required by the organization.

2.3 Expedited Review

1.0 Purpose

The purpose of this policy 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

It is the policy of the Organization that:

2.1. Expedited review will be conducted in accordance with HHS regulations at 45 CFR 46.110 and will satisfy the criteria for IRB approval described in HRPP policy 2.5 (Criteria for Approval) and in 45 CFR 46.111, as applicable.

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, the HIPAA Privacy Rule (as applicable), and CUCU HRPP policies.

2.3. Expedited review will not be used for initial or continuing review of: (1) classified research (per OHRP Expedited Review Categories (1998), section D); or (2) research involving prisoners.

2.4. 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).

2.5. 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.

2.6. 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.

2.7. 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.

2.8. Complaints which are considered minor, unexpected incidents involving no more than minimal risk to subjects or others, and noncompliance which is neither serious nor continuing 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).

3.0 Definitions

3.1. Expedited Review: 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.

3.2. Minimal Risk: 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(j)).

4.0 Expedited Review Categories

4.1. The following categories of research may be eligible for review through the expedited review procedure. Research activities must be no more than minimal risk. For research subject to the Common Rule, inclusion of research activities on the list of OHRP Expedited Review Categories (63 FR 60364-60367, November 9, 1998) 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.

(a) Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required.

Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)

(b) Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

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 IRB Office and processed in accordance with HRPP policy 2.1 (Submission of Items for Review by the IRB).

5.2. Appointment of Designated Expedited Reviewers

5.2.1. An IRB member may serve as an expedited reviewer once they have been judged by the IRB Chair/designee to be sufficiently qualified and experienced. Specifically, the reviewer must have:

5.2.1.1. An acceptable level of knowledge about the area of research under review.

5.2.1.2. An understanding of the categories of research that qualify for expedited review.

5.2.1.3. The ability to apply the IRB approval criteria and determine conditions required for IRB approval.

5.2.1.4. An absence of a COI in accordance with HRPP policy 1.7 (IRB Member, Consultant, and Staff COI Identification & Management).

5.2.2. An IRB Administrator who is also a board member may serve as an expedited reviewer, provided they meet the requirements above.

5.3. Expedited Review Procedures

5.3.1. The expedited reviewer must be satisfied that they have sufficient information to make the determinations required for IRB approval in accordance with 45 CFR 46.111and HRPP policy 2.5 (Criteria for IRB Approval).

5.3.1.1. The expedited reviewer must be satisfied that they have the appropriate expertise to review the protocol. If they do not, then the reviewer may request that a consultant with appropriate expertise be obtained, in accordance with HRPP policy 1.6 (IRB Composition, Leadership, Qualifications, and Responsibilities) section 3.1.3.

5.3.2. The expedited reviewer is expected to consult the IRB study files in InfoEd (including but not limited to the IRB application, full protocol, investigator's brochure, questionnaires and surveys, recruitment and other subject facing materials, and consent documents), applicable regulations, and HRPP policies, as necessary during their review of the protocol.

5.4. Criteria for Expedited IRB Approval and Other Determinations

5.4.1. The expedited reviewer(s) must determine whether the criteria for IRB approval have been (or continue to be) met, per HRPP policy 2.5 (Criteria for IRB Approval).

5.4.2. As appropriate and as relevant to the specific review (such as review of new protocols, continuing reviews, review of requests for modifications in protocol or ICF or other types of IRB reviews as described previously) the expedited reviewer must also determine:

5.4.2.1. Whether continuing review is required, and if so, whether it is required more often than annually. In making this determination the expedited reviewer may consider factors including but not limited to the nature of the risks associated with the research; the degree of uncertainty regarding the risks involved; the vulnerability of the participants; the experience of the investigator in conducting the research; the IRB's previous experience with that researcher or sponsor); the projected rate of enrollment. If the expedited reviewer determines that continuing review is required, the rationale for conducting continuing review will be recorded in accordance with 45 CFR 46.115(a)(3).

5.4.2.2. 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).

5.4.2.3. Whether the research needs verification from sources other than the PI that no material changes have occurred since the previous IRB review, as required at 45 CFR 46.108(a)(3)(ii).

5.4.2.4. Whether the current consent form is still accurate and complete.

5.4.2.5. 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.

6.0 Expedited Review Actions

6.1. Approval: initiation of the research is authorized (when institutional requirements are satisfied).

6.1.1. All of the criteria for approval are satisfied and no changes are required.

6.2. Conditional approval; final approval contingent upon Expedited Reviewer/designee review and acceptance of specified modifications and/or submission of additional documents unrelated to the regulatory criteria for approval.

6.2.1. All the criteria for IRB approval are satisfied provided the investigator makes the specified changes and/or submits the specified documents. The requirements for final approval and release are considered minor and not substantive in nature.

6.3. Tabled; re-review required.

6.3.1. The expedited reviewer requires additional information in order to determine whether the criteria for approval have been satisfied.

Note: Prior to tabling a protocol, the expedited reviewer may continue communication with the investigator to resolve issues related to the protocol that prevent approval (for example that relate to the regulatory criteria for approval).

6.4. Refer to full Board

6.4.1. The expedited reviewer is unable to determine that the protocol satisfies the regulatory requirements for expedited review (for example, on closer examination it appears the protocol or the modification constitutes greater than minimal risk); or the expedited reviewer determines that the regulatory criteria for approval are not met; or the expedited reviewer considers the protocol has serious deficiencies which would merit disapproval; or the expedited reviewer believes the research would be more appropriately reviewed by the convened IRB.

Note: The Expedited Reviewer may not disapprove research. Research which does not satisfy regulatory criteria for approval, or which has serious deficiencies which would merit disapproval must be referred to the full IRB.

7.0 Development of IRB Expedited Review and Final Approval Letters

7.1. Expedited review letters, which reflect the determinations of the expedited reviewer(s), are developed by the IRB Administrators, in consultation with the IRB Executive Chair and/or expedited reviewers as appropriate.

7.2. The IRB review letters will clearly document the determinations of the Expedited Reviewer and will include:

7.2.1. The decision to approve, require modifications to secure approval, or table.

7.2.2. List any modifications or clarifications required by the Expedited Reviewer.

8.0 Deadlines for PI Responses

8.1. The PI is given 90 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 90-day period, or by the expiration of an extension provided by the IRB Chair/designee, the study may 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, in consultation with the IRB Chair, board members and/or other expedited reviewers as appropriate.

9.1.1. If, on consultation with the Chair, the IRB Administrator determines that the investigator's response to the review is inadequate, incomplete, or contains significant changes not initially reviewed by the IRB, the analyst may re-review (or refer back to another expedited reviewer for re-review) and further communicate with the investigator or may refer the submission for review by the full convened IRB.

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 conditional approval by expedited reviewer.

10.1.1.2. Date all conditions set by the expedited reviewer 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 regulations.

10.1.3. Verification that the research is classified as minimal risk.

10.1.4. The applicable expedited review category or categories.

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 expedited reviewer 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: Full and Conditional Approval must be completed and maintained in the InfoEd online platform. The reviewer's determination must include: a) the category or categories 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 email that minutes documenting all actions reviewed and approved by the expedited review procedure are available for review in InfoEd.

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 IRB Office must receive verification of approval or completion of review by components of the HRPP as described in HRPP Policy 1.10 (Other HRPP Committee Review of Research) and as required by the organization.

2.4 IRB Review of Changes in Previously Approved Research

2.0 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)) 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 IRB staff.

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)), 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 IRB Chair under HHS 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 affect 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 Chair or Director 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 Request of Modifications to Protocols (other than Single Subject Protocol Deviation)

4.1. The PI must submit a Request for Modifications in accordance with HRPP policy 2.1 (Submission of Items for Review by the IRB).

4.2. The Request for Modifications 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 IRB 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 Request for Modifications.

5.0 Procedure for Single Subject Protocol Deviation*

5.1. A Single Subject Protocol Deviation Request must be submitted to the IRB and be approved by either the 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 IRB.

5.3. The 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 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 IRB Chair or designee.

5.6. All minor single subject protocol deviation requests approved by the IRB Chair or designeewill 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)).

6.2. The IRB 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 Request for Modifications, the revised IRB application, and other required documents must be submitted in accordance with thispolicy.

6.2.2. If the change was initiated for a single subject, the Single Subject ProtocolDeviation 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)) and HRPP policy 5.1 (Obtaining Informed Consent from Research Subjects).

7.2. The IRB 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 Request for Modifications is submitted to the IRB 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 IRB Office will submit the Request for Modifications 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.

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 greater than 10% .
- Increase in study wide accrual of subjects greater than 10% 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.
- Removal 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 §_.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 to 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, consent document, 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 CU investigator.

2.5 Criteria for IRB Approval

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.

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 (where applicable)

3.1.1.2. Evaluate the research design 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 lessrisk, 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 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) 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 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. 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 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.

2.6 Exempt Research

1.0 Purpose

The purpose of this policy and procedure is to describe the Organization's requirements for determining if a research proposal is eligible for exemption under 45 CFR 46.104(d), with appropriate protections in place for research subjects.

2.0 Policy

It is the policy of the Organization that:

2.1. All proposed exempt research must be reviewed and approved by the Creighton University IRB Office prior to initiation.

2.2. The IRB Office 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. Exempt human subject research must be conducted in accordance with sound ethical standards and all applicable HRPP and institutional policies.

3.0 Categories of Exemption

3.1. The following research is exempt from 45 CFR 46:

3.1.1. 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 (45 CFR 46.104(d)(1))

3.1.1.1. 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 must not be regulated by 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. Informed consent must be obtained from the prospective subject or their parent or guardian.

3.1.2. 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) (45 CFR 46.104(d)(2)).

3.1.2.1. Research involving the observation of public behavior of minors is only eligible for exemption if the investigator does not participate in the activities being observed AND if criterion (i) or (ii) above are met.

3.1.2.2. Research involving the use of survey or interview procedures involving minors is not eligible for exemption under this category.

3.1.2.3. Research involving minors is not eligible for exemption under criterion (iii) above.

3.1.2.4. Research regulated by US FDA is not eligible for exemption under this category.

3.1.3. 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 HRPP policy 2.8 (Limited IRB Review) (45 CFR 46.104(d)(1)).

3.1.3.1. 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.

3.1.3.2. Consent of the subject is required, as per section 6.7 below.

3.1.3.3. 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.

3.1.3.4. Research involving minors is not eligible for exemption under category 3.

3.1.3.5. The research is not regulated by FDA.

3.1.4. 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)).

3.1.4.1. 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 HRPP policy 5.2 (Waiver or Alteration of Informed Consent and HIPAA Authorization).

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 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)).

3.1.5.1. 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).

3.1.5.2. 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.

3.1.5.3. There must be no statutory requirement that the project be reviewed by an Institutional Review Board (IRB).

3.1.5.4. The research is not regulated by 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 46.104(d)(6)).

3.1.7. Categories 7: Storage or maintenance for secondary research for which broad consent is required. Storage or maintenance of identifiable private information or identifiable biospecimens for potential secondary research use if an IRB conducts a limited IRB review and makes the determinations required by §46.111(a)(8).

3.1.8 : Category 8: Secondary research for which broad consent is required. Research involvingthe use of identifiable private information or identifiable biospecimens for secondary research use, if the following criteria are met:

(i) Broad consent for the storage, maintenance, and secondary research use of the identifiable private information or identifiable biospecimens was obtained in accordance with §46.116(a)(1) through (4), (a)(6), and (d);

(ii) Documentation of informed consent or waiver of documentation of consent was obtained in accordance with §46.117;

(iii) An IRB conducts a limited IRB review and makes the determination required by §46.111(a)(7) and makes the determination that the research to be conducted is within the

scope of the broad consent referenced in paragraph (d)(8)(i) of this section; and

(iv) The investigator does not include returning individual research results to subjects as part of the study plan. This provision does not prevent an investigator from abiding by any legal requirements to return individual research results.

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 46.104(b)(3)).

4.1.1. Research involving children may be exempt under category 2 only if the research activities are those involving educational tests or observation of public behavior where the investigators do not participate in the activity being observed. The use of survey or interview procedures is eliminated from this exemption, and so is research involving the observation of public behavior if the investigators participate in the activity being observed. To be exempt, these activities must also meet the condition that the data are recorded without individual identifiers, or the condition that disclosure of the recorded responses would not place the subjects at risk of criminal or civil liability or be damaging to their financial standing, employability, or reputation.

4.1.2. Research involving children is not exempt under category 3 (benign behavioral interventions).

4.2. Federally funded research involving prisoners is not exempt, except for research aimed at involving a broader subject population that only incidentally includes prisoners (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 Director, IRB 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 Director, IRB Chair or IO review.

5.0 Procedures

5.1. Protocols which may be eligible for exemption are submitted to the IRB Office using InfoEd.

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 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 Minimal Risk Research Checklist which includes the category under which the research qualifies for exemption.

5.3.4. Communicate the determination with the PI (or his/her designee).

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 (per HRPP policy 2.3: Expedited Review of Research).

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.

6.7.1. The IRB and/or the IRB Chair or his/her designee may determine whether this informed consent must be documented by a consent form signed by the subject or his/her LAR, parent or legal guardian.

6.8. 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 45 CFR 46.104(d)(2)(iii) or 45 CFR 46.104(d)(3)(i)(C)), the IRB must conduct a limited review as described in HRPP policy 2.8 (Limited IRB Review).

6.9. 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 45 CFR 46.104(d)(4)(iii)), the IRB Office 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 IRB 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 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 IRB Office must receive verification of approval or completion of review by the following committees/offices as applicable:

8.1.1. Conflict of Interest Committee.

2.7 Continuing Review of Research

1.0 Purpose

The purpose of this policy is to describe the Organization's requirements for continuing review of approved research.

2.0 Policy
It is the policy of the Organization that:

2.1. Non-exempt research shall undergo continuing review at intervals appropriate to the degree of risk.

2.1.1 Minimal risk research will not be required to undergo continuing review unless the full IRB has demonstrated that the requirement of continuing review enhances the protection of human subjects in a specific study.

3.0 Continuing Review Frequency

3.1. Greater than minimal risk research shall undergo continuing review at intervals appropriate to the degree of risk, but not less than once per year, except as described in section 3.3 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. 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 the convened IRB determines otherwise, continuing review is not required for exempt research.

3.4.1. If the IRB determines that continuing review is required for a specific research protocol which was eligible for exemption under categories 2 and 3 (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).

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. In addition to the criteria in HRPP policy 2.5 (Criteria for IRB Approval), 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 appropriate to the degree of risk. In making this determination, the IRB might consider the nature of risks posed by the research, the degree of uncertainty regarding the risks involved, the vulnerability of the participants, the experience of the investigator, the IRBs previous experience

with that investigator or sponsor, the projected rate of enrollment, and/or 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 45 CFR 46.108(a)(3)(ii)).

4.1.1.3. Whether the current consent form is still accurate and complete.

4.1.1.4. Whether the research should have a third party observe the consent process.

4.1.1.5. Whether the research requires an audit of research records in accordance with HRPP policy 1.21 (Post Approval Monitoring of Research) and HRPP policy 8.4 (Review of Noncompliance Involving the PI and Study Personnel).

4.1.1.6. 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.

