INSTITUTIONAL REVIEW BOARD

STANDARD OPERATING PROCEDURES

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KCU Institutional Official

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1 Institutional Review Board

KCU fosters a research environment that promotes respect for the rights and welfare of individuals recruited for, or participating in, research conducted by or under the auspices of the Organization. In support of this, KCU has established an Institutional Review Board (IRB). The KCU IRB, in partnership with its research community, is responsible for ensuring the ethical and equitable treatment of all human subjects in research conducted under KCU's auspices.

1.1 Mission

The mission of the IRB is to:

- Safeguard and promote the health and welfare of human research subjects by ensuring that their rights, safety and well-being are protected;
- Provide guidance and support to the research community in the conduct of research with human subjects;
- Assist the research community in ensuring compliance with relevant regulations;
- Provide timely and high quality education, review, and oversight of human research projects; and
- Facilitate excellence in the conduct of human subjects research.

The IRB includes mechanisms to:

- Monitor, evaluate and continually improve the protection of human research participants
- Exercise responsible oversight of human subjects research
- Educate IRB members, investigators, and staff about their ethical responsibility to protect research participants
- When appropriate, intervene in research and respond directly to concerns of research participants.

1.2 Organizational Authority

[Reserved] KCU Human Research Protection Program operates under the authority of the Organization policy "ORSP Office of Research and Sponsored Programs (ORSP) adopted on [DATE]. As stated in that policy, the operating procedures in this document "…serve as the governing procedures for the conduct and review of all human research conducted under the auspices of the KCU." The ORSP Policy and these operating procedures are made available to all KCU investigators and research staff and are posted on the ~~ORSP~~ Research Compliance website (www.KCUMB.edu).

1.3 Definitions

Common Rule. The Common Rule refers to the "Federal Policy for the Protection of Human Subjects" adopted by a number of federal agencies. Although the Common Rule is codified by each agency

separately, the text is identical to DHHS regulations in 45 CFR 46 Subpart A. For the purposes of this document, references to the Common Rule will cite the DHHS regulations.

Clinical Trial. Per the Common Rule and NIH Policy, clinical trial 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 the interventions on biomedical or behavioral health-related outcomes.

Human Subject Research. Human Subject Research means any activity that meets the definition of "research" and involves "human subjects" as defined by either the Common Rule or FDA regulations.

Note: The terms "subject" and "participant" are used interchangeably in this document and have the same definition.

Research. The Common Rule defines research as a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalized knowledge. Activities which meet this definition constitute research whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities.

For purposes of this part [the Common Rule], the following activities are deemed not to be research: (1) Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected. (2) Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. Such activities are limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products). Such activities include those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters). (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. (4) Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions.

For the purposes of this policy, a **"systematic investigation"** is an activity that involves a prospective study plan that incorporates data collection, either quantitative or qualitative, and data analysis to answer a study question. Investigations designed to develop or contribute to **generalizable knowledge** are those designed to draw general conclusions (i.e., knowledge gained from a study may be applied to populations outside of the specific study population), inform policy, or generalize findings.

Human Subject. A human subject as defined by the Common Rule is a living individual about whom an investigator conducting research: (i) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or (ii)

Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.

- **Intervention** means both physical procedures by which information or biospecimens are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.
- **Interaction** means communication or interpersonal contact between investigator and subject.
- **Private information** means 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).
- **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. [45 CFR 46.102(e)(5)]. Note: This definition is within the Common Rule. For a discussion of identifiability under HIPAA, please see Section 25.1.
- **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 [45 CFR 46.102(e)(6)]

  Note: FDA regulations have a different definition of "human subjects research". See Section 25.4 for the FDA definitions and details on FDA-regulated research..

Test Article. *Test article* means any drug for human use, biological product for human use, medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under FDA regulations. (See Section 25.4 for details on FDA regulated research)

1.4 Ethical Principles

KCU is committed to conducting research with the highest regard for the welfare of human subjects. With the exception of transnational research, where consideration of alternative ethical principles may apply (see Section 25.3), KCU upholds and adheres to the principles of *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects in Research* by the National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research. These principles are:

1. **Respect for Persons**, which involves the acknowledgment and support of autonomy, and protection of those with diminished autonomy
2. **Beneficence**, which involves ensuring that possible benefits of research are maximized and possible harms are minimized
3. **Justice**, which involves the fair distribution of the benefits and burdens of research through the equitable selection of subjects

The KCU IRB, in partnership with its research community, including researchers and research staff, IRB members and chairs, IRB staff, the organizational official, employees and students, is responsible for

ensuring the ethical and equitable treatment of all human subjects in research conducted under its auspices.

1.5 Regulatory Compliance

Human subjects research at KCU is conducted in accordance with applicable regulations and requirements including, but not limited to, the following:

Research conducted, supported, or otherwise subject to regulation by any federal department or agency which adopts the Common Rule is reviewed and conducted in accordance with the Common Rule. Although the Common Rule is codified by each agency separately, the text is identical to DHHS regulations in 45 CFR 46 Subpart A. For the purposes of this document, references to the Common Rule will cite the DHHS regulations.