4.1.1.7. Whether subject accrual is adequate to achieve the scientific goals of the study.

4.1.1.8. 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 Investigator Responsibilities

5.1. If continuing review is required (as per section 3.3 above), a continuing review application must be submitted thru InfoEd prior to expiration date of the approved protocol.

5.2. The investigator must update the record in Clinicaltrials.gov as applicable, per HRPP policy 1.29 (Clinicaltrials.gov Reporting).

5.3. If the research is completed, the investigator will be responsible for the activities described in HRPP policy 2.9 (Closure of On-Going Research).

5.4. If the research is closed because an investigator does not submit for continuing review, the investigator will be responsible for the activities described in HRPP policy 2.9 (Closure of On-Going Research).

6.0 IRB Responsibilities

6.1. Continuing review, when it is required, is conducted by the convened IRB, except under the following circumstances:

6.1.1. Research which satisfies the requirements of OHRP Expedited Review Categories (1998) and HRPP policy 2.3 (Expedited Review), expedited category 8 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 where no subjects have been enrolled and no additional risks have been identified; or where the remaining research activities are limited to data analysis.

6.1.2. Research which satisfies the requirements of OHRP Expedited Review Categories (1998) and HRPP policy 2.3 (Expedited Review), 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.

6.2. The IRB Office will send emails to the PI and the Lead Coordinator and/or Regulatory Contact at least 60 days and 45 days prior to the date of expiration.

6.3. Protocols initially approved by IRB-01 or IRB-02 will undergo continuing review at either the IRB-01 or the IRB-02 meeting.

6.4. For continuing review by the convened IRB, IRB members will be provided documents for review as defined in HRPP policy 2.2 (Full IRB Review).

6.5. 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.

6.6. 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.

6.6.1. 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).

6.6.2. The Investigator and the Lead Coordinator and/or Regulatory Contact will be notified by email or through the InfoEd portal that a study is expired and that investigators are no longer authorized to conduct research activities or enroll subjects.

6.6.3. If the investigator believes that it would be in the best interest of a subject participating in an expired research study to continue research activities, the investigator must contact the IRB.

6.6.3.1. The IRB Chair or designee has the authority to grant approval of the request for one or more subjects provided (1) the research interventions hold out the prospect of direct benefit to the subjects, or (2) withholding those interventions poses increased risk to the subjects.

6.6.3.2. If the IRB Chair or designee decides that already enrolled subjects should continue to receive the interventions that were being administered to subjects under the research protocol, data collection (especially safety information) should also continue for such subjects.

6.6.4. If the investigator does not respond to the "Approval Expired" notification from the IRB Office within 30 calendar days, the study will be considered closed.

6.7. The expiration date for the next continuing review will be based on the date that the convened IRB gave conditional re-approval of the research (as per section 5.7 above).

6.8. The IRB Office will keep appropriate records of all continuing review activity in accordance with 45 CFR 46.115(a)(3).

2.8 Limited IRB Review

1.0 Purpose
The purpose of this policy is to describe the Organization's requirements and procedure for limited IRB review.

2.0 Policy
It is the policy of the Organization that the Organization may utilize limited review as described in 45 CFR 46.104(d)(2, 3, 7 or 8).

3.0 Criteria to be used for Limited Review

3.1 For purposes of conducted Limited IRB Review for research exempt under categories 2 or 3 the following determination must be made:

3.1.1 There are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of study data.

3.2 For purposes of conducting Limited IRB Review for Broad Consent under the Revised Common Rule, the following determinations must be made:

3.2.1 Broad Consent for storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens is obtained under the protocol;

3.2.2 Broad Consent is appropriately documented, or waiver of documentation is appropriate, and

3.2.2 If there is a change made for research purposes in the way the identifiable private information or identifiable biospecimens are stored or maintained, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

2.9 Closure of On-Going Research

1.0 Purpose
The purpose of this policy is to describe the criteria for, and 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

2.1. All research activities, including analysis of identifiable data, must cease when a research study has closed.

2.2. Studies may be closed by the PI or sponsor at any time, or by the IRB if subject accrual has been judged to be inadequate to achieve the scientific goals of the study, or by the IRB if the study remains in standard follow-up without additional research interventions or protocol dictated assessments, or by the IRB if the investigator has failed to respond to the "Approval Expired" notification from the IRB Office that IRB approval for a study has expired.

2.3. The investigator is responsible for notifying the IRB when a study is closed, and for making appropriate updates on ClinicalTrials.gov as appropriate, and for posting the consent forms on ClinicalTrials.gov as required.

2.4. Studies closed by the IRB due to inadequate accrual or closed in standard follow-up, may be reactivated under certain circumstances; studies closed by the IRB for failure to respond to "approval expired" notification require submission of a new application.

3.0. Definitions

3.1. Closure of a study means that all research interventions, including analysis of identifiable data, have been or must be ceased. Closure 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 if subject accrual has been judged to be inadequate to achieve the scientific goals of the study.

3.1.5. By the IRB if the study remains in standard follow-up without additional research interventions or protocol dictated assessments.

3.1.6. By the IRB if the investigator has failed to respond to the "Approval Expired" notification from the IRB Office that IRB approval for 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 (see HRPP policy 8.6 (IRB Study Hold, Suspension and Termination)).

4.0. Closure for Inadequate Accrual

4.1. Single site studies where CU is the sole participant, or multi-institution studies where CU is a participant but there is no external funding, may be closed by the IRB for low or no accrual.

4.1.1. Low accrual is defined as less than 1/2 of expected accrual based on the total accrual divided by the estimated time to accrue subjects in initial IRB application.

4.2. Studies with low or no accrual after two review cycles will be required to provide an explanation and a detailed plan to increase accrual. Plans to increase accrual might include, but are not limited to:

4.2.1. additional sites.

4.2.2. additional investigators.

4.2.3. additional study personnel, such as coordinators.

4.2.4. expanded study populations or less restrictive inclusion or exclusion criteria.

4.2.5. augmented education/training of referring practitioners, as applicable.

4.2.6. new advertising.

4.2.7. extension of the expected time to achieve target accrual.

4.3. Failure to accrue a minimum number of subjects by the next review cycle, without acceptable justification by the investigator may lead to closure of the study.

4.4. The IRB may allow certain studies involving rare conditions to continue despite poor or no accrual.

5.0. Closure of Studies in Standard Follow-Up

5.1. Studies may remain in standard follow-up for no more than three review cycles, and then may be closed, unless:

5.1.1. the study is collecting data in any form (such as survival); or

5.1.2. the organization is contractually required to keep the study open; or

5.1.3. the study includes a tissue bank at the organization; or

5.1.4. the investigator can provide adequate justification for the study to remain open.

6.0 Closure Procedures

6.1. 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.

6.2. The investigator is responsible for notifying the IRB when a study is closed. This is done by submitting a Request for Study Closure through InfoEd.

6.3. 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).

6.4. When a study is closed, the investigator is responsible for posting the consent forms on ClinicalTrials.gov as required.

6.5. If a study is closed by the IRB (per section 3.1.4 or 3.1.5. above), the investigator may request reactivation, with adequate justification, within 30 calendar days from the date of completion. Reactivation after the 30 calendar days grace period requires submission of a new IRB application.

6.6. If a study is closed by the IRB for failure to respond to “approval expired” notification (per section 3.1.6 above), investigators wishing to continue the research must submit a new application.

Section 3: Special Issues

3.1 Assessing the Need for Increased Monitoring, Interim Continuing Review, and Verification from Sources Other than the PI

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 that all non-exempt research other than that governed by 45 CFR 46.109(f) will be assessed at both initial and continuing review in accordance with the requirements set forth by HHS regulations at 45 CFR 46.108(a)(3), 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 where there is an expectation of high morbidity and mortality due to the underlying medical condition of the subjects.

3.1.2. 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.

3.1.3. Studies where a scientific subject matter expert – IRB member or outside consultant – has indicated the need for interim review or additional monitoring.

3.1.4. 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 the Research Compliance Auditor. 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 CU 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 RCO Auditor will perform the necessary verification by conducting an audit.

3.2 Data and Safety Monitoring

2.0 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 greater than minimal risk 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 (DSMP)

3.1. The DSMP must be developed to fit the design and risk profile of the research. It should include, as appropriate, elements such as:

3.1.1. The specific data that will be reviewed

3.1.2. The frequency and duration of review (when monitoring will start and when it will end).

3.1.3. The identities of the persons or groups conducting the review

3.1.4. The conditions under which specific subjects should be withdrawn

3.1.5. As appropriate based on the design and risk profile of the research, the conditions under which the study will be halted (that is, study stopping rules based on efficacy, toxicity and futility)

3.2. 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 (DSMB)

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.

4.1.2.6. Research involving a particularly vulnerable population, for whom closer monitoring will provide additional meaningful protection.

5.0 Review of the DSMP by the IRB

5.1. The IRB will consider the adequacy of the DSMP based on the conditions described in section 3.1 above.

5.2. For studies that do not have a data monitoring committee the IRB will carefully review the data and safety monitoring plan and determine whether a data monitoring committee would provide meaningful additional protection for subjects.

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 and IND Safety Reports by the IRB

6.1. It is the responsibility of the investigator to obtain copies of, and review, DSMB and IND Safety Reports, as they are produced.

6.2. The PI is responsible for submitting copies of all DSMB and IND Safety Reports to the IRB at the time of continuing review (or interim reporting period as mandated by the IRB), except as mandated in HRPP Policy 3.2.6.3 (immediately below).

6.3. If the DSMB or IND Safety 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 and/or IND Safety Reports will be followed promptly by a Request for Modifications to the protocol.

6.3.1. If the DSMB or IND Safety Report recommends halting the protocol or accrual, the report must be provided to the IRB in a Reportable New Information submission no later than 5 business days after the PI's initial receipt of the report.

6.3.2. If the DSMB or IND Safety Report recommends substantive changes to the protocol and/or informed consent document, the report must be provided to the IRB in a Reportable New Information submission no later than 10 business days after the PI's initial receipt ofthe report.

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.

3.3 Privacy Interests and Confidentiality of Research Data

2.0 Purpose

The purpose of this policy is to describe the Organization's requirements for 1) protection of privacy interests of research subjects, and 2) maintenance of confidentiality of data. For the purposes of this policy "subjects" and "participants" are synonymous and includes those persons participating in a data registry or biobank.

2.0 Policy

It is the policy of the Organization that:

2.1. The privacy interests of participants, and the confidentiality of research data will be protected in consideration of the risk to subjects and the nature of the research performed.

2.2. 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 Protection of Privacy

4.1. 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. 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 as appropriate:

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. Persons present during the informed consent process or during research activities will be limited as much as is possible to those listed on the IRB application or involved in the clinical care of the participant, or with the consent of the participant.

4.1.5. The research activities are performed in as private a place as possible.

5.0. Protection of Confidentiality

5.1. 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. 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:

5.1.1. 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, the risk to the subject associated with a breach of confidentiality and the physical medium on which the data is stored. PHI must be stored in a manner that is compliant with the HIPAA Privacy Rule, and other regulations and laws as applicable.

5.1.2. 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.
5.1.3. 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.

5.1.4. 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).

5.2. Certificate of Confidentiality

5.2.1. Research is automatically covered by an NIH Certificate of Confidentiality whenever the study is funded in whole or in part by the NIH and involves identifiable, sensitive information.

5.2.1.1. Identifiable sensitive information means information about an individual, obtained during the course of 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.

5.2.1.2. Researchers may also apply to the NIH for a Certificate of Confidentiality for research not funded by NIH. Generally, NIH will consider these requests for research on a topic that is within the NIH mission or HHS health-related research mission, and for research information that is collected, used, or stored in the US.

5.2.1.3. When research is covered by an NIH Certificate of Confidentiality, researchers:

5.2.1.3.1. 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

5.2.1.3.2. 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.

5.2.1.3.3. May disclose information if:

5.2.1.3.3.1. 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.

5.2.1.3.3.2. necessary for the medical treatment of the individual to whom the information, document, or biospecimen pertains and made with the consent of such individual;

5.2.1.3.3.3. made with the consent of the individual to whom the information, document, or biospecimen pertains; or

5.2.1.3.3.4. made for the purposes of other scientific research that is in compliance with applicable Federal regulations governing the protection of human subjects in research.

5.2.1.4. When research is covered by an NIH Certificate of Confidentiality, researchers must inform participants (for example, in the consent document) of the protections and limitations of certificates of confidentiality.

5.2.1.5. 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 that research is federally funded, the other researcher or organization must comply with applicable requirements when research is covered by a certificate of confidentiality.

5.2.1.6. All identifiable, sensitive information collected or used for research under an NIH Certificate of Confidentiality are protected by the certificate in perpetuity. Investigators and participants should be made aware that in the event of a lapse in NIH funding the protections of the Certificate may no longer apply. Therefore, the consent form for subsequent subjects should be amended to remove any guarantees of protection for these new subjects.

5.2.2. Investigators whose research is funded by the Centers for Disease Control and Prevention (CDC), Food and Drug Administration (FDA), Health Resources and Services Administration (HRSA), Indian Health Service (I), and Substance Abuse and Mental Health Services Administration (SAMHSA) may also have access to Certificates of Confidentiality thru those agencies.

3.4 Use of Protected Health Information in Research

2.0 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) all other applicable HIPAA policies and procedures adhered to by the Organization.

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 may 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 is a neutral intermediary (person or system), who is a CU 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 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 164.508I.

4.1.1. The Organization may utilize 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 164.508I(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 164.508I(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 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 a designated honest broker.

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 164.514I

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 IRB Office and the CU Privacy Officer) 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 the Office of the General Counsel.

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 a designated honest broker.

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 46.104(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 the Office of the General Counsel 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 CU 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.

3.5 Subject Recruitment Through Advertisements

2.0 Purpose

The purpose of this policy is to describe the Organization's requirements for recruitment of subjects through advertisements. For purposes 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
It is the policy of the Organization that:

2.1. All advertisements related to research for which the CU IRB is the IRB of record must be reviewed and approved by the IRB before the material can be used to recruit potential subjects.

2.2. All advertisements related to research for which the Organization is relying on another IRB as the IRB of record, must adhere to this policy; however, the IRB will not routinely review such advertising unless requested to do so by the investigator or the reviewing IRB.

2.3. Advertising must be clear, promote equitable enrollment and not represent undue influence or coercion.

2.4. For the purpose of this policy, references to information provided to, or decisions made by, potential subjects also means information provided to, or decisions made by, parents, guardians or legally authorized representatives (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 those described in the consent document and the protocol.

3.2.2. Claims, either explicit or implicit, that the research procedures (e.g. experimental interventions) 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 (monetary or related to free or reduced price for services), 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. Information about the type, amount, and availability of compensation may be included in an advertisement for research if

the information about the compensation appears in font and size that is consistent with the rest of the advertisement.

3.2.7. Any exculpatory language.

4.0 Printed Advertisement

4.1. All printed advertisements developed by the investigator or staff, or developed by an outside sponsor must be uploaded to InfoEd and reviewed and approved 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 protocol 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 of risks and discomforts, if any. If potential benefits are stated in recruitment material then the 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 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 protocol 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 matches the language and basic formatting 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 and Review of Advertisements

7.1. Final versions of all advertisements including print media, audio scripts for radio, video scripts for television, and screenshots of online advertising (including all webpages linked to the advertisement) related to research for which the CU IRB is the IRB of record, must be submitted to the IRB in accordance with HRPP policy 2.1 (Submission of Items for Review) for review and approval. Copies will be maintained by the IRB Office.

7.1.1. Submission of planned advertising to the IRB 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.

7.1.2. 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 HRPP policies 2.3 (Expedited Review).

7.1.3. The IRB approval letter will cite the approved version of the advertisement.

7.2. Advertisements related to research for which the Organization is relying on another IRB as the IRB of record need not be submitted to the IRB for review unless such review is requested by the investigator or by the reviewing IRB.

3.6 Subject Recruitment Through Direct Invitation

2.0 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 medical record or on file with the custodian of an IRB approved potential research subject database.

3.2. Honest Broker refers to a person, appropriately trained and designated by the Organization, whose responsibility it is to de-identify protected health information and provide that de-identified information to investigators.

4.0 Invitations to Patients

4.1. This section applies to patients (present and former) associated with CU.

4.2. Distribution Lists based on Clinical Databases, Potential Research Subject 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 IRB must approve subject recruitment plans, which include directed invitations to former or present patients.

4.3.2. Only patients who have opted-in to be contacted for research may be included in Distribution Lists.

4.3.3. Once a distribution list is approved by the IRB, it must be kept on a secure/encrypted CU computer for no more than 6 months. After that time, the distribution list must be re-submitted to the IRB as a request for modification.

4.3.4. The list must be deleted/destroyed once it is no longer in use.

4.3.5. Patients who have not opted-in for inclusion on a distribution list 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.

4.4. 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. Emails containing PHI must be sent on to the individual to whom the PHI belongs.

4.5.3. The subject line must clearly identify "CU 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 protocol 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.

4.5.5.7. Information for the patient on how to change their research recruitment option if desired.

4.5.6. Email invitations to patients obtained through IRB approved Distribution Lists must be sent by via the central email approved in connection with the creation of the Distribution List.

4.5.7. The recruitment email invitation may be sent to potential subjects no more often than weekly unless specifically authorized by the IRB.

4.5.8. 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 “CU 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 protocol 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. Frequency and number of calls must be specified by the investigator in the IRB application or study protocol 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 protocol 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 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, information on how to change their research recruitment option if desired.

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 Creighton University. 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; 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 namesor

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 6 months without an extension of IRB approval. The list must be deleted/destroyed once it is no longer in use.

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 Creighton University email 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 CU "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 protocol 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 or study protocol 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 protocol 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.

3.7 Finder's Fees and Recruitment Bonuses

2.0 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 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.

3.8 Research Subject Compensation and Reimbursement

2.0 Purpose

The purpose of this policy and procedure is to describe the Organization's requirements and limitations regarding compensation and reimbursement of research subjects.

2.0 Policy

It is the policy of the Organization that:

2.1. Compensation for research subjects may be acceptable if 1) the possibility of undue influence is minimized, and 2) the compensation is considered reasonable payment for time spent, or, if minimal risk research, a reasonable incentive for participation.

2.2. 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. Compensation not be presented to the potential subject as a benefit in either the process of consent or in the potential benefits section of the consent form.

2.3. Reimbursement for study-related travel and out of pocket expenses is acceptable.

2.4. Investigators should attempt to minimize financial sacrifice on the part of subjects and, as possible and appropriate, offer equitable reimbursement for costs.

3.0 Definitions

3.1. Compensation refers to monetary or other payment to the subject primarily intended to compensate for time spent in participating in the research activities, but also, in limited circumstances, as incentive to participate.

3.2 Reimbursement refers to monetary payment to offset expenses incurred as a direct result of participating in research activities. This includes travel expenses, lodging, meals, daycare, and may also include specific costs associated with research interventions (for example, costs of medications or therapies).

4.0 General Principles

4.1. Compensation for participation in research is not a requirement.

4.2. The amount or type of compensation should not serve as undue inducement to potential subjects.

4.3. For research posing greater than minimal risk to subjects, the 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.

4.4. For research posing minimal risk to subjects, since the risks associated do not exceed those of daily life or routine physical or psychological examination, compensation is not an inducement to offset risk. Therefore, compensation for minimal risk research may represent a reasonable incentive for participation.

4.5. Reimbursement for expenses is not a requirement; however, participation in research should, if possible, not require any financial sacrifice on the part of the subject. Investigators must provide adequate justification for failure to reimburse reasonable expenses.

4.6. The IRB will consider financial burden imposed on subjects as a consequence of participating in the research when evaluating whether risks are minimized and whether the risk-benefit relationship of the research is acceptable.

5.0 Specific Requirements for Compensation

5.1. 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 rate is $20/hour.

5.2. The IRB has the authority to review the level of compensation and, in appropriate circumstances, limit the total value.

5.3. Research interventions include 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, their time may be included in determining appropriate compensation.

5.4. Compensation above these levels must be specifically justified by the investigator and must comply with the general principles described in Section 4.0 of this policy.

5.5. The terms of the compensation must be disclosed in the IRB approved protocol and ICF, and discussed during the informed consent process, but the total amount of compensation should not be emphasized.

5.6. Compensation 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 may not be contingent upon the subject completing the study. If a subject does not complete the study, prorated payments 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.

5.7. The preferred form of compensation to subjects is a Cash Debit Card; however, subjects may be paid in any manner consistent with the policies of the relevant component of the Organization with adequate justification and IRBapproval.

5.8. The IRB does not allow bonuses to be 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.

5.9. 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.

5.10. 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.

5.11. 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.

5.12. Monetary payments for involvement of young children <7 years of age in research should not be made directly to the minor (though parents may still be compensated as per 5.3 above). It may be appropriate to offer young children an age appropriate token for their participation, such as a small toy. Direct payment to older children (7-12 years) may be made with appropriate justification. Adolescents (>13 years) may be directly compensated.

5.13. Due to the concerns relating to the potential subject's overestimating the value of compensation the CU 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.

5.14. 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.

6.0 Requirements for Reimbursement

6.1. Any costs to the subject that may result from participation in the research must be justified and disclosed in the consent form.

6.2. The terms of the reimbursement must be disclosed in the IRB application and ICF and discussed during the informed consent process.

6.3. Any reimbursement for costs incurred by subjects must be equitable, based on actual or reasonably estimated costs.

6.4. Eligibility for reimbursement for travel associated expenses may not be contingent on arbitrary distance threshold (that is, investigators may not offer reimbursement only for subjects who travel more than X miles).

6.5. The preferred form of reimbursement to subjects is a Cash Debit Card; however, subjects may be reimbursed in any manner consistent with the policies of the relevant component of the Organization or with the terms of a Clinical Trial Agreement as applicable.

3.9 Contraception Requirements

1.0 Purpose

The purpose of this policy is to describe the Organization's requirements regarding the avoidance of pregnancy for subjects participating in research.

2.0 Policy

It is the policy of the Organization that pre-menopausal subjects who are capable of becoming pregnant must avoid pregnancy while participating in research with the potential for reproductive toxicity or fetal harm.

2.1. As a Catholic institution, Creighton University endorses abstinence as the preferred method of pregnancy prevention.

2.2. When required by a study Sponsor, the Sponsor will provide information regarding contraception in the consent documents for research with the potential for reproductive toxicity or fetal harm.

2.2.1. In addition to conforming to the requirements of the study Sponsor, contraception language included in CU consent documents must conform to the CU IRB Standard Operating Procedure on the Inclusion of Pregnancy Prevention Language in Consent Documents.

2.2.2. When contraception language is required by the study Sponsor it is the responsibility of the investigator to discuss the risks and benefits of each form of contraception with potential study participants to ensure that subjects are making an informed choice.

3.10 Pregnancy Testing

2.0 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. Person of childbearing potential (POCBP) for the purpose of this policy is a person 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 women 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 CU or 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. 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 whether their parent/guardian will be informed of the test results.

4.7.1. Nebraska and Arizona state law permit minor subjects to consent to pregnancy testing and family planning services without parental permission.

4.7.2. In general, when parents will be informed of a minor's pregnancy results, the requirement to disclose results must be supported by a rationale involving medical necessity, for example, a risk to the life or health of the pregnant minor or the fetus based on the condition of pregnant minor.

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 women 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.

4.10. Any subject with a positive pregnancy test should be referred to the subject's 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.

3.11 Collecting Data from Pregnant Partners of Research Subjects

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 the subject 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 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 HHSregulations.

4.0 IRB Review

4.1. Protocols for collection of pregnancy outcome data should be submitted to the IRB.

4.2. If there is a high likelihood that subjects or partners of subjects will become pregnant duringthe course of the research, the collection of pregnancy outcome data may be included in the initial submission of the protocol.

4.2.1. The protocol submitted at the time of initial 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 protocol 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 research must satisfy requirements of subpart B. Non-Federally funded research 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. A Research application to collect pregnancy outcome data and or information on the infant 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 the partner's permission.

3.12 Ethical Access

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 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.

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 oftwo conditions applies:

3.2.1.1. The investigator has an existing clinical relationship with the patient. In contrast tosection 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 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 approved protocol.

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 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).

3.13 Use of Placebo or Wash-Out of Effective Therapy in Clinical Trials

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 treatment 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, injection, device, or procedure 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.

3.14 Managing Radiographic Incidental Findings in Human Subjects Research

2.0 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 applicable 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 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.

Section 4: Vulnerable Populations

4.1 Additional Protections for Vulnerable Populations

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).

2.2. It is the policy of the Organization thatthe 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 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 persons 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 persons (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 conditions 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.

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, 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 by submitting a Request for Modifications via InfoEd. The IRB will review the submission to determine that the vulnerable subject(s) has appropriate additional protections.

6.6.1. Subjects participating in research funded by a Common Rule department or agency 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).

6.6.3 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).

4.2 Research Involving Pregnant Women, Human Fetuses, and Neonates (Nonviable or of Uncertain Viability)

1.0 Purpose

The purpose of this policy 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

It is the policy of the Organization that:

2.1. Non-exempt research involving pregnant women, fetuses, and neonates (nonviable or of uncertain viability) funded by a Common Rule department or agency will be reviewed and approved in accordance with the requirements of HHS regulations at 45 CFR 46 Subpart B, and applicable state law.

2.2. Other non-exempt research involving pregnant women, fetuses, and neonates (nonviable or of uncertain viability) will be reviewed and approved in accordance with 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. 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 person shall be assumed to be pregnant if they exhibit 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. For research which is subject to HHS regulations at 45 CFR 46 subpart B pregnant women may be involved in research if all of the following conditions are met.

4.1.1.1. 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.

4.1.1.2. 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.

4.1.1.3. 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 determining the viability of a neonate.

4.1.2. For research which is not subject to HHS regulations at 45 CFR 46 subpart B pregnant women may be involved in research if all of the conditions in section 4.1.1 are met, with the following exceptions:

4.1.2.1. 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.

4.1.2.2. 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.

4.1.2.3. The IRB may decide that the consent of the father is not a requirement for research which holds out the prospect of direct benefit solely to the fetus.

4.2. Research Involving Neonates of Uncertain Viability

4.2.1. Neonates of uncertain viability may only 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 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.

4.2.1.5. 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.

4.2.2. If a neonate of uncertain viability is determined, after delivery, to be viable, that neonate 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 Nonviable Neonates

4.3.1. Nonviable neonates may only be involved in research if:

4.3.1.1. Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.

4.3.1.2. Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate.

4.3.1.3. Individuals involved in the research will have no part in determining the viability of the neonate.

4.3.1.4. The vital functions of the neonate will not be artificially maintained.

4.3.1.5. The research will not terminate the heartbeat or respiration of the neonate.

4.3.1.6. There is no additional risk to the neonate resulting from the research.

4.3.1.7. The purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means.

4.3.1.8. 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.

4.3.1.8.1. The waiver and alteration provisions at 45 CFR 46.116€ and 45 CFR46.116(f) do not apply.

4.3.1.8.2. The consent of the father is not required where the pregnancy resulted from rape or incest.

4.3.1.8.3. The consent of a legally authorized representative of either or both of the parents of a nonviable neonate is not permitted.

4.4. Research involving placenta, dead fetus, or fetal material

4.4.1. Research involving the placenta 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 Creighton University policies.

4.5. Research not otherwise approvable

4.5.1. Research which is subject to HHS regulations at 45 CFR 46 subpart B but which does not satisfy the requirements of 45 CFR 46 subpart B, and which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates, may be conducted only if the additional requirements of 45 CFR 46.207 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 ofthe 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 Compliance with 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 InfoEd.

4.3 Research Involving Prisoners

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 research involving prisoners that is funded by a Common Rule department or agency 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 research involving prisoners that is not funded by a Common Rule department or agency, 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 interaction or intervention with 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 CU IRB does not allow exemption from IRB review of federally funded research involving prisoners or for non-federally funded involving interaction or intervention with prisoners.

6.4. The CU 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 5.4 (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 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).

4.4 Research Involving Children

1.0 Purpose

The purpose of this policy is to describe the Organization's requirements for research involving children.

2.0 Policy
It is the policy of the Organization that:

2.1. Federally funded non-exempt research involving children will be reviewed and approved in accordance with the requirements of HHS regulations at 45 CFR 46 Subpart D, 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. Other non-exempt research (non-federally funded research and non-FDA regulated) involving children will be reviewed and approved in accordance with 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: 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 underage of nineteen years, his or her minority ends."

3.1.2. In the state of Arizona, the age of majority is defined, according to Arizona Revised Statute 8-531, as eighteen years of age.

3.1.3. 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.

3.1.4. If the research is conducted in another state under the oversight of the CU IRB, the age of majority is set by that state.

3.2. Assent: 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: 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: 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: a child's affirmative decision to decline participation in research.

3.6. Minimal risk: "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: 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: a child's biological or adoptive parent.

3.10.2. In Arizona the governing statute is Arizona Rev Stat 14-201.

3.10. Guardian: an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care.

3.10.1. In Nebraska the governing statute is Neb Rev Stat 30-2627.

3.10.2. In Arizona the governing statute is Arizona Rev Stat 14-201.

3.11. Permission: the agreement (consent) of parent(s) or guardian(s) to the participation of the child or ward in research.

3.12. Ward (of the State): a child who, as determined by the State where the child resides, is a foster child, is a ward of the State, or is in the custody of a public child welfare agency

4.0 Categories of Research

HHS regulations specify that research involving children must be approvable under one or more of the following four categories and meet the specified criteria. For the purposes of this policy, "IRB" refers both to the convened IRB and to an expedited reviewer as described in HRPP 2.3 (Expedited Review).

4.1. Research not involving greater than minimal risk (45 CFR 46.404)

4.1.1. The IRB will determine and document 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, 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)

4.2.1. The IRB finds and documents 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, 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)

4.3.1. The IRB finds and documents 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, 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)

4.4.1. The IRB will submit this category of research to HHS for approval, if the research is funded by HHS.

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, or 406.

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 ofchildren.

4.4.2.3. The research meets applicable requirements of 45 CFR 46; 46.408; 46.409 (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.

4.5. Research Involving Wards

4.5.1. HHS regulations at 45 CFR 46.409 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 providing all ofthe requirements under Subpart D are met.

4.5.1.2. Wards may participate in research classified as 45 CFR 406 or 407only 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 takeinto 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. In the State of Arizona, children who are wards of the state can be included in research as consistent with federal HHS statute 45 CFR 46.409.

4.5.5. If a child becomes a ward while participating in the research, the IRB must be promptly notified and Request for Modifications 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(f).