Research that involves drugs, medical devices or biologics may be covered by FDA regulations. (See Section 25.4 for a detailed discussion of FDA-regulated research) Research subject to **FDA regulations** is reviewed and conducted in accordance with applicable regulations including, but not limited to, 21 CFR 50, 21 CFR 56, 21 CFR 312 and 21 CFR 812.

Research involving the use of Protected Health Information is reviewed and conducted in accordance with the **Health Insurance Portability and Accountability Act** (HIPAA), 45 CFR Part 160, 162, and 164. (See Section 25.1 for a detailed discussion of HIPAA)

Research conducted or supported by the U.S. **Department of Education (ED)** is subject to the Common Rule with regulations published at 34 CFR 97. In addition to the Common Rule, human subjects research involving education records conducted at institutions receiving ED funding must comply with additional requirements, including the Family Educational Rights and Privacy Act (FERPA) (34 CFR 99) and the Protection of Pupil Rights Amendment (PPRA) (34 CFR 98). Investigators should consult these regulations and resources provided by ED when developing their research protocol. The IRB will evaluate the research in accordance with these regulations when applicable. (See Section 26.2 for a detailed discussion of ED requirements)

Research supported by the **Department of Defense (DoD)** is reviewed and conducted in compliance with 32 CFR 219, 10 USC 980, applicable parts of title 21 CFR (50, 56, 312, 600, 812), DoD Instruction 3216.02, DoD Directive 3210.07, and applicable additional requirements from respective DoD component(s). (See Section 26.1 for a detailed discussion of DoD requirements)

Research conducted or supported by the **Department of Justice (DoJ)** is subject to the Common Rule, including Subpart C, with regulations published at 28 CFR 46. The DoJ has established additional requirements for research conducted with the federal Bureau of Prisons (28 CFR 512) and research involving the National Institute of Justice (28 CFR 22). Investigators should consult these regulations and resources provided by NIJ when developing their research protocol. The IRB evaluates the research in accordance with these regulations when applicable. (See Section 26.4 for a detailed discussion of DoJ requirements)

1.5.1 Management of pre-existing studies once the revised Common Rule goes into effect

The revised Common Rule establishes that all studies approved, waived under .101(i), or determined exempt before January 21, 2019 will be subject to the old rule through the close of study. All studies approved or determined exempt on or after January 21, 2019 will be subject to the new rule. However, KCU may transition individual studies and agree to comply with the new rule if desirable.

1.6 Federalwide Assurance (FWA) and IRB Registration

The federal regulations require that federally-funded human subject research only be conducted at facilities covered by a Federalwide Assurance (FWA) approved by the DHHS Office for Human Research Protections (OHRP). An FWA is an organization's assurance to the federal government that human subject research conducted at that site complies with federal regulations pertaining to the protection of human subjects.

When human subjects research is not subject to the Common Rule or FDA regulations, KCU ensures that human research subjects benefit from equivalent protections by applying the Common Rule standards, with purposeful deviations that do not meaningfully diminish protections as noted within this manual.

Likewise, federal regulations require IRBs to register with DHHS if they will review human subjects research conducted or supported by DHHS or research subject to FDA regulations.

The HHS registration system database can be used to verify the status of KCU's FWA, IORG, and IRB registration.

KCU's Federal Registration Numbers	
FWA	00000017
IORG	0000461
IRB Registration	00000782

1.7 Research Under the Auspices of KCU

Research under the auspices of KCU includes research conducted at or using any property or facility of KCU, conducted by or under the direction of any employee or agent of KCU (including students) in connection with his or her KCU position or responsibilities, or involving the use of KCU's non-public information (e.g., medical records) to identify, contact, or study human subjects. The research may be externally funded, funded from internal sources, or conducted without direct funding.

All human subjects research under the auspices of KCU is under the jurisdiction of the KCU IRB. Human subjects research that KCU is engaged in (per OHRP or FDA guidelines) is under the jurisdiction of the KCU IRB, unless KCU chooses to rely upon another IRB for review and ongoing IRB oversight of the research (the IRB of record for the research).

Employee or Agent. For the purposes of this document, *employees or agents* refers to individuals who: (1) act on behalf of the organization; (2) exercise organizational authority or responsibility; or (3) perform organizationally designated activities. "Employees and agents" can include staff, students, contractors, and volunteers, among others, regardless of whether the individual is receiving compensation.