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, 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, 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 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 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.

5.4. Documentation of permission by parents/guardians may be waived if the IRB determines the conditions of 45 CFR 46.117(c)are satisfied.

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 CFR46.408(a)].

6.3. Assent is required from children 7 to 18 years of age in the state of Nebraska and 7 to 17 years of age in the state of Arizona 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)]. 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)]. OR

6.3.3. The research meets the requirements for a waiver of assent under 45 CFR 46.116(f).

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 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 in the state of Nebraska or 13 and 17 in the state of Arizona the following procedure for assent must be followed:

7.2.1. The child should be given a copy of the Informed Consent/Assent Form.

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 appropriate signature blank on the Informed Consent Form.

8.0 Consent of Subjects Reaching the Age of Majority

8.1. Children who reach the age of majority while actively participating in a 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 informed consent document as "subject" without parental co signature.

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 Written Assent)

9.1. Children who reach the age of written assent while actively participating in a study must give their written assent to continue participation in the research at the first visit after reaching that age if they are capable of providing assent. Subjects must then sign an Informed Consent Form (which must also be signed by the parent or guardian).

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 written assent.

9.3. If, upon reaching the age of written 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 written assent, the subject refuses to provide written 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-01 (Biomedical IRB) or IRB-02 (Social Behavioral IRB) will review greater than minimal risk research involving children in accordance with the authority granted to them in HRPP policy 1.2 (Authority Granted to the IRB by the Organization).

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 utilizethe 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 and 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 InfoEd.

4.5 IRB Review of Research Involving Subjects with Impaired Decision-Making Capacity

1.0 Purpose

The purpose of this policy 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), 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 procedure(s) involved in the research. If there is no applicable law addressing this issue, legally authorized representative means 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” (45 CFR 46.102(i)). “Legally authorized representative” in the context of research is, however, not defined in the Nebraska revised statutes. OHRP Guidance 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©.”

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. Under Arizona law (Arizona Rev. Stat 36-3231), the following persons may serve as a Legally Authorized Representative – by order of preference:

3.2.2.1. The patient/research subject’s designated healthcare power of attorney

3.2.2.2. A court appointed guardian for purposes of healthcare decisionmaking.

3.2.2.3. The patient/research subject’s spouse unless the patient/subject and spouse are legally separated.

3.43 Adult assent is defined as the affirmative agreement of a decisionally impaired person to participate in research.

3.4. Dissent is defined as an objection to participation. In general, dissent is considered meaningful if it is unequivocal or sustained after an effort to relieve concerns and/or distress (Black B, et al; Am J Geriatr Psychiatry 18(1), 77-85, 2010)

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: a) adjudicated by the Court, or b) determined by an investigator, who, by their professional training, licensure, or experience, is qualified to determine capacity, or c) determined by an independent assessor.

4.2. The method utilized to determine capacity may vary depending on the characteristics of the 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, but are not limited to:

4.2.1. Clinical interviews

4.2.2. Mini-Mental Status Exam (MMSE)

4.2.3. 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 and/or an independent monitor of the consent/assent process.

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 only if an LAR provides consent on their behalf.

5.2. 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 exhibits unequivocal or sustained dissent 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 Chair. The full IRB will be notified of the IRB Chair's decision, and the board has the authority to accept the IRB Chair's decision, require additional actions, or require withdrawal of the subject.

6.4. If a decisionally impaired person exhibits unequivocal or sustained dissent 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 Chair. The full IRB will be notified of the IRB Chair's decision, and the board has the authority to accept the IRB 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 provides consent, and the decisionally impaired person provides assent (as described in section 6 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 provides consent, and the decisionally impaired person provides assent (as described in section 6 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 section 6 above).

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, 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
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. Informed consent (permission) of the LAR will be documented in accordance with HRPP Policy 5.1 (Obtaining Informed Consent from Research Subjects)

12.2. As appropriate, subjects with impaired decisional making capacity will be provided with an 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 Information Sheet Template.

4.6 Research Involving Employees of the Organization and Students as Subjects

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.

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.

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 research protocol 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 research 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.

Section 5: Informed Consent

5.1 Obtaining Informed Consent From Research Subjects

1.0 Purpose

The purpose of this policy is to describe the Organization's requirements for the process and documentation of informed consent.

2.0 Policy

It is the policy of the Organization that:

2.1. 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 and CU HRPP policies.

2.2. Informed consent will be appropriately documented in accordance with, and to the extent required by 45 CFR 46.117 and CU 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 has prospectively obtained the legally effective informed consent of the subject 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 obtaining and documenting valid informed consent from the subject prior to their 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, HRPP policies, and 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), or

through an electronic signature process 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 in the research 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 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. For non-exempt, federally funded research, informed consent must begin with a concise and focused presentation (summary) of the key information that is most likely to assist a prospective subject 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.

Note: CU IRB strongly recommends that consent documents for all research, not just non-exempt federally funded research, utilize a key summary in order to facilitate greater comprehension among study subjects.

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 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 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 must minimize the potential for coercion and undue influence.

3.11. Obtaining informed 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. Obtaining informed 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. Obtaining informed consent for 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. Obtaining assent for the participation of minors in research must be conducted in accordance with HRPP policy 4.4 (Research Involving Children).

3.15. Obtaining assent for the participation of decisionally impaired individuals in research and consent from the LAR acting as a surrogate on behalf of the decisionally impaired individual 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, other laws and regulations, and/or HRPP policy. This requirement is satisfied by utilizing the appropriate CU ICF Template.

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 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 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, NIH, sponsors/CROs, other institutions and investigators, third party payers, or others will, as necessary, have access to research records containing PHI.

4.1.1.11. A statement that federally funded interventional and observational trials must be listed on ClinicalTrials.gov.

4.2. Additional Elements of Informed Consent (45 CFR 46.116(b))
When appropriate, the consent process and form must provide some or all the following information, in accordance with Federal Regulations at 45 CFR 46.116, other laws and regulations, and/or HRPP policy. This requirement is satisfied by utilizing the appropriate ICF template available on the IRB website.

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 study 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 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 that may result from participation in the research.

4.2.5. The consequence(s) of a subject 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.

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, the investigator may 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 Department of Defense research, a description of the additional elements for informed consent are found in HRPP policy 1.14 (Research Subject to Department of Defense Regulatory Requirements).

4.2.16. For Department of Justice research, a description of the additional elements for informed consent are found in HRPP policy 1.15 (Research Subject to Department of Justice Regulatory Requirements).

4.3 Elements of Broad Consent for the Storage, Maintenance, and Secondary Research Use of Identifiable Private Information or Identifiable Biospecimens (45 CFT 46.116(d))

Broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens (collected for either research studies other than the proposed research or nonresearch purposes) is permitted as an alternative to the informed consent requirements in 45 CFR 46.116(c) and (d) and the requirements codified in this policy at 4.1. (Basic Elements of Informed Consent) and 4.2 (Additional Elements of Informed Consent). If a subject or the subject's LAR is asked to provide broad consent, the following elements shall be provided to each subject or the subject's LAR in a written consent form:

4.3.1. The information required in 45 CFR 46.116(b)(2), a description of any reasonably foreseeable risks or discomforts to the subject; 45 CFR 46.116(b)(3), A description of any benefits to the subject or to others that may reasonably be expected from the research; 45 CFR 6.116(b)(5), A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained; 45 CFR 46.116(b)(8), A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled; 45 CFR 46.116(c)(7), 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; and 45 CFR 46.116(c)(8), A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions.

4.3.2. A general description of the types of research that may be conducted with the identifiable private information or identifiable biospecimens. This description must include sufficient information such that a reasonable person would expect that the broad consent would permit the types of research conducted.

4.3.3. A description of the identifiable private information or identifiable biospecimens that might be used in research, whether sharing of identifiable private information or identifiable biospecimens might occur, and the types of institutions or researchers that might conduct research with the identifiable private information or identifiable biospecimens.

4.3.4. A description of the period of time that the identifiable private information or identifiable biospecimens may be stored and maintained (which period of time could be indefinite), and a description of the period of time that the identifiable private information or identifiable biospecimens may be used for research purposes (which period of time could be indefinite).

4.3.5. Unless the subject or legally authorized representative will be provided details about specific research studies, a statement that they will not be informed of the details of any specific research studies that might be conducted using the subject's identifiable private information or identifiable biospecimens, including the purposes of the research, and that they might have chosen not to consent to some of those specific research studies.
4.3.6. Unless it is known that clinically relevant research results, including individual research results, will be disclosed to the subject in all circumstances, a statement that such results may not be disclosed to the subject.

4.3.7. An explanation of whom to contact for answers to questions about the subject's rights and about storage and use of the subject's identifiable private information or identifiable biospecimens, and whom to contact in the event of a research-related harm.

5.0 ICF and Information Sheet Templates

All investigators are required to utilize one or more of the templates, available on the IRB website, applicable:

5.1. ICF template(s)

Note: the ICF template may be used to document consent (or permission) from an adult, parent or guardian, or LAR.

5.2. Information Sheet(s)

Note: the Information Sheet template may be used for Child, Youth or Decisionally Impaired Subjects.

6.0 Process of Informed Consent

6.1. Informed consent may only be obtained from subjects who have the legal and mental capacity to provide 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).

6.2. Prospective subjects 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.

6.3. 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.

6.4. The process of informed consent can be described as the transmission of relevant information to the prospective subject. The exchange of information between the PI/designee and the prospective subject should occur by face-to-face contact. However, depending upon the nature and risks of the study or other factors, the IRB may permit a process including remote consent, as described in HRPP policy 5.3 (Use of a Remote Consent Process).

6.5. 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.

6.6. The PI/designee involved in the process of consent should take all necessary steps to minimizethe 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.

6.7. The PI/designee will consider additional protection for prospective subjects who may 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. Such additional protections may include but are not limited to 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.

6.8. The PI/designee must fully explain the rights of research subjects and provide the prospective subject with a written copy of the "Rights of Research Subjects."

6.9. The prospective subject 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 might 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 is uncomfortable making a decision, he/she should be encouraged to consult with family members or other individuals of their choosing.

6.10. The PI/designee have a legal and an ethical obligation to ensure that the prospective subject has sufficient knowledge and comprehension of all 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.

6.11. In certain studies, it may be appropriate to seek active re-consent from subjects. 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.

6.12. Each subject must be given a copy (paper or electronic) of the signed and dated ICF after signing. If the IRB has approved a waiver of signed informed consent, each subject must be offered a copy (paper or electronic) of the unsigned ICF.

6.13. 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).

7.0 Documentation of Informed Consent

7.1. Unless a waiver of the requirement to obtain signed consent has been granted 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.

7.2. Study personnel who are permitted to document informed consent must be:

7.2.1. Authorized by the PI.

7.2.2. Listed by name in the IRB Application and consent form.

7.2.3. Approved by the IRB.

7.3. Individuals authorized to document consent must have the:

7.3.1. Sufficient knowledge of the protocol.

7.3.2. Sufficient knowledge of CU HRPP policies and of their responsibility to protect the rights and welfare of subjects.

7.3.3. Required licensure to perform the procedures described in the protocol, as applicable.

7.4. Once it is determined the prospective subject has fully understood all 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 should sign and date the current IRB-approved ICF at the time of consent.

7.5. Provided the IRB has not approved an alternate method of communication and consent (per HRPP policy 5.3 Use of a Remote Consent Process) the subject, PI (or other person authorized to document consent), and the witness (if required per section 7.6 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 provided valid informed consent.

7.6. 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 or ICF as study personnel.

8.0 Documentation in the Research and Medical Records

8.1. The research record must contain the original signed ICF. If signature is obtained electronically, then the research record must either include a printed copy of the electronically signed form, or an electronic copy of the form with the e-signature attached.

8.2. For any protocol where a research procedure or intervention may result in a billable charge, the subject's medical record must contain a copy of the signed ICF.

8.2.1. The IRB Chair/designee may waive this requirement with adequate justification from the investigator (for example, but not limited to, if inclusion of the CF in the medical record would represent a physical or financial risk to subjects if a breach of confidentiality occurred).

8.3. For all studies greater than minimal risk, the process of consent must be documented in themedical 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.

9.0 Special Consent Circumstances

9.1. Additional requirements for the process and documentation of informed consent for non-English speaking persons, or persons with additional needs or vulnerabilities participating in human subject research are described in HRPP policy 5.7 (Obtaining Informed Consent from Non-English Speaking Persons, or Persons with Additional Needs or Vulnerabilities).

10.0 Requirements for Re-Consent of Subjects

10.1. A formal re-consent procedure is not required for minor changes in protocol or the ICF.

10.1.1. 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.

10.1.2. 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.

10.2. 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 through the use of an IRB-approved revised ICF or an addendum to the ICF.

10.2.1. 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.

10.3. When new information could potentially have a significant impact on the health and welfare of subjects (for example, information concerning a serious adverse event), subjects should be notified immediately in person, or by telephone, video-conferencing, or use of desktop, mobile or web-based applications or similar technologies with the transmission of information documented and witnessed.

10.3.1. Notification of subjects 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.

10.3.2. The PI must notify the IRB when all subjects have been contacted. This notification should include identification of subjects by number and the date they were contacted.

10.4. If modification of ICFs or information sheets are made by the investigator at the time of continuing review, re-consent of currently enrolled subjects is not required except as described in section 10.1, 10.2 or 10.3 above.

10.5. Since consent must be an on-going process throughout the duration of the study, investigators should regularly verbally reaffirm the subject’s willingness to continue participation in the study as well as solicit and answer questions from the subject.

10.6. Subjects withdrawing consent to participate in a study may be asked to allow continued follow-up of clinical outcomes to be used for research purposes. The subject's agreement to use of clinical follow-up data must be documented in the research record or medical record.

11.0 Telephone Consent
Refer to HRPP policy 5.3 (Use of a Telephone Consent Process).

12.0 Short Form
Refer to HRPP policy 5.5 (Use of the Short Form Consent Document).

13.0 Waiver or Alteration of Informed Consent
Refer to HRPP policy 5.2 (Waiver or Alteration of Informed Consent and HIPAA Authorization).

14.0 Waiver of the Requirement to Obtain a Signed ICF
Refer to HRPP policy 5.4 (Waiver of the Requirement to Obtain Signed Consent Form).

5.2 Waiver or Alteration of Informed Consent and HIPAA Authorization

1.0 Purpose

The purpose of this policy is to describe the Organization's requirements for granting a waiver or alteration of informed consent with or without waiver of HIPAA authorization in research.

2.0 Policy

It is the policy of the Organization that

2.1. Waiver or alteration of the requirement for informed consent may be approved, provided that the IRB finds and documents the criteria specified in 45 CFR 46.116(f) have been met.

2.2. Waiver of authorization under the HIPAA Privacy Rule may be approved, provided that the IRB (acting as the Privacy Board) finds and documents the criteria specified in 45 CFR 164.512(I)(2)(ii) have been met.

2.3. 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) have been satisfied.

2.4. 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(f) and 45 CFR 164.512(I)(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. The IRB may allow a waiver or alteration of informed consent and HIPAA authorization provided the requirements of 45 CFR 46.116(f) (and 45 CFR 164.514(I)(2)(ii) if applicable) are met; specifically:

3.1.1. The research involves no more than minimal risk to the subjects (45 CFR 46.116(f)(3)(i)).

3.1.1.1. For research subject to the HIPAA Privacy Rule, 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(I)(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(j)).