Engagement. The Department of Health and Human Services (DHHS) regulations [45 CFR 46.103[a]] require that an institution "engaged" in human subject research conducted or supported by a Federal Department or Agency provide the Office for Human Research Protection (OHRP) with a satisfactory assurance of compliance with the DHHS regulations, unless the research is exempt under [45 CFR 46.104]. *"In general, an institution is considered engaged in a particular non-exempt human subjects research project when its employees or agents for the purposes of the research project obtain: (1) data about the subjects of the research through intervention or interaction with them; (2) identifiable private information about the subjects of the research; or (3) the informed consent of human subjects for the research."* Institutions that receive an award through a grant, contract, or cooperative agreement directly from DHHS for the non-exempt human subjects research (i.e. awardee institutions), are also considered engaged in research even where all activities involving human subjects are carried out by employees or agents of another institution.

When external organizations and researchers wish to conduct research that is under the auspices of KCU, the external organization or researchers must consult with the KCU IRB staff prior to initiating any research activities at or involving KCU.

The IO, IRB Chair, and Vice Chair, with the assistance of the IRB staff and legal counsel as needed, are authorized to determine whether KCU is engaged in a particular research study. Investigators and other institutions **may not** independently determine whether KCU is engaged in a particular research study.

When KCU is engaged in research, the Institutional Official may choose to enter into an agreement to cede review to an external IRB.

For additional information on engagement please refer to OHRP's Guidance on Engagement on Institutions in Human Subjects Research.

1.8 Written Procedures

These Standard Operating Procedures (SOPs) for the IRB detail the procedures, standards, and requirements for research with human subjects under the auspices of KCU and the requirements of the KCU IRB. This is not a static document. The SOPs are reviewed at a minimum of every two years and revised by the IRB Chair, Research Compliance Administrator and Institutional Official. The IO will approve all revisions of the SOPs.

The KCU IRB will keep the research community apprised of new information that may affect the human research protection program, including laws, regulations, policies, procedures, and emerging ethical and scientific issues on its website, through email, and/ or other forums.

The following officials, administrative units and individuals have primary responsibilities for human subject protections:

1.8.1 Institutional Official

The ultimate responsibility resides with the **Institutional Official (IO)** of the program. The IO is legally authorized to represent KCU. The IO is the signatory of the FWA and assumes the obligations of the FWA. At KCU, the Vice Provost of Research is the Institutional Official. The IO is responsible for ensuring that the KCU IRB has the resources and support necessary to fulfill its responsibilities and to comply with the regulations and requirements that govern human subject research. Such resources include, but are not limited to:

- Staffing commensurate with the size and complexity of the research program;
- Appropriate office space, meeting space, equipment, materials, and technology;
- Resources for the production, maintenance, and secure storage of IRB records;
- Resources for auditing and other compliance activities and investigation of noncompliance;
- Access to legal counsel;
- Support for evaluation of Conflict of Interest;
- Support for Community Outreach; and
- Ensuring that the IRB, investigators, and staff receive training related to human research protections.

At a minimum of annually, the IO reviews IRB functions, requirements, and resources and makes adjustments as needed.

The IO is also responsible for:

- Fostering, supporting and maintaining a culture that supports the ethical conduct of research involving human subjects and compliance with applicable regulatory and other requirements;
- Ensuring that the IRB functions independently by, among other mechanisms, being directly accessible to the IRB Chair(s) and members if they experience undue influence or if they have concerns about the function of the IRB;
- Oversight of the Institutional Review Board (IRB);
- Oversight over the conduct of human subjects research under the auspices of KCU;
- Providing training and educational opportunities for IRB members and staff to support their ability to review research in accordance with ethical standards and applicable regulations;
- Providing training and educational opportunities for investigators and research staff to support their ability to conduct research in accordance with ethical standards and applicable regulations; and
- Taking action as necessary to ensure the protection of human subjects and compliance with regulatory and other requirements.

The IO has the authority to suspend, terminate, or disapprove research or take other actions, such as sanctions or restrictions of research privileges or uses of research data, as necessary, to ensure the proper conduct of research, the protection of human subjects, the autonomy and authority of the IRB, compliance with regulatory and other requirements, or to protect the interests of KCU. However, the IO may not approve research that has been disapproved (or not yet approved) by the IRB.

The IRB Office will support the continuing education of the IO by providing information and updates on topics related to human research protections.

The IO is made known to employees of the organization and is accessible by phone, email, in person or other methods of communication. The IRB Chair and IRB members have access to the IO for any concerns or issues related to the IRB.

In the performance of these duties, the IO has the authority to delegate such activities as may be necessary in order to effectively administer the program. However, the IO is ultimately responsible and is expected to be knowledgeable about human subject protections and research at the organization.

1.8.2 IRB Staff

In addition to the leadership structure described above, the staffing for the IRB includes the Research Compliance Administrator. The IRB staff for KCU must comply with all ethical standards and practices. The duties and responsibilities for all staff are found in their respective job descriptions, and their performance is evaluated on an annual basis. The IRB staff report to the IO, who has day-to-day responsibilities for its operations.

1.8.3 Institutional Review Board (IRB)

KCU has one internal IRB, appointed by the Institutional Official (IO). The IRB prospectively reviews and makes decisions concerning all non-exempt human subjects research under the auspices of KCU unless it has been determined that KCU is not engaged in the research or KCU has entered into agreement with an external IRB to serve as the IRB of record. The IRB is responsible for the protection of the rights and welfare of human research subjects, through review and oversight of safe and ethical research. It discharges this duty by complying with the requirements of federal and state regulations, the FWA, and organizational policies.

The IRB functions independently of, but in coordination with, other organizational committees and officials. The IRB, however, makes independent determinations whether to approve, require modification in, or disapprove research based upon whether human subjects are adequately protected.

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 research that has not been approved or has been disapproved by the IRB.

KCU may also rely on external IRBs including those of various hospitals, clinics, and others. External IRBs are primarily relied upon for the review and oversight of studies not occurring on KCU's premises. KCU may also enter into reliance agreements for other reasons, for example, when required as a term or condition of a grant.

1.8.4 Legal Counsel

The KCU may rely on the Organization's Legal Counsel or designee for the interpretation of state law and the laws of other jurisdictions where research is conducted as they apply to human subjects research. Counsel is available to provide guidance on other relevant topics as needed. When there are any conflicts between federal or national law and other applicable laws, the Legal Counsel will determine the appropriate resolution.

1.8.5 Department Chairs and/or Organizational Leaders Department Chairs and organizational leaders are responsible for ensuring that the investigator is qualified by training and experience to conduct the proposed research.

Department chairs/leaders are required to review all proposals before they are submitted to the IRB for review. The signature of the Department chair or leader (1) indicates that the investigator is qualified and has the necessary credentials and resources to safely conduct the study, and (2) attests to the scientific validity of the study, meaning that:

- The research uses procedures consistent with sound research design; and
- The research design is sound enough to reasonably expect the research to yield the expected knowledge.

1.8.6 Principal Investigators

The Principal Investigator (PI) is ultimately responsible for the protection of the human subjects participating in research they conduct or oversee. The PI is expected to abide by the highest ethical standards when developing a research plan and to incorporate the principles of the Belmont Report. The PI is expected to conduct research in accordance with the IRB approved research plan and to personally conduct or oversee all aspects of the research. In addition to complying with all applicable regulatory policies and standards, PIs must comply with organizational and administrative requirements for conducting research. The PI is responsible for ensuring that all investigators and research staff complete all organization required trainings as well as training for their specific responsibilities in any given research study. When investigational drugs or devices are used, the PI is responsible for ensuring an appropriate plan for their storage, security, dispensing, accounting, and disposal.

The IRB reviews investigator qualifications when reviewing research and may determine that an investigator may not serve as PI or may require the addition of other investigators to supplement the expertise available on the research team or to conduct or oversee certain aspects of the research.

The PI for human subjects research under the auspices of KCU must be the individual who assumes full responsibility for a research project, including the supervision of any co-investigators, research assistants, staff and students. The Institutional Review Board (IRB) generally only recognizes one principal investigator per human subjects' research study, no matter how many research sites may be involved.

Other individuals may be named co-investigators. The principal investigator must possess the expertise, time and commitment to conduct and provide the necessary oversight for all aspects of the study, and must be willing to accept full responsibility for the study. In multi-site studies for which KCU is the coordinating institution, the principal investigator assumes the responsibility for the conduct of the study at each performance site and by each site-specific principal investigator. The following classes of individuals may exercise the privilege of being named as principal investigator or project directors at KCU:

1. KCU individuals with a paid faculty appointment, other than visiting and per-diem faculty, with the approval of the department Chair;
2. KCU unpaid (volunteer) faculty by exception only, with written justification by an appropriate chair or administrator, with final case-by-case approval by the Vice Provost of Research;
3. KCU individuals in permanent, non-faculty staff positions, with the approval an appropriate chair or administrator, with final case-by-case approval by the Vice Provost of Research;
4. Faculty members from affiliated institutions may be approved to serve as principal investigators on a KCU project on a case-by-case basis with final case-by-case approval by the Vice Provost of Research.
5. PsyD. Students under the supervision of a faculty advisor for their dissertation research.

Individuals who are debarred, disqualified, or otherwise restricted from participation in research or as a recipient of grant funds for research by a federal, state, or other agency **may not** serve as PI.

Individuals with a history of compliance issues related to the conduct of research (e.g., recipients of a FDA Warning Letter) will be considered on a case-by-case basis. Factors to consider include whether corrective actions have been accepted as adequate, whether information from an audit or quality review indicates that the issues have been resolved, and similar considerations.

1.8.7 [THIS SECTION IS CURRENTLY NON-APPLICABLE AND RESERVED] Other Related Units

1.8.8 Sponsored Programs Administration

Sponsored Programs Administration staff review all research agreements with grantors and sponsors including federal, foundation, industry, and non-profit. This review ensures that all terms of the award (grant or contract) are in compliance with organizational policies. Only designated senior individuals within Sponsored Programs Administration have the authority to approve funding proposals and to execute research agreements on behalf of the organization.