3.1.2. The research could not practicably be carried out without the requested waiver or alteration (45 CFR 46.116(f)(3)(ii)); (45 CFR 164.512(I)(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.

Note: 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.

3.1.3. 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 (45 CFR 46.116(f)(3)(iii)).

3.1.3.1. For research subject to the HIPAA Privacy Rule, 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(I)(2)(ii)(C)).

3.1.4. The waiver or alteration will not adversely affect the rights and welfare of the subjects (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 99) 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.

3.1.5. 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)

4.1. The IRB may allow a waiver of parental/guardian consent (permission) provided the requirements of 45 CFR 46.408(c) are met; specifically;

4.1.1. 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 males and females about their use of alcohol and/or illicit drugs, providing referrals to outpatient resource, and an annual follow up for three years. The questions are reasonably commensurate with questions asked during routine medical services which the adolescents are permitted by law to receive without parental permission and the provision of outpatient referrals 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 99) 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.

4.1.2. 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 IRB may allow a waiver or alteration of informed consent in research involving public benefit and service programs conducted by or subject to the approval of state or local officials provided the requirements of 45 CFR 46.116(e) are met; specifically;

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. Responsibilities of IRB

6.1. 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).

6.2. Research which involves PHI 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 or exempt review as appropriate.

6.3. 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.

6.4. Documentation of IRB approval of waiver or alteration of informed consent and HIPAA authorization will appear in the IRB review letter for all approvals (expedited and full Bord) and in the meeting minutes (for studies approved at the full Board).

5.3 Use of a Remote Consent Process

1.0 Purpose

The purpose of this policy and procedure is to describe the Organization's requirements for use of remote informed consent process. For the purpose of this policy remote consent includes telephone, video-conferencing, or use of desktop, mobile or web-based applications or similar technologies.

2.0 Policy

2.1. It is the policy of the Organization that remote consent may be used in both clinical and non-clinical research, provided such communication satisfies requirements of HHS regulations at 45 CFR 46.116 and 45 CFR 46.117, and satisfies the additional requirements in the policy.

2.1.1. The convened IRB or a qualified expedited reviewer (if the research or change in protocol qualifies for expedited review) may authorize use of remote consent or documentation for new subjects, or re-consent for current 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.

2.1.1.3. Direct face-to-face contact with the research staff would place an unreasonable burden on the subject (for example, because of distance), or

2.1.1.4. Requirement for direct face-to-face contact would prohibit enrollment of a potential subject in research with the prospect of direct benefit, or

2.1.1.5. Provision of new information to the subject would be inappropriately delayed by requiring direct face-to-face contact with the research staff.

2.1.2. The IRB Chair or designee may authorize use of remote consent or documentation for a single subject if:

2.1.2.1. Direct face-to-face contact with the research staff would place an unreasonable burden on the subject (for example, because of distance), OR

2.1.2.2. Requirement for direct face-to-face contact would prohibit enrollment of a potential subject in research with the prospect of direct benefit, OR

2.1.2.3. 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 Remote 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" must be provided to the subject for review prior to the remote consent process. These items can be provided to the subject in paper form by mail or fax, in PDF or equivalent form electronically, or through InfoED or another desktop, mobile or web-based application remotely.

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 CFR46.116(a)).

3.1.3. If the subject agrees to participate in the research or the screening:

3.1.3.1. If the ICF is supplied in paper form the subject is instructed to sign and date the ICF and return the signed document to the investigator by mail, fax, a scanned copy via email, or a photograph of the signed ICF sent via text or email.

3.1.3.2. If the ICF is supplied in PDF or equivalent form the subject is instructed to print, sign and date the ICF and return the signed document to the investigator by mail, fax a scanned copy via email or a photograph of the signed ICF sent via text or email.

3.1.3.3. If the ICF is supplied remotely through a desktop, mobile, or web-based application, the subject is instructed to sign through that application.

3.1.3.4. If the signed ICF (noted in sections 3.1.3.1. or 3.1.3.2. above) cannot be collected by the investigator, the subject may supply a dated attestation by a witness who participated in the call and by the investigator who conducted the consent discussion during the call that the subject confirmed that he/she agreed to participate in the study and signed the informed consent.

3.1.3.5. In all cases, the investigator must verify the identity of the person signing the form or providing the electronic signature. Verification of identity and signature can be accomplished by

direct (or video) observation of the process of signing, or by using information from some form of official identification, such as a birth certificate, a government-issued passport, or a driver's license, or via security questions, or by the written attestation of a witness to the signature.

3.1.3.6. No research interventions (including screening) can be conducted until a signed copy of the ICF has been received by the investigator by email, fax, mail, or text except when specifically authorized by the IRB or by the IRB Chair or designee.

3.1.3.7. 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", "remote consent obtained 10/27/08").

3.1.3.7.1. If a "signed" ICF in the form of a photograph is provided to the investigator, the investigator shall sign and data a clean copy of the ICF and append the photo to the signed ICF.

3.1.3.8. A copy of the countersigned ICF signed by the investigator must be provided to the subject (unless the subject has the ability to print the signed ICF through the desktop, mobile or web-based application).

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 remote 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 remote consent.

3.1.5.2. The date and time of remote 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. Remote Consent may be utilized for enrollment of new subjects provided the research constitutes no more than minimal risk OR 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.

3.2.3. Some minimal risk survey only research may be eligible for waiver of the requirement for the investigator to obtain a signed informed consent form under 45 CFR 46.117(c)(1)(ii).

3.3. Re-consent to disclose new information or protocol changes

3.3.1. Remote 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. Remote 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).

5.4 Waiver of Requirement to Obtain Signed Consent Form

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, 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'swishes will govern.

3.1.1.2. The oral or written information provided to subjects includes all requiredand 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)).

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.

3.2. 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 (for example, an information letter).

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 of IRB approval of waiver of requirement to obtain signed ICF will appear in the IRB review letter.

5.5 Use of the Short Form Consent Document

1.0 Purpose
The purpose of this policy is to describe the Organization's requirements for use of a short form written consent document for enrollment in research.

2.0 Policy
It is the policy of the Organization that:

2.1. The use of a short form written consent document is permissible in accordance with HHS regulations at 45 CFR 46.117(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. The IRB may require that a translated CF be prepared and used for research where it is reasonable to expect that a significant number of non-English speaking persons will participate.

2.3. Use of 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. 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 Definitions

3.1. Qualified Interpreter: as defined in addendum B to HRPP policy 5.7 (Obtaining Informed Consent from Non-English Speaking Persons, or Persons with Additional Needs or Vulnerabilities). Generally, it must be an individual fluent in English and in the spoken language of the subject, and preferably who has a basic understanding of the medical or other scientific terminology related to the research.

4.0 Use of the Short Form

4.1. 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

4.1.1. 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 45 CFR 46.116(a)(5)(i)) was presented first to the subject, before other information, if any, was provided.

4.2. Investigators must complete a Request for Modifications InfoEd requesting the use of a short form, and the request must be approved by IRB or IRB reviewer prior to use of the requested short form.

4.3. The approval to use the short form is valid for two weeks and may be used for one subject only. The approval period can be extended by the IRB Chair/designee with adequate justification.

4.4. 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. The completed Short Form Request and the translated Short Form must be submitted to the IRB for expedited review and approval before use.

4.5. A Qualified Interpreter who is fluent in both English and the language of the subject/LAR must be identified.

4.5.1. If a prospective subject/LAR/parent wishes to designate his/her own interpreter a Qualified Interpreter must also be present to ensure the quality and accuracy of the interpretation and this must also be documented. A minor cannot be used as an interpreter.

4.6. A witness who is fluent in both English and the language of the subject/LAR must be identified and must fill the same requirements as a qualified interpreter.

4.6.1. The Qualified Interpreter may also serve as the witness (with the exception that study staff may not serve as witness).

4.7. The interpreter must be involved in the process of consent as follows:

4.7.1. The subject/LAR should be given a copy of the short form.

4.7.2. The person obtaining consent, with the assistance of the interpreter, should explain the use of the short form.

4.7.3. The person obtaining consent, with the assistance of the interpreter, must

4.7.3.1. 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 45 CFR 46.116(a)(5)(i)) before other information about the research.

4.7.3.2. 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.

4.7.4. The complete ICF, which has been approved by the IRB, will serve as the summary required by 45 CFR 46.117(b)(2).

4.7.5. 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.

4.8. Upon conclusion of the consent process the subject/LAR, person obtaining consent, and the witness must sign the forms as follows:

4.8.1. The subject/LAR must sign and date the short form.

4.8.2. The person obtaining consent must sign and date the English version of the complete ICF.

4.8.3. The witness to the oral presentation of the ICF must sign both the Short Form, as well as the English version of the complete ICF.

4.9. A copy of the signed and dated short form and the English version of the complete ICF must be given to the subject/LAR.

4.10. Depending on the nature and duration of the research, the IRB Chair/designee may determine that the English version of the complete ICF must be translated into a language understandable to the subject with a copy given to the subject as soon as possible after enrollment in the research using the short form. In general, this may be required for studies which are significant risk and of long duration.

4.11. The process of consent must be documented in the medical or individual study subject record (if applicable). This documentation should include the names of the individuals involved in the process of consent, including the names and contact information of the interpreter and the witness.

4.12. 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.

5.6 Exceptions from Informed Consent Requirements for Emergency Research

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 CU IRB does not provide review or oversight to Emergency Research.

5.7 Obtaining Informed Consent from Non-English Speaking Persons, or Persons with Additional Needs or Vulnerabilities

1.0 Purpose
The purpose of this policy is to describe the Organization's requirements for the process and documentation of informed consent for non-English speaking persons, or persons with additional needs or vulnerabilities participating in human subject research. For general considerations of informed consent see HRPP 5.1 (Obtaining Informed Consent from Research Subjects).

2.0 Policy
It is the policy of the Organization that:

2.1. Non-English speaking persons, or persons with additional needs or vulnerabilities will be offered accommodations and additional protections regarding the process and documentation of informed consent.

3.0. Specific Protections and Requirements

3.1. Non-English Speaking Subjects

3.1.1. Expected Enrollment of Non-English Speaking Subjects. 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.

3.1.1.1. Consent forms must be prepared by a qualified translator, as defined in the addendum A to this policy.

3.1.1.2. A Qualified Interpreter, as defined in addendum B to this policy, must be identified.

3.1.1.3. 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.

3.1.1.4. Upon conclusion of the consent process the subject and the Interpreter must sign and date the non-English version of the ICF.

3.1.1.4.1. If the Interpreter is not present in person during the informed consent process, he/she may sign utilizing a remote consent process as described in HRPP policy 5.3 (Use of a Remote Consent Process)

3.1.1.5. The person obtaining consent must sign and date the English version of the ICF.

3.1.1.6. The process of consent must be documented in the medical or individual study subject record (if applicable). This documentation should include the names of the individuals involved in the process of consent, including the name and contact information of the interpreter.

3.1.2. 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:

3.1.2.1. 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.

3.1.2.2. If the research offers the prospect of direct therapeutic benefit, the person can be enrolled using the IRB-approved short form as per the requirements of HRPP policy 5.5 (Use of the Short Form Consent Document).

3.2. Visually Impaired or Blind Subjects

3.2.1. For research where it is reasonable to expect that a significant number of blind or low vision subjects will participate, the investigator must describe a plan to assure that materials are available to assist the prospective subject in the process of consent. This may include large font (electronic or paper) consent forms, audio version of consent form, Braille consent form, or other technology as appropriate.

3.2.2. If Braille CF is utilized, the IRB may require a transcription into print text or review of the document by a qualified person who reads Braille in order to ensure that a Braille ICF is accurate.

3.2.3. If an unexpected blind or visually impaired subject is encountered, the IRB Chair or designee may authorize use of any of the above methods or technologies as appropriate.

3.2.4. If possible, the subject should sign or make an X to signify consent. A witness unaffiliated with the research team must observe the consent process and witness the signature or mark. The witness must sign the consent form attesting that the information in the consent document and any other written information was accurately.

3.3. Hearing Impaired or Deaf Subjects

3.3.1. For research where it is reasonable to expect that a significant number of hearing impaired or deaf subjects will participate, the investigator must describe a plan to assure that the process of consent can be conducted in an appropriate manner. This may include use of an American Sign Language (ASL) interpreter, or appropriate assistive technologies.

3.3.2. If an unexpected deaf or hearing impaired subject is encountered, the IRB Executive Chair or designee may authorize use of any of the above methods or technologies as appropriate.

3.4. Illiterate or Low Literacy Subjects

3.4.1. For research where it is reasonable to expect that a significant number of illiterate or low literacy subjects will participate, the investigator must describe a plan to assure that the process of consent can be conducted in an appropriate manner. This may include reading the CF to the subject, use of a pre-recorded audio version of consent form, or other technology as appropriate.

3.4.2. If an unexpected illiterate subject is encountered, the IRB Chair or designee may authorize use of any of the above methods or technologies as appropriate.

3.4.3. If possible, the subject should sign to signify consent. If the subject is unable to sign, he/she may make an X to signify consent. A witness unaffiliated with the research team must observe the

consent process and witness the mark. The witness must sign the consent form attesting that the information in the consent document and any other written information was accurately explained to, and apparently understood by, the subject and that consent was freely given.

Addendum A

Minimal Requirements for Translation of Informed Consent Documents
Translation of Consent forms into a language other than English must be performed by qualified persons, with adequate competence in English and the language of the translation, and preferably with knowledge of research methodology.

A. For research conducted solely within the Organization acceptable translation by a "qualified" translator includes, in order of preference:

- Translation provider by a translator certified by The American Translators Association
- Translation provided by a translator certified by any other non-profit organization, or Federal, State or Municipal government agency
- Translation accompanied by a certification statement; specifically, that the document translation is complete and accurate, and by the translator's certification that he or she is competent to translate. A person deemed "competent to translate" includes (a) foreign language instructors employed by an accredited university or college; or (b) graduate students in foreign language currently in training at an accredited university or college; or (c) a bilingual person able to write in two languages with equal fluency (including members of the research team). For research involving greater than minimal risk (per 45 CFR 46.102(j)), translation accompanied by a certification statement (category 3) must be accompanied by a back-translation by a different person or group, preferably of categories 1 or 2.

B. For multi-institution research where the Organization is a participating site, translation must be accompanied by documentation that the translation was performed by a "qualified" individual, as defined above.

Addendum B

Minimal Requirements for Interpretation

- Interpretation must be performed by qualified persons, who are fluent in both English and the language of the subject, and preferably with knowledge of research methodology.

Qualified interpreters include, in order of preference:

- A person holding certification by the National Board of Certification for Medical Interpreters, the Certification Commission for Healthcare Interpreters, or any similar credentialling body, or certified by any other non-profit organization, or Federal, State or Municipal government agency.

- A person employed by, or contracted by, the Organization to provide interpretation services in a clinical context. This includes commercial interpretation services (such as CyraCom) or study site staff who are fluent in both English and the language of the subject.
- Study personnel who are fluent in both English and the language of the subject.
- Other persons, including (a) foreign language instructors employed by an accredited university or college; or (b) graduate students in foreign language currently in training at an accredited university or college; or (c) a bilingual person; specifically, a person using or able to speak in two languages with equal fluency.