When the grant or contract agreement includes human research activities that will be conducted by investigators who are not employees or agents of KCU, a subcontract is executed between KCU and the collaborating institution. The subcontract includes the requirement for the collaborating institution to assure compliance with federal regulations for the protection of human subjects in research and to provide documentation of current and ongoing IRB approval. The collaborating institution must also ensure that key personnel involved in human subject research are in compliance with the NIH policy on

education in the protection of human research subjects and provide documentation of education of key personnel to KCU.

1.8.9 [THIS SECTION IS CURRENTLY NON-APPLICABLE AND RESERVED] Relationship Among Components

1.8.10 Study-Specific Coordination

In addition to IRB approval, PIs must obtain and document the approval, support, or permission of other individuals and departments or entities impacted by the research as well as approval by other oversight committees, including, but not limited to:

- Facilities where research activities will occur
- Departmental approvals
- Records access permissions (e.g., Educational Records)
- Institutional Biosafety Committee
- Radiation Safety Committee
- Research Conflict of Interest Committee

When applicable, a letter of support, collaboration, permission, or approval from the designated authority, should be included in the Initial Study Application to the IRB. The application will be reviewed in the IRB Office to ensure that all necessary letters are included. The IRB may request review by or consultation with any of the above listed or other organizational committees or components even when such review or consultation is not required by policy.

If the research sites, or research personnel, are also under the jurisdiction of another IRB, documentation of the external IRB's approval or agreement to cede or waive review is required.

Other committees and officials may not approve research involving human subjects to commence that has not been approved or has been disapproved by the IRB.

2 Quality Assurance

KCU performs the following Quality Assurance and Improvement activities for the purposes of monitoring the safety of ongoing studies and measuring and improving human research protection effectiveness, quality, and compliance with organizational policies and procedures and applicable federal, state, and local laws.

2.1 External Monitoring, Audit, and Inspection Reports

The IRB, IO, and any applicable department chair should be notified in advance, whenever possible, of upcoming audits or inspections of research whether the study is reviewed by the KCU IRB or an external IRB on KCU's behalf.

When research is under the oversight of the KCU IRB, all reports from external monitors, auditors, or inspectors must be submitted to the IRB for review. The IRB Chair or designee will review such reports to monitor for issues that could impact the rights or welfare of human subjects and for issues indicative of possible serious or continuing noncompliance. If such issues are identified, the report will be forwarded to the convened IRB to determine what additional actions are necessary, if any.

When KCU is engaged in research reviewed by an external IRB, all reports from audits or inspections must be submitted to the KCU IRB for review. The IRB may require corrective and preventative actions, a follow up review, or other actions as needed to ensure the protection of human subjects and to support compliance.

2.2 Investigator Compliance Reviews

The IO or IRB Chair or, on occasion, other internal or external staff, may conduct post-approval directed (for cause) and routine (not for cause) compliance reviews of human subjects research conducted under the auspices of KCU. Additionally, the IRB may appoint a subcommittee for the purpose of conducting a for-cause or not for-cause compliance review of one or more research plans under its jurisdiction. The subcommittee may be composed of IRB members and Compliance staff from within, or individuals from and outside of the organization.

Compliance reviews are conducted to assess investigator compliance with federal, state, and local law, and KCU policies, and to identify areas for improvement, and to provide recommendations based on existing policies and procedures. The results of compliance reviews will be reported to the KCU IRB (when the KCU IRB is the IRB of record), the investigator, and other KCU leadership, as appropriate. Any IRB reporting and evaluation of noncompliance will be handled according to the procedures of the IRB of record.

If it is identified during the course of a review that subjects in a research project may have been exposed to unexpected serious harm or risk of harm, the reviewer will promptly report such findings to the IO and the IRB of record.

If issues are identified that indicate possible misconduct in research, the procedures in the *KCU research misconduct policy* will be initiated. If the potential research misconduct also involves potential noncompliance with the IRB-approved protocol, any investigations will be coordinated

between the IRB and the research misconduct committee.

Compliance reviews may include:

- Requesting progress reports from investigators
- Examining investigator-held research records and records held by pharmacy or other ancillary services
- Reviewing source documentation
- Reviewing the recruitment process and materials
- Reviewing consent materials and the documentation of consent
- Observing the consent process and other research activities
- Interviewing investigators and research staff
- Interviewing research subjects
- Reviewing projects to verify from sources other than the investigator that no unapproved changes have occurred since previous review
- Conducting other monitoring or auditing activities as deemed appropriate by the ORSPORSP or IRB.

2.3 IRB Compliance Reviews

The IO or, on occasion, other internal or external staff, will periodically review the activities of the IRB to assess compliance with regulatory requirements and to identify areas for improvement; this will include a review of IRB records at least annually.

Review activities may include:

- Review of the IRB minutes to evaluate whether adequate documentation of the meeting discussion and any required determinations has occurred and that quorum was met and maintained
- Reviewing IRB files to evaluate whether adequate documentation of exemptions, expedited review, and other outside of committee reviews has occurred
- Reviewing consent forms to evaluate whether all required elements are included
- Reviewing the IRB databases to evaluate whether all required fields are completed accurately
- Verifying IRB approvals for external sites or investigators
- Reviewing metrics (for example, time from submission to first review) to evaluate the quality, efficiency, and effectiveness of the IRB review process
- Reviewing the workload of the IRB and IRB staff
- Other review activities as appropriate

If substantive deficiencies are identified in the review, a corrective action plan will be developed by the IO. The IO, IRB staff, and IRB Chair will have responsibility for implementing and reporting progress on the corrective action plan.

3 Education & Training

3.1 Training / Ongoing Education of IRB Chair, Members, and Staff

Recognizing that a vital component of a comprehensive human research protection program is an education program, KCU is committed to providing training and on-going education for IRB members and the staff of the IRB, related to ethical concerns and regulatory and organizational requirements for the protection of human subjects.

Orientation

New IRB members, including alternate members, will meet with the IRB Chair or IRB Staff for an orientation session. At the session, IRB processes, regulations, and resources will be reviewed and the new member will be provided with a copy of the IRB Member Handbook. The handbook includes copies of the following and other relevant information:

- Belmont Report
- KCU SOPs
- Federal regulations relevant to the IRB
- Tools used by IRB reviewers (checklists etc.)
- IRB Meeting Schedule
- Contact Information for IRB Office

Initial Education

IRB members and IRB staff must complete the required modules in the CITI Course in the Protection of Human Research Subjects, or other training determined to be equivalent by the IO.

Continuing Education

To ensure that oversight of human research is ethically grounded and the decisions made by the IRB are consistent with current regulatory and policy requirements, training is continuous for IRB members throughout their service on the IRB.

In addition to CITI training, KCU may use the following activities as a means for offering continuing education to IRB members and IRB staff:

- In-service training at IRB meetings
- Training workshops
- Webinars
- Email distribution of articles, announcements, presentations, and other materials relevant to human subject protections

IRB members are also required to complete CITI basic or refresher training every 2 years.

The activities for continuing education may vary on a yearly basis depending on areas of need, as determined by the IO or IRB Staff. Whenever possible, the IO provides support for staff and IRB members to attend PRIM&R, OHRP, and other relevant conferences.

The IO and IRB Staff determines minimum requirements for continuing education and tracks participation. Fulfillment of training requirements is included as part of the evaluation of the performance of IRB members, alternates, and staff.

3.2 Training / Ongoing Education of Investigators and Research Team

As stated previously, a vital component of a comprehensive human research protection program is an education program for all individuals with human subject responsibilities. KCU is committed to providing training and on-going education for investigators and research staff members on human subject protections and other relevant topics.

3.2.1 Initial Education

Investigators and research staff who interact or intervene with subjects, or who use subject's identifiable information for the purposes of research, must complete KCU's CITI Courses relevant to the type of research being conducted and the investigator or staff member's responsibilities.

Evidence of current training (date of completion within 2 years of application date) for each member of the research team must be included with every new study application and applications to add study personnel. New study applications and additions of study personnel will not be moved forward for IRB review without evidence of training.

Waiver of Initial Education

If individuals can provide documentation verifying that they have successfully completed human subject research training equivalent to that required by the KCU, they may request a waiver of KCU's specific training requirements. IRB Staff and the IRB Chair will review the documentation and determine if it satisfies organizational standards.

3.2.2 Continuing Education

Initial training is considered current for a period of 2 years by which time investigators and research staff must complete basic or refresher CITI training or provide evidence of equivalent training as described above. There is no exception to this requirement.

Training will be verified at the time of continuing review, submission of a progress report and/or with applications to add study personnel. If training has not been completed or has lapsed and is not completed in a timely manner, the investigator or staff member may be removed from the study or otherwise restricted from participating in the research.

In addition to the basic requirements described above, KCU will periodically provide training on topics relevant to human subject protections, regulations, policies and standards, and IRB submission processes and requirements. Training may be provided via in-service, workshops, webinars, e-Learning,

or through the distribution of articles, presentations, and other materials. Investigators and staff may request training or offer training suggestions by contacting the IRB Staff and/or IO.

4 KCU Institutional Review Board

KCU has established an Institutional Review Board (IRB) to ensure the protection of human subjects in research conducted its auspices. All non-exempt human research conducted under the jurisdiction of KCU must be reviewed and approved by the KCU IRB, or another IRB with a signed reliance agreement with KCU and approval from the IRB Office prior to the initiation of the research.