Section 6: FDA Regulated Drugs and Devices

6.1 Research Involving Investigational and Marketed Drugs

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 CU IRB does not provide review and oversight of research involving investigational and marketed drugs.

2.2 It is the policy of the Organization that research involving investigational and marketed drugs conducted by CU-affiliated personnel will be reviewed and approved by a qualified external IRB as defined in CU HRPP Policy 1.4, and that the external IRB conducting review and approval will maintain oversight of these studies.

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. Marketed Drug is a drug or biologic approved by FDA for marketing and is generally in use for treatment purposes.

6.2 Research Involving Investigational and Marketed Devices

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

2.0 Policy

2.1. It is the policy of the Organization that the CU IRB does not provide review and oversight of research involving investigational and marketed devices.

2.2 It is the policy of the Organization that research involving investigational and marketed devices conducted by CU-affiliated personnel will be reviewed and approved by a qualified external IRB as

defined in CU HRPP Policy 1.4, and that the external IRB conducting review and approval will maintain oversight of these studies.

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. Marketed Device is a device approved by FDA for marketing and is generally in use for treatment or diagnostic purposes.

6.3 Humanitarian Use Device (HUD)

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 by CU affiliated personnel will be reviewed and approved by a qualified external IRB as defined in CU HRPP Policy 1.4, and that the external IRB conducting review and approval will maintain oversight of the use of the HUD.

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.

6.4 Emergency Use of a Test Article

1.0 Purpose
The purpose of this policy 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
It is the policy of the Organization that:

2.1. CU IRB does not provide review or oversight of the emergency use of a test article (investigational drug, biologic, or device) as defined by applicable FDA regulations at 21 CFR 56.102(d).

2.2 Emergency use of a test article (investigational drug, biologic, or device) by CU-affiliated personnel must be reported to a qualified external IRB as defined by CU HRPP Policy 1.4 as soon as possible but no later than five days following the use of the test article as required by 21 CFR 56.104(c).

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).

6.5 Expanded Access to Investigational Drugs and Devices for Treatment Use

1.0 Purpose

1.1. The purpose of this policy and procedure is to describe the requirements for utilization of an investigational drug or device (test article) for treatment use. This applies to expanded access for individuals or groups of patients with serious or immediately life- threatening diseases or conditions who lack therapeutic alternatives (compassionate use).

1.2. Emergency use of a test article on a human patient is permissible in a life-threatening or severely debilitating circumstance where no standard medically acceptable treatment is available and where there is not sufficient time to obtain IRB approval prior to the emergency use of the test article.

2.0 Policy

2.1. It is the policy of the Organization that CU IRB does provide review and approval of expanded access to investigational drugs and devices for individuals or groups of patients with serious or immediately life- threatening diseases or conditions who lack therapeutic alternatives (compassionate use). Compassionate use of investigational drugs and devices by CU affiliated personnel must be reviewed and approved by a qualified external IRB as defined in CU HRPP Policy 1.4.

3.0 Definitions

3.1. Expanded Access: Expanded access refers to the treatment use of an investigational drug or device for patients with serious or immediately life-threatening diseases who lack therapeutic alternatives

3.1.1. The primary purpose of the expanded access use is to diagnose, monitor, or treat a patient's disease or condition rather than to obtain the kind of information about the drug that is generally derived from clinical trials. The terms expanded access, treatment use, and compassionate use may be used interchangeably.

3.2. Immediately life-threatening disease or condition: a stage of disease in which there is reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment.

Section 7: Human Biologic Materials and Data Registries

7.1 Banking Human Biological Material

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 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 CU 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 a 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 a 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) or under the exemption at 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 ofwho 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.

7.2 Use of Human Biological Material in Research

1.0 Purpose
The purpose of this policy and procedure is to describe the Organizations 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, 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); 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 immediate 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 elsewhere by the investigator 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.

4.4. The use of coded HBM previously stored in an HBM bank or elsewhere by the investigator 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 (undercategory 5 or 8), 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), or under the exemption at rev 45 CFR 46.104(d)(8).

7.3 Data Registries

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 IRB.

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 CU 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 IRB 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 CU 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 IRB. 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 CU IRB 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, the CU Privacy Officer, 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 CU 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.

7.4 Effective Date of this Policy

7.1 The terms of this policy shall apply from the date on which the policy is adopted by majority vote by the CU IRB.

7.1.1 Biobanks, biorepositories, and Data Registries established at CU prior to the adoption of this policy are grandfathered under this policy so long as the terms of the bank, repository, and/or registry complied with the terms of 45 CFR 46 at the time of its creation.

Section 8: AEs, Unanticipated Problems, and Compliance

8.1 Review of Adverse Events and Adverse Device Effects

1.0 Purpose
The purpose of this policy is to describe the process for reporting research related Adverse Events (AEs) and Adverse Device Effects (ADEs) to the IRB, and the process for review of AEs and ADEs.

2.0 Policy
It is the policy of the Organization that:

2.1. Internal AEs must be promptly reported to the IRB if the PI determines that the AE is unexpected, AND related to, or possibly related to, the research intervention or procedures.

2.2. External AEs must be reported to the IRB if the PI determines that the external AE is unexpected AND related or possibly related to the research intervention or procedure AND serious AND the external AE requires a change to the protocol and/or informed consent form and/or re-consent of subjects.

2.3 External UADEs must be reported to the IRB if the PI determines that the external UADE is unexpected AND related or possibility related to the research intervention or procedure AND serious AND the external AE requires a change to the protocol and/or informed consent form and/or reconsent of subjects.

3.0 Definitions

3.1. Adverse Event (AE) is defined as any untoward or unfavorable occurrence in a human subject temporally associated with the subject's participation in the research (whether or not related to participation in the research). An 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.

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; or (c) or similar materials.

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. An 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: 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. Events may also be considered serious when they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition (21 CFR 312.32(a)).

3.2. Adverse Device Effect (ADE) is defined as an adverse effect caused by, or associated with, use of a medical device in a clinical investigation.

3.2.1. 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)).

3.2.2. Serious UADE: An UADE which results in any of the outcomes as described above for serious AEs, or one in which required intervention to prevent permanent impairment or damage.

3.3. Internal AE: An AE experienced by a subject in a study conducted at the Organization or at an external site under the jurisdiction of the CU 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 CU IRB).

NOTE: While CU IRB does not provide review or oversight to FDA regulated research, CU IRB nevertheless adopts the FDA definitions of Adverse Event (AE), Serious AE (SAE), Adverse Device Effect (ADE), Unanticipated Adverse Device Effect (UADE), and Serious UADE as CU investigators conducting FDA-regulated research under the oversight of an external IRB are required to report a subset of Serious AEs and Serious UADEs to the CU IRB (see sections 2.2 and 2.3, above).

4.0 Investigator Responsibilities

4.1. Internal AEs

4.1.1. Internal AEs must be promptly reported to the IRB if the PI determines that the AE is unexpected, AND related to, or possibly related to, the research intervention or procedures. Internal

AEs meeting the above conditions must be reported no later than two business days following PI notification that the event occurred, or within 24 hours if the internal AE is fatal.

4.1.1.1. Except for congenital anomalies or birth defects, and cancer, internal AEs occurring more than 90 days after the subject has completed study interventions are generally considered unrelated and are therefore not reportable.

4.1.2. Internal AEs that occur on studies for which the Organization is relying on another IRB must be reported to the IRB if the PI determines that the AE is unexpected, AND related to, or possibly related to, the research intervention or procedures.

4.1.2.1. Internal AEs that occur on studies for which the Organization is relying on another IRB must also be reported to that IRB in accordance with the reliance agreement.

4.2. External AEs

4.2.1. External AEs must be reported to the IRB if the PI determines that the external AE is unexpected AND related or possibly related to the research intervention or procedure AND serious AND the external AE requires a change to the protocol and informed consent form and re-consent of subjects. External AEs meeting the above conditions must be reported no later than five business days following PI notification that the event occurred.

4.2.2. 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.

4.2.3. 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.

4.3. External UADEs

4.3.1. External UADEs which occur at other institutions must be reported to the CU IRB 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).

4.3.2. 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 IRB Responsibilities

5.1. AEs reported to the IRB will be reviewed by an IRB Administrator, in consultation with the IRB Chair, IRB Director, or designee to determine if the AE satisfies the criteria for reporting per 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 Chair/designee will take all actions necessary to protect human subjects in accordance with HRPP policy 8.6 (Study Hold, Suspension, and Termination).

5.3. All internal AEs which satisfy the criteria for reporting per section 4.1.1, and all internal or external UADEs will be referred to the convened IRB.

6.0 IRB Responsibilities

6.1. The convened IRB will review reports of SAEs and UADEs in accordance with HRPP policy 2.2 (Full IRB Review).

6.2. To approve the SAE or UADE 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(c)(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 subjects.

6.3.5. The current continuing review schedule is appropriate.

6.4. The IRB must determine if the AE/UADE is an Unanticipated Problem in accordance with HRPP policy 8.3 (IRB Review of Unanticipated Problems Involving Risk to the Subject or Others).

7.0 Reporting AEs/UADEs 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).

8.2 Review of Study Related Complaints

1.0 Purpose
The purpose of this policy is to describe the process for reporting research related complaints to the RCO and the IRB, and the process for review of complaints.

1.1. For the purposes of this policy "complaints" includes problems, concerns, or questions raised by current, prospective, or past research participants or their representatives regarding their participation in human subject research. Complaints by research personnel or other interested parties regarding the functioning of one or more components of the HRPP will be addressed as per HRPP Policies 1.22 (Assessment of the HRPP) and/or HRPP Policy 8.5 (Noncompliance by the IRB or Other Components of the HRPP).

2.0 Policy
It is the policy of the Organization that:

2.1. Complaints involving the human research protection program be promptly reported to the RCO and to the IRB.

2.1.1. Complaints made directly to PIs and/or study team members must be reported to the IRB within 5 business days of the PI and/or study team member becoming aware of the complaint.

2.2. Complaints under the jurisdiction of the IRB will be investigated and resolved as appropriate and reported to Organizational officials.

2.3. Findings of serious or continuing noncompliance and suspensions or terminations of IRB approval as a result of a complaint will be promptly reported to OHRP, FDA and sponsors or funding agency heads in accordance with HRPP policy 8.7 (Reporting Incidents to Institutional Officials and Federal Agencies).

3.0 Complainant (or Other Reporters') Responsibilities

3.1. Complaints from current, prospective, or past research participants or their representatives may be received by the Principal Investigator, other investigators, study staff, IRB members, IRB staff, the Research Compliance Office, or any other Organizational officials.

3.2. Any complaint that is received by the investigator or study staff that involves risk to participants or others or changes the risk-benefit profile of the study, or which cannot be resolved by the investigator must be promptly reported to the IRB.

3.3. 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 at continuing review.

4.0 IRB Responsibilities

4.1. Complaints received by the IRB, or reported to the IRB by the investigators will be reviewed by the IRB Chair and/or IRB Director. Complaints found not to relate to human subject research will be referred to the Research Compliance Office.

4.2. Complaints related to human subject research will be further reviewed by the RCO Auditor. Additional information will be obtained from the complainant, the study documents, the investigator or research staff, or from other sources as appropriate. Based on this initial review, in consultation with the IRB Chair and IRB Director or designees, the RCO Auditor 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), HRPP Policy 8.3 (IRB Review of Unanticipated Problems Involving Risk to the Subject or Others), or HRPP Policy 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-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).

4.3. The IO will be notified of all complaints which involve risk to participants or others, or which change the risk-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 Responsibilities

5.1. Complaints that do not involve risk to participants or others, or do not change the risk-benefit profile of the study are reported to the IRB (either at the time of continuing review, or as a special notification item).

5.2. Complaints that involve risk to participants or others, or change the risk-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.

6.0 Reporting Complaints to Organizational Officials, OHRP, 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).

8.3 Review of Unanticipated Problems Involving Risk to the Subject or Others

1.0 Purpose
The purpose of this policy is to describe the process for reporting potential unanticipated problems (UPs) involving risk to the IRB, and the process for review of potential UPs.

2.0 Policy

It is the policy of the organization that:

2.1. The IRB will comply with HHS regulations at 45 CFR 46.108(a)(4)(i); and any additional requirements of Common Rule agencies (as applicable).

2.2. Any AE, UADE, noncompliance event, complaint, or other incident, regardless of the level of associated or potential risk, which appears to meet the criteria for classification as a UAP will be submitted to the full IRB for review.

2.3. The convened IRB is responsible for determining whether the event, incident, outcome, or complaint meets the criteria for classification as a UAP.

3.0 Definitions

3.1. Unanticipated Problems Involving Risk to Subjects or Others (UAP) is defined as an event that meets the criteria below:

3.1.1. 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.

3.1.2. 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.

3.1.3. 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 modifications.

3.1.4. Though not a required criterion for definition of an event as a UAP, the event generally warrants 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 UAP may arise from an AE, UADE, noncompliance, participant complaint, or other incident (including new information such as IND safety reports, DSMB reports, or other outcome information).

Note: UAPs may occur in research other than clinical trials, and may involve risks other than physical harm (for example, a stolen laptop or thumb drive containing identifiable information leading to risk of loss of confidentiality).

4.0 Investigator (or Other Reporters') Responsibilities

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 must be promptly reported to the IRB as a Reportable New Information submission thru InfoEd.

5.0 IRB Responsibilities

5.1. The IRB Chair, Director, or designee will review reports under Section 4.1 thru 4.5 above in accordance with the criteria specified in HRPP policies 2.2 (Full IRB Review), HRPP policies 8.1 (IRB Review of Adverse Events and Adverse Device Effects), HRPP policies 8.2 (IRB Review of Study Related Complaints), and HRPP policies 8.4 (Review of Noncompliance Involving the PI and Study Personnel), and will make determinations (including referral to the convened IRB) as described in those policies.

5.2. Events reviewed by the IRB Chair, Director, or designee in accordance with the above policies will be referred to the convened IRB if a preliminary determination is made by the Chair or Director that the event may constitute a UAP.

5.3. The convened IRB will determine whether or not the event is a UAP in accordance with Section 3.1 of this policy.

5.4. 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.

5.5. In addition to the required actions specified in HRPP policy 2.2 (Full IRB Review), IRB actions in response to a UAP may include, but are not limited to:

5.5.1. Requiring modification of the protocol.

5.5.2. Requiring modification of the information disclosed during the consent process.

5.5.3. Requiring notification of current participants when such information might relate to participants' willingness to continue to take part in the research.

5.5.4. Requiring provision of additional information to past participants.

5.5.5. Requiring current participants to re-consent to participation.

5.5.6. Modification of the continuing review schedule.

5.5.7. Monitoring of the research.

5.5.8. Monitoring of the consent process.

5.5.9. Referral to other organizational entities.

6.0 Reporting UPs to Institutional Officials, OHRP, 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).

8.4 Review of Noncompliance Involving the PI or Study Personnel

1.0 Purpose
The purpose of this policy is to describe the process for reviewing and reporting incidents of noncompliance by the PI and/or study personnel.

2.0 Policy
It is the policy of the Organization that:

2.1. Reports of noncompliance with Federal Regulations, HRPP policies, or the requirements or determinations of the IRB, or the provisions of the IRB approved research study must be promptly reported to the IRB.