KCU may authorize the use of external IRBs to serve as the IRB of record for research under the auspices of KCU (See Section 5). The authorized external IRBs have the same authority as the on-site IRBs. All determinations and findings of the authorized external IRB acting in its capacity as the IRB-of-record for a study conducted at KCU are equally binding on the specific study at KCU.

4.1 IRB Authority

The IRB derives its authority from KCU policy, as cited in Section 1.2. Under the federal regulations, IRBs have the authority:

1. To approve, require modifications to secure approval, or disapprove human subjects research activities, including exempt research activities under 45 CFR 46.104 for which limited IRB review is a condition of exemption (under 45 CFR 46.104(d)(2)(iii), (d)(3)(i)(C), and (d)(7), and (8));
2. To require that informed consent is obtained and documented in accordance with regulatory and policy requirements unless the criteria for the waiver or alteration of such requirements has been satisfied and approved by the IRB. The IRB may require that information, in addition to that specifically mentioned in the regulations, be given to the subjects when in the IRB's judgment the information would meaningfully add to the protection of the rights and welfare of subjects;
3. For research subject to the Common Rule: To conduct continuing review of research requiring review by the convened IRB at intervals appropriate to the degree of risk of the research, but not less than once per year, except as described in Section 10.5;
4. To suspend or terminate approval of research not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to participants;
5. To observe, or have a third party observe, the consent process; and
6. To observe, or have a third party observe, the conduct of the research.

The IRB functions independently. Attempts to coerce or otherwise unduly influence the actions of the IRB are forbidden by policy, and are to be reported as described in Section 4.6. Likewise, the IRB must remain free from the influence of financial and other organizational interests. No individual with responsibility for the business and financial interests of the organization may serve on the IRB.

Research that has been reviewed and approved by the IRB may be subject to review and disapproval by officials of KCU. However, those officials may NOT approve research if it has not been approved or has been disapproved by the IRB. Reviewing officials may strengthen requirements and/or conditions, or add other modifications before approval, or may require approval by an additional committee, office, or

person. Previously approved research proposals and/or consent forms must be re-approved by the IRB before initiating any changes or modifications that result from such additional organizational reviews.

4.2 Roles and Responsibilities

4.2.1 Chair of the IRB

The IO appoints a Chair and Vice Chair of the IRB. Any change in appointment, including reappointment or removal, requires written notification.

The IRB Chair should be a highly-respected individual, fully capable of managing the IRB and the matters brought before it with fairness and impartiality. The task of making the IRB a respected part of the research community falls primarily on the shoulders of the Chair. The IRB must be perceived to be fair, impartial, and immune to pressure by administration, the investigators whose research plans are brought before it, and other committees and departments.

The IRB Chair is responsible for conducting IRB meetings and expedited reviews and may serve as signatory for correspondence generated by the IRB.

The IRB Chair is authorized to take immediate action to suspend a study or studies if subjects may be at risk of harm, when serious noncompliance may have occurred, or for any other reason where such action would be deemed appropriate. Such action requires subsequent notice to and review by the convened IRB.

The IRB Chair may designate other experienced IRB members to perform duties such as expedited reviews and other IRB functions.

The IRB Chair advises the IO about IRB member performance.

The performance of IRB Chair will be reviewed by the IO. Feedback from this evaluation will be provided to the Chair. If the Chair is not acting in accordance with the IRB's mission, following policies and procedures, has an undue number of absences, or not fulfilling the responsibilities of the Chair, s/he may be removed.

4.2.2 Vice Chair of the IRB

The Vice Chair serves as the Chair of the IRB in the absence of the Chair and has the same qualifications, authority, and duties as the Chair.

The performance of IRB Vice Chair will be reviewed by the IO. Feedback from this evaluation will be provided to the Vice Chair. If the Vice Chair is not acting in accordance with the IRB's mission, following policies and procedures, has an undue number of absences, or otherwise not fulfilling their responsibilities, s/he may be removed.

4.2.3 IRB Members

The role of an IRB member is to ensure that human research activities comply with federal regulations, state and local laws, and organizational policies and procedures, by:

- Completing member education and training, both initial and on-going (See Section 3.1)
- Maintaining the confidentiality of IRB deliberations and research reviewed by the IRB
- Conducting and documenting reviews in a timely fashion
- Attending IRB meetings as scheduled
- Recusing self from reviewing or voting on research when s/he has a conflict of interest (See Section 22.2)
- Participating in subcommittees of the IRB if requested and available
- Conducting themselves in a professional and collegial manner

Members should attend all meetings for which they are scheduled. If a member is unable to attend a scheduled meeting, they should inform the IRB staff. If a member's availability changes and they are no longer able to regularly attend IRB meetings or will be absent for an extended period of time, they should inform the IRB Staff. The IRB Staff will assess the situation, including the availability of the alternate when applicable, and make recommendations to the IRB Chair to ensure the IRB is able to meet quorum requirements and has the necessary expertise to review the research, which regularly comes before it.