2.2. The PI is ultimately responsible for the proper conduct of research and for assuring that noncompliance is promptly reported in accordance with this policy, and for implementing any required corrective action plan.

2.3. Incidents of noncompliance will be promptly addressed by the IRB and appropriate action taken in order to ensure protection of the rights and welfare of research subjects.

2.4. Findings of serious or continuing noncompliance and suspensions or terminations of IRB approval as a result of noncompliance will be promptly reported to OHRP, sponsors or funding agency heads in accordance with the requirements of 45 CFR 46.108(a)(4), and the Organization's FederalWide assurance, as specified in HRPP policy 8.7 (Reporting Incidents to Institutional Officials and Federal Agencies).

3.0 Definitions

3.1. Noncompliance is defined as any failure to follow federal regulations (including but not limited to 45 CFR 46, including any applicable subparts), HRPP policies, the requirements or determinations of the IRB or the provisions of the IRB approved research study. Noncompliance may be serious and/or continuing, or neither serious nor continuing. 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 a violation of applicable federal regulations, HRPP policies, or the determinations of the IRB which (a) significantly increases the risk to subjects, or otherwise compromises the rights and welfare of research subjects; or (b) appreciably decreases the potential direct benefit to subjects; or (c) compromises the scientific integrity of the research.

3.1.1.1. In accordance with OHRP guidance, non-exempt human subject research conducted without IRB review and approval or without appropriate informed consent, or significant modifications to IRB-approved research without IRB approval is considered serious non-compliance.

3.1.1.2. The IRB may decide that certain classes or types of non-compliance (for example, protocol violations involving drug dosing errors) represent serious noncompliance.

3.1.2. Continuing noncompliance is defined as (1) repeated incidents of the same or substantially similar noncompliance after the investigator or staff has been notified that the action represents non-compliance or despite appropriate retraining and/or a specific corrective action plan; or (2) repeated incidents of the same or substantially similar noncompliance of such a nature that the investigator should have reasonably been expected to know that such an action was noncompliance.

4.0 Reporting Noncompliance to the IRB

4.1. Reports of possible noncompliance by the PI or study team must be made to the IRB within ten (10) business days of the study team becoming aware of the event, or five (5) business days when the possible noncompliance was associated with harm to subjects or others. Reports of noncompliance made by any other person should be made as soon as feasible.

4.1.1. Persons reporting possible noncompliance may do so anonymously and may use any mechanism they wish to report to the IRB or RCO.

5.0 IRB Responsibilities

5.1. Upon receipt of a report of possible noncompliance the following will occur:

5.1.1. The IRB will conduct the initial investigation. Additional information will be obtained from the reporter, RCO or HRPP records, and/or from other sources as appropriate.

5.1.2. If the initial investigation discloses that no noncompliance occurred, the IRB reviewer responsible will notify the reporter, and no further action need be taken.

5.1.3. If the initial investigation confirms that noncompliance occurred, the IRB reviewer responsible, in consultation with the IRB Chair, Director, or designee, will determine:

5.1.3.1. Whether the noncompliance may represent serious or continuing noncompliance.

5.1.3.2. 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).

5.1.3.3. Whether additional investigation is necessary, by the IRB, or by other parties including but not limited to the Research Compliance Auditor, Institutional Compliance Officer, CU General Counsel, other IRB Administrators, other IRB members and internal consultants.

5.1.4. If the report of noncompliance comes from someone other than the investigator the IRB will notify the PI (and other involved individuals) of the investigation, and the investigator will be provided an opportunity to provide any relevant information and/or records that should be considered.

5.1.5. During the investigation, the investigator (or other relevant party) will have a reasonable opportunity to provide additional information.

5.1.6. The IRB, Institutional Official (IO) and Institutional Compliance Officer will be informed of any ongoing investigations as soon as is appropriate to do so.

5.2. After completion of the investigation by the IRB and review by the Chair, Director, or designee, the following will occur:

5.2.1. A report determined to be possibly serious or continuing noncompliance, will be referred to the convened IRB, along with the results of the investigation.

5.2.2. A report determined to be neither serious, nor continuing will be sent to the convened IRB as a notification item.

5.3. Lists of protocol violations noted by a sponsor, CRO or Audit committee may be submitted to the IRB at the time of discovery and will be reviewed by the IRB in consultation with the IRB Chair, Director, or designee. Incidents determined to be possibly serious or continuing noncompliance, will be referred to the convened IRB for action, and incidents determined to be neither serious nor continuing will be sent to the convened IRB as a notification item, as described above.

5.3.1 It is the responsibility of the PI to be familiar with the reporting requirements of the IRB and to promptly report incidences of serious or continuing noncompliance to the IRB. Failure to report serious or continuing noncompliance to the IRB may itself be the basis for an IRB determination of serious or noncompliance. An egregious failure or pattern of failures to report serious or noncompliance to the IRB may result in sanctions from the IRB up to and including disqualification of a PI.

6.0 IRB Responsibilities

6.1. Noncompliance which may represent serious or continuing noncompliance will be referred for review by the convened IRB. The convened IRB will determine:

6.1.1. Whether the incident represents serious and/or continuing noncompliance.

6.1.2. Whether the incident is an unanticipated problem involving risk.

6.1.3. Whether the corrective action plan is adequate.

6.1.4. Whether the research continues to satisfy the approval criteria at 45 CFR 46.111.

6.1.5. Whether subject accrual should be allowed to continue.

6.1.6. Whether currently enrolled subjects should be notified of information related to the incident.

6.1.7. Whether previously enrolled subjects who have completed participation in the study should be notified of information related to the incident.

6.2. After making the determinations above, the IRB may take action including, but not limited to:

6.2.1. Requiring 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.

6.2.2. Auditing the research, or any of the investigator's other active or completed studies.

6.2.3. Requiring additional investigator or study staff education and training.

6.2.4. Suspending or terminating the research.

6.2.5. Making recommendations to the IO regarding restrictions on, or termination of, other protocols submitted by the investigator, or regarding other sanctions against the investigator or staff including withdrawal or modification of pending or published manuscripts and/or destruction of research data or biological materials.

6.3. After completion of the review by the convened IRB the investigator (or other relevant party) will be informed of the results of the review, and of any determinations and requirements by the IRB.

7.0 Reporting Noncompliance to Organizational Officials, OHRP, 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).

8.5 Noncompliance by the IRB or Other Components of the HRPP

1.0 Purpose
The purpose of this policy is to describe the process for reviewing and reporting incidents of noncompliance by the IRB and/or other components of the HRPP.

2.0 Policy
It is the policy of the Organization that:

2.1. Reports of noncompliance with Federal Regulations related to human subjects research or HRPP policies by the IRB or other components of the HRPP shall be reviewed, investigated and reported as outlined below.

2.2. Findings of serious or continuing noncompliance will be reported to OHRP and sponsors or funding agency heads in accordance with the requirements of 45 CFR 46.108(a)(4), and the Organization's Federalwide assurance, as specified in HRPP policy 8.7 (Reporting Incidents to Institutional Officials and Federal Agencies).

3.0 Definitions

3.1. Noncompliance by the IRB or other components of the HRPP is defined as failure to follow federal regulations (including but not limited to 45 CFR 46 and applicable subparts), HRPP policies, and/or

Organizational policies. Noncompliance may be serious and/or continuing, or neither serious nor continuing.

3.1.1. Serious noncompliance by the IRB or other components of the HRPP is defined as a violation of federal regulations, HRPP policies, and/or Organizational policies which (a) significantly increases the risk to subjects, or otherwise compromises the rights and welfare of research subjects, or (b) places the Organization at risk of significant regulatory, financial, or reputational harm.

3.1.2. Continuing noncompliance by the IRB or other components of the HRPP is defined as (1) repeated incidents of the same or substantially similar noncompliance, after the IRB or other component has been notified that the action represents non-compliance, or despite appropriate retraining and/or specific corrective action, or (2) repeated incidents of the same or substantially similar noncompliance of such a nature that the IRB or other component of the HRPP should have reasonably been expected to know that such an action was noncompliance.

4.0 Responsibilities of the IRB, Chief Compliance Officer (CCO) and Institutional Official (IO)

4.1. Upon receipt of a report of noncompliance attributable to any component of the HRPP:

4.1.1. The IRB will conduct the initial investigation. Additional information will be obtained from the reporter, IRB or HRPP records, and/or from other sources as appropriate.

4.1.2. If the initial investigation does not confirm that noncompliance occurred, the IRB will prepare a report to the IO describing the allegation, and explaining why it does not represent noncompliance. The IO may accept the report and notify the IRB, or may request clarification or additional information, or may conduct further investigation by enlisting the University's Auditor or CCO.

4.1.3. If the initial investigation confirms that noncompliance occurred, the Director of the IRB or designee will prepare a report to the IO describing the noncompliance. The report will classify the noncompliance as minor, serious and/or continuing and include a proposed corrective action plan (CAP) as appropriate.

4.1.4. The IO may:

- Accept the report and CAP as proposed
- Request modifications to the CAP
- Request clarification or additional information
- Conduct further investigation

4.1.5 Upon conclusion of the investigation of noncompliance, a report of the noncompliance and the CAP will be presented to the IRB, IO and other organizational officials as appropriate.

4.2. The IRB Director/designee, Research Compliance Director, and/or IO, as appropriate, will initiate all necessary action(s) to ensure that human subjects are fully protected, and the interests of the Organization are appropriately considered.

4.3. A record of the report and actions taken under this policy will be maintained by the IRB.

5.0 Reporting Noncompliance to Organizational Officials, OHRP 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).

8.6 Study Hold, Suspension, and Termination

1.0 Purpose
The purpose of this policy is to describe the process for study holds, study suspensions, and study termination.

2.0 Policy
It is the policy of the Organization that:

2.1. The IRB has the authority to accept a study hold imposed by the PI, sponsor, DSMB, FDA or other funding agency, and the IRB Chair or the convened IRB has the authority to release that hold.

2.2. The IRB or the IRB Chair has the authority to suspend IRB approval of research, and the convened IRB has the authority to release that study suspension.

2.3. The IRB or the Organization has the authority to terminate IRB approval of research.

2.4. Suspensions or terminations of IRB approval as a result of noncompliance will be promptly reported to OHRP and sponsors or funding agency heads in accordance with the requirements of 45 CFR 46.108(a)(4), and the Organization's FederalWide assurance, as specified in HRPP policy 8.7 (Reporting Incidents to Institutional Officials and Federal Agencies).

3.0 Definitions

3.1. Study Hold: A planned or 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 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 Chair or designee (in consultation with the IO as appropriate), that all or some research activities in one or more protocols must be temporarily suspended to protect the rights, safety, or welfare of human subjects.

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 or 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.

3.4. Organization Directed Termination of IRB Approval: A directive by the Institutional Official (IO) that an IRB approved study be terminated.

4.0 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 IRB by email or letter. When the IRB 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 IRB by email or letter.

4.5.1. If the study hold was initiated for subject safety concerns only the convened IRB 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 convened IRB or the IRB Chair or designee 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 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 IRB 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 IRB 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 convened IRB has the final authority to act on any appeals and the decision of the Board cannot be overturned.

5.9. The convened IRB has the sole authority to release a study suspension.

6.0 Termination of IRB Approval

6.1. The convened 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 has 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 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 Chair, Research Compliance Director, IRB Director, 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 seek consultation with the IRB or any other persons. The PI will be afforded due process and may be offered the opportunity to meetwith

the IO. The investigator may bring legal counsel who will be restricted to observation only. The decision of the IO regarding any appeal is final.

8.0 Reporting Suspensions and Terminations to OHRP and Department and Agency Heads
Suspensions and terminations are reported in accordance with HRPP policy 8.7 (Reporting Incidents to Institutional Officials and Federal Agencies).

8.7 Reporting Incidents to Institutional Officials and Federal Agencies

1.0 Purpose
The purpose of this policy is to describe the Organization's requirements to ensure prompt reporting of incidents to Institutional Officials, Federal Agencies (including OHRP) and other Common Rule Departments and Agencies, and to AAHRPP.

2.0 Policy
It is the policy of the Organization that:

2.1. Unanticipated problems involving risk to the subject or others (UAPs), serious or continuing noncompliance, suspensions of IRB approval, and terminations of IRB approval will be promptly reported to the Institutional Official (IO).

2.2. Unanticipated problems involving risk to the subject or others (UAPs), serious or continuing noncompliance, suspensions of IRB approval, and terminations of IRB approval related to research subject to 45 CFR 46 be reported to OHRP and other Common Rule Department or Agencies in accordance with 45 CFR 46.108(a)(4) and 45 CFR 46.113 as applicable.

2.3. Unanticipated problems involving risk to the subject or others (UAPs), serious or continuing noncompliance, suspensions of IRB approval, and terminations of IRB approval related to research not subject to 45 CFR 46 will be reported to OHRP and funding agencies at the discretion of the Institutional Official.

2.4. The Organization will report to AAHRPP as soon as possible (but generally within 48 hours) after the Organization becomes aware of: (1) any negative actions by a government oversight office related to human research protections; (2) any litigation, arbitration, or settlements initiated related to human research protections; and (3) any press coverage of a negative nature regarding the Organization's HRPP.

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 IRB Responsibilities

4.1. The IRB Director 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.

5.0 Institutional Responsibilities

5.1. For research subject to the 45 CFR 46, the IO or designee 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.

5.2. For research no subject to 45 CFR 46 written reports may be submitted to OHRP and Department or Agency heads at the discretion of the IO. The decision to report will be made by the Institutional Official after due consideration of recommendations of the IRB and the IRB Director.

5.4. Copies of the report (including any additional materials submitted to OHRP or Department or Agency heads) will be made available to the PI after submission.

5.5. Reporting events which occur at institutions not under the jurisdiction of the CU IRB are the responsibility of the external institution.

5.6. Reporting of events which occur at other institutions when CU acts as the reviewing IRB for that institution will be reported either by CU or by the relying institution, as described in HRPP Policy 1.3 (CU IRB Serving as the Single IRB for Multisite Research) and per the terms of the reliance agreement.

6.0 Investigator Responsibilities

6.1. 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.

6.1.1. It is the responsibility of the PI to be aware of reporting deadlines, including those established by 45 CFR 46 and by applicable common rule departments or agencies.

6.2. 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.

6.2.1. It is the responsibility of the PI to be aware of reporting deadlines, including those established by sponsors and CROs (as applicable).

7.0 Contents of Reports

7.1. Reports to the IO, OHRP, and Common Rule Department or Agencies must include the information described in OHRP document "Guidance on Reporting Incidents to OHRP (2011)", or any succeeding guidance.

8.0. Reports to AAHRPP

8.1. The IRB will report to AAHRPP as soon as possible but generally within 48 hours after the organization or any researcher (if the researcher is notified rather than the organization) becomes aware of:

8.1.1. Any negative actions by a government oversight office, including, but not limited to, OHRP Determination Letters, FDA Warning Letters, FDA 483 Inspection Reports with official action indicated, FDA Restrictions placed on IRBs or Investigators, and corresponding compliance actions taken under non-US authorities related to human research protections.

8.1.2. Any litigation, arbitration, or settlements initiated related to human research protections.

8.1.3. Any press coverage (including but not limited to radio, TV, newspaper, online publications) of a negative nature regarding the Organization's HRPP.

8.2. Investigators and research teams are responsible for notifying the IRB if they become aware of any of the actions noted above.

9.0 Emergency Preparedness/Continuity of Operations Plan (EP/COOP)

1.0 Emergency Preparedness /Continuity of Operations Plan (EP/COOP)

1.1. Purpose
CU Human Research Protection Program (HRPP) and Institutional Review Board is committed to the safety and protection of research participants, as well as IRB and HRPP staff, and investigators and research staff, and the operations and facilities of the research enterprise.

The purpose of this Emergency Preparedness /Continuity of Operations Plan (EP/COOP) is to provide the framework for restoring essential functions to the HRPP and the CU IRB in the event of an emergency that affects its operations. It is a supporting document to the Creighton University Emergency Operations Plan (EOP). This document establishes the EP/COOP procedures for any operational disruption, including but not limited to:

Loss of access to a facility (such as damage to the building),

Loss of service due to a reduced workforce (such as due to pandemic virus) and

Loss of service due to protracted equipment or systems failure (such as IT systems failure).

The intent of this HRPP EP/COOP is to lay out procedures to allow the HRPP, in the event of an emergency, to implement actions to promptly begin continuity operations and to maintain essential functions until full operative capacity can be resumed.

1.2. Scope
This document applies to all personnel in the CU HRPP and all locations where essential functions of the CU HRPP are conducted. It also applies to the array of emergencies and hazards that could threaten the performance of essential HRPP functions. The plan covers the Human Research Protection Program and the CU Institutional Review Board.

This plan does not apply to temporary disruptions of service including temporary disruptions in IT systems or power outages and any other scenarios where essential functions can be readily restored in the primary facility within 3 business days.

1.3. Responsibility
It is the responsibility of the entire team to ensure the success of the CU HRPP EP/COOP implementation during and after an emergency; however, there are specific roles that hold explicit responsibility and decision-making authority during implementation.

Implementation and operationalizing of the CU HRPP EP/COOP: The Director of Research Compliance will act as the primary point of contact (POC) for all members of the HRPP team regarding day-to-day

operations of the HRPP EP/COOP. The Director of Research Compliance will initiate appropriate internal and external notifications, support the decision-making procedures of the Director of the IRB, Research Compliance Director, and Institutional Official (IO), and maintain the CU HRPP EP/COOP for the duration of the emergency to ensure the essential functions of the HRPP. The IO or designee, the Institutional Review Board (IRB) Director, and the Board Chairs and Vice-Chairs will all play critical roles in the EP/COOPs implementation.

Strategic Coordination and Communication: The Director of Research Compliance is responsible for providing strategic decision-making for all elements of CU HRPP EP/COOP operations. They will communicate with CU Public Safety; coordinate communications with the IRB and representatives of components of the HRPP, and principal investigators (PIs); and coordinate the release of information with University Communications and Marketing.

If the Director of Research Compliance is unable to fulfil this responsibility, the IRB Director or designee will take over those responsibilities. They will be aided by (or as necessary, replaced by) and IRB Chair, as determined by the IO.

Research Stoppage: The IO, in consultation with the Director of Research Compliance, IRB Director, and Board Chairs, is responsible for the final decision-making regarding the stoppage of any and all research activities, including new IRB reviews.

Periodic Evaluation of the Emergency Plan: The Director of Research Compliance, in consultation with the IRB Director, is responsible for evaluating the CU HRPP EP/COOP and making changes, when appropriate. This evaluation shall occur at least annually.

Periodic Review of the CU HRPP EP/COOP Training and Education Plan: The Director of Research Compliance, in consultation with the IRB Director, is responsible for ensuring the educational materials are reviewed and updated as necessary, based on the outcome of the periodic evaluation of the emergency preparedness plan.

1.4. Planning Assumptions

The following assumptions have guided the development of this plan:

The institutions are vulnerable to a full range of hazards (man-made, natural, technological disasters and potentially hazardous materials (area/department dependent) that may constitute an emergency.

An emergency and any resulting impacts may occur during normal business hours and during off hours and may adversely affect the ability of the CU HRPP to initiate or sustain its essential functions.

The Director of Research Compliance, in consultation with the IO, has authority to implement the CU HRPP EP/COOP under emergency conditions affecting CU HRPP, even if the institution has not activated incident command or declared an emergency.

Critical personnel and other resources may be requested of the institution by the Director of Research Compliance or IO and will be made available to the extent possible if required to sustain or recover essential functions.

Leadership and all personnel will continue to recognize their responsibilities to public safety and human subjects research protection and will exercise their authority to implement the CU HRPP EP/COOP in a timely manner when confronted with emergencies as described above.

All personnel have been trained in the CU HRPP EP/COOP and know and understand their role.

2. Implementation Procedures

Depending on the nature of the risk and the potential impact to the HRPP and the institution, the Director of Research Compliance, in consultation with the IO, the IRB Director, IRB Chairs, and representatives from components of the HRPP as appropriate, will determine which actions need to be undertaken to minimize the impact on research activities and mitigate risk to research participants, study team members, and the institution.

2.1. Assess the nature of the risk and the potential impact to the HRPP.

2.2.1.1 Once an emergency or threat is identified the Director of Research Compliance and IO will determine the response based on the nature of the event.

2.2.1.2 The Director of Research Compliance or IO shall contact the appropriate Institutional personnel and/or committees [University Preparedness Committee (UPC), Critical Incident Response Team (CIRT), and Emergency Officer within the CU Department of Public Safety] to determine whether there are Institutional plans already in place to address the event (as per the institutional EOP plan on file with the Research Compliance Office). If these institutional plans are activated, the HRPP will proceed in accordance with those plans and determine whether communication with the research community is necessary to alert them to the activation of the emergency preparedness plan.

2.2. Assess and mitigate the impact(s) to HRPP operations.

2.2.1 IRB Meetings: If the emergency may prevent one or more IRB meetings from occurring, the Director of Research Compliance in consultation with the IRB Director will determine whether to cancel or reschedule the meetings after identifying currently approved protocols which may expire prior to IRB review. If research will expire, the IRB Office will follow CU HRPP Policies regarding

lapses in approval. If the meeting(s) can be held safely remotely, execute remote IRB meeting procedures.

2.2.2 If it is expected that IRB meetings will be impacted for a prolonged period of time, arrangements may be made to rely on one or more external IRBs. The IO, in consultation with the Director of Research Compliance and the IRB Director, will determine whether it is in the best interests of the institution and research subjects to make arrangements (contractual or MOU where appropriate) in advance of an emergency to rely upon other organizations or commercial entities for IRB review.

2.2.3 HRPP Staff protocol processing and review: If staff will be unable to complete protocol processing and review responsibilities, or if capacity will be limited, the IRB Director, and RCO leadership shall work with the staff to prioritize initial reviews, or reviews of Continuing Reviews (CRs), protocol modifications, or other submissions. In general review priority will be based on (1) potential for direct benefit to subjects of the research, (2) number of subjects impacted, (3) importance of trial to the organization (as determined by the Institutional Official) and (4) contractual and/or funding requirements (as more fully described in section 2.4 below).

2.2.4 If research will expire, the IRB will follow CU HRPP Policies regarding lapses in approval.

2.2.5 Data and records: If electronic records are unavailable, the AVCRA thru the COOP coordinator will consult with CU Information Technology (IT) support to implement alternative procedures to access backup data and/or email. If access to and functionality of RSS cannot be promptly restored, substitution of PDF forms and/or use of paper forms will be instituted.

2.2.6 The IRB will maintain PDFs of application and other forms on cloud platforms and local hard drives, and paper forms on site.

2.3. Assess and mitigate the impact on on-going research.

2.3.1 General approach for on-going research

Based on the nature and severity of the emergency, and the effects on the IRB operations and research infrastructure, modifications in on-going research protocols may be necessary to accommodate various situations. These situations include (but not limited to) decreased availability of research staff, closure of research space, closure or decreased availability of clinical space (impacting administration of research interventions, data collection and/or safety evaluation), decreased availability of the research intervention (for example, investigational or other products), reduced ability of research participants to travel to research site.

Options include:

2.3.1.1 Continued enrollment but with protocol modifications (including modification of research plan and/or informed consent process)

2.2.1.2 Restriction of all or some further subject enrollment

2.2.1.2.1 with continuation of research interventions and data collection for currently enrolled subjects.

2.2.1.2.2 with discontinuation of further research interventions but continuation of data collection for currently enrolled subjects.

2.2.1.2.3 discontinuation of all research interventions and data collection on currently enrolled subjects.

2.3.2 At the beginning of an emergency, the Director of Research Compliance, in consultation with appropriate institutional stakeholders, may categorize on-going research protocols in order pre-identify appropriate mitigation actions should the emergency progress and enrollment or study halts become necessary.

Studies may be broadly assigned to one of several categories.

Within each category, consideration will be made based on the risk to the individual subject (for example, risks associated with traveling) and, in the case of an infectious disease bioemergency, the risk of spread of infection to others (based on face-to-face contact with investigator or other subjects).

Category 1 – High direct benefit and/or potential for harm to subjects if stopped.

Protocols in which serious or immediate harm could be caused to the research participants if stopped. This category might include (1) research protocols involving treatments for acute, life-threatening health conditions, or (2) protocols where stopping the intervention could be harmful.

Category 2 – Moderate direct benefit and/or potential for harm to subjects or scientific value if stopped.

Protocols which, if stopped, may pose a risk to the research participant, or may cause significant harm to the scientific value of the study. This category might include (1) protocols in which research participants are receiving interventions or clinical care that is very interrelated to their research participation, (for example, where research test results coming back that might have clinical implications for their care), or (2) some protocols evaluating treatments for chronic conditions, or (3) protocols with less than high direct benefit to subject but where, if stopped or

delayed, the potential societal benefit of the science would be significantly and adversely impacted (for example, research where an assessment is only valuable if collected at a very specific time).

Category 3 – Low or no direct benefit to research participants OR low or no direct benefit to research participants and vulnerable subject population OR delays have limited impact on scientific objectives.

This category might include (1) research with healthy volunteers, or (2) protocols with low or no direct benefit which involve research participants at higher risk for adverse outcome based on the nature of the emergency (for example, persons at higher risk for poor outcomes associated with an infectious disease bioemergency), or (3) cohort and natural history studies where delays in data collection have limited impact on scientific objectives, or where endpoints could be shifted to compensation for delay.

In addition, in the case of an infectious disease bioemergency, research may also fall into a fourth category:

Category 0 – No face-to face contact with investigators by research subjects.

This category might include (1) medical records research with waiver of consent, or (2) HBM research w/ waiver of consent, or with sole consent by clinician obtaining tissue for clinical purposes, or (3) Internet based research w/o face-to-face contact.

2.3.3 Specific strategies:

2.3.3.1 Deviations and Modifications to Existing Research:

The Director of Research Compliance, in consultation with the IRB Director and IO as appropriate, may allow investigators to implement procedures to minimize burden on subjects and/or maintain research integrity without modification to the IRB application or formal IRB approval.

Specifically, the IO and Director of Research Compliance may allow minor changes to the study (such as to decrease number of study visits, or to give a “window” for a visit) to proceed without IRB review and approval, provided such changes are temporary and do not increase the risk of harm to participants or adversely impact the data. Such changes would be reported to the IRB until the time of continuing review.

Major changes to the study (for example, changes in method or dose timing of agent administered, major changes in data collection which affect primary endpoints of the research)

would continue to be submitted as separate protocol deviations and reviewed and approved before implementation.

As always, changes necessary to eliminate apparent immediate hazards to the subject may be made without prior approval of the IRB (per 45 CFR 46.108(a)(3)(iii), 21 CFR 56.108(a)(4) and HRPP Policy 2.4).

2.3.3.2 In-person interactions with research subjects: If studies involve in-person interactions with research subjects, investigators (in consultation with the IRB Chair, Director, or designess) will determine whether the studies may be conducted as written, or whether interactions need to be altered to adhere with emergency mitigation strategies.

If in-person interactions cannot be accommodated, the investigator will need to advise the IRB whether the research can safely continue in a manner which allows for protection of subjects and staff and generates scientifically valid data.

In a manner similar to the way they perform scientific review of clinical research, Departments and/or Colleges should consider conducting a risk-analysis regarding the impact of emergencies on their planned research, and an emergency mitigation strategy for ensuring the safety of research participants.

2.3.3.3 Safety monitoring: If trial participants are unable to come to the investigational site for protocol specified visits, alternative methods for safety assessments must be considered. This may include utilizing phone contact, virtual/telehealth visits, alternative locations for assessment (including alternate laboratory sites, study visit sites, or imaging centers) to assure the safety of research study participants.

2.2.3.4 Sponsored research: When studies have an external sponsor, each PI must coordinate with the sponsor to confirm mitigation plans. The PI and study team must document any mitigation strategies that are implemented.

2.2.3.5 Clinical care and/or research facility considerations: If the emergency impacts clinical care standards which may in turn impact research, the PI must consult with the IRB regarding any changes to protocol activities, and document which do and do not require IRB review. Emergency response plans must be considered for each existing research location and any changes to research locations.

2.2.3.6 Regulatory Flexibility: When studies are not subject to the Common Rule or to FDA regulations, the IRB may employ “equivalent protections” in protecting the rights and welfare of research participants. For example, the IRB may consider extending continuing review dates during the emergency and allowing more widespread use of waivers of documentation of consent.

2.2.3.7 Halting existing research: The IO, in consultation with the Director of Research Compliance, IRB Director, and/or IRB Chairs, may consider halting enrollment of new subjects into active research, and/or stopping some or all study activities, for some or all active protocols. As noted above, specific criteria for halting research will be determined based on the nature of the emergency and its expected effect on IRB and clinical research infrastructure.

2.4. Assess and mitigate impact on future research

During the emergency, the IO, in consultation with the Director of Research Compliance, IRB Director, and/or IRB Chairs, may consider limiting acceptance for review of new protocols submitted to the IRB, based on the nature of the emergency and its expected effect on IRB and clinical research infrastructure.

2.4.1 If limiting acceptance is deemed necessary, priority for review will be based (in order of importance) on:

(1) potential for direct benefit to subjects of the research.

(2) impact of protocol on research and clinical infrastructure.

(3) number of potential subjects impacted.

(4) importance of trial to the organization as determined by the IO; and

(5) contractual and/or funding requirements.

Research which is directly related to the operations or understanding of the emergency will also have priority.

2.5. Conduct an After-Action Review upon completion of the emergency.
Following any emergency, the Director of Research Compliance will convene a team to collect information on critical issues requiring leadership attention, lessons learned, and best practices associated with the response. The review will focus on what did and did not facilitate response efforts and the findings will be used to develop recommendations to improve procedures for future event response operations.

The After-Action Review will be shared with the IO, appropriate stakeholders, and the CU Critical Incident Response Team (CIRT) for inclusion in the overall incident file. Once developed, new or updated procedures should be evaluated for effectiveness in an exercise and any formal updates should be included in the amended CU HRPP EP/COOP document.

3. Plan maintenance

The Director of Research Compliance, in consultation with the IRB Director, will periodically review and update the CU HRPP EP/COOP based on legislative changes, CU guidance, departmental or personnel changes, and procedural changes based on lessons learned from exercises and actual events.

4. Training and Education

The IRB Office will provide targeted communications and education/training regarding the CU HRPP to researchers and research staff, IRB Chairs and IRB members, study team members and PIs.