The performance of IRB members will be reviewed by the IO, the IRB Chair, and the IRB Office. Feedback from this evaluation will be provided. Members who are not acting in accordance with the IRB's mission, not following policies and procedures, have an undue number of absences, or otherwise not fulfilling the responsibilities of membership, may be removed by the IO or his/her designee.

4.2.4 Alternate members

The appointment and function of alternate members is the same as that for primary IRB members. An alternate's expertise and perspective should be comparable to those of the primary member. The role of the alternate member is to serve as a voting member of the IRB when the regular member is unavailable to attend a convened meeting, in part or in full, or when the regular member has a conflict of interest in regards to a protocol under review. When an alternate member substitutes for a primary member, the alternate member will receive and review the same materials prior to the IRB meeting that the primary member would have received.

The IRB roster identifies the primary member(s) or class of members (e.g., physician scientist) for whom each alternate member may substitute. When both the regular member and the alternate is in attendance at an IRB meeting, only one may be counted towards quorum and vote. The IRB minutes will document when an alternate member replaces a primary member.

Experienced alternate members may be designated by the Chair to conduct reviews.

4.2.5 Subcommittees of the IRB

The IRB Chair, in consultation with the IO, may appoint one or more other IRB members to a subcommittee of the IRB to review issues and to make recommendations to the IRB (e.g., to supplement

the IRB's review of research proposals or to review of reports of potential unanticipated problems or noncompliance). The size and composition of the subcommittee shall depend on the scope of duties delegated by the IRB Chair. Any such subcommittee cannot approve research or issue determinations that require review by the convened IRB.

4.3 Composition of the IRB Membership

The IRB must promote respect for its advice and counsel in safeguarding the rights and welfare of the research that comes before it and possess the professional competence necessary to review specific research activities. The structure and composition of the KCU IRB is based upon regulatory requirements and the characteristics of the research it reviews. A member of the IRB may fill multiple membership position requirements (e.g., nonscientific and unaffiliated).

- The IRB will have at least five members with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the organization. The IRB shall not consist entirely of members of one profession
- The IRB will be sufficiently qualified through the experience and expertise of its members, and the diversity of the members, including consideration of 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
- In addition to possessing the professional competence necessary to review specific research activities, the IRB will be able to ascertain the acceptability of proposed research in terms of organizational commitments and regulations, applicable law, and standards of professional conduct and practice. The IRB will therefore include persons knowledgeable in these areas
- The IRB will include members who are knowledgeable about and experienced working with subjects vulnerable to coercion or undue influence (e.g., children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons) that are regularly included in the research under its review
- Every nondiscriminatory effort will be made to ensure that the IRB does not consist entirely of men or entirely of women, including the organization's consideration of qualified persons of both sexes, so long as no selection is made to the IRB solely on the basis of gender
- The IRB includes at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in nonscientific areas
- The IRB includes at least one member who is not otherwise affiliated with the organization and who is not part of the immediate family of a person who is affiliated with the organization
- The IRB Chair and Vice Chair are voting members of the IRB.

Individuals from other business units at KCU may provide information to the IRB and attend IRB meetings when invited as guests.

On an annual basis, the IRB Chair, the IO, and the IRB Office review the membership and composition of the IRB to determine if it continues to meet regulatory and organizational requirements.

4.3.1 Appointment of Members to the IRB

When the need for a new IRB member or alternate is identified, the IRB Staff or IRB Chair informs the IO who seeks out qualified candidates.

The final decision in selecting a new member is made by the IO, in consultation with the IRB Chair.

Initial appointments are made for a Two-year term. Subsequent appointments are made for a renewable two-year period of service. Any change in appointment, including reappointment or removal before the end of a member's term, requires written notification. Members may resign by written notification to the IO, the IRB Chair and the IRB Office.

The IRB Staff will ensure that changes in IRB membership are reported via the federal IRB registration in accordance with the instructions provided on OHRP's website.

4.4 Liability Coverage for IRB Members

The KCU insurance coverage applies to employees and any other person authorized to act on behalf of KCU for acts or omissions within the scope of their employment or authorized activity.

4.5 Use of Consultants

When necessary, the IRB Chair or the IO may solicit individuals from within or outside the organization with the expertise to assist in the review of research or issues which require expertise beyond or in addition to that available on the IRB. The IRB Office will ensure that all relevant materials are provided to the consulting reviewer prior to the convened meeting or expedited review.

The IRB Staff reviews the COI policy for IRB members with consultants and consultants must confirm that they do not have a conflict of interest prior to review. Individuals who have a conflicting interest or whose spouse or immediate family members have a conflicting interest will not be invited to provide consultation.

The consultant's findings will be presented to the IRB for consideration either in person or in writing. If in attendance at an IRB meeting, consultants may provide information and assist in the IRB's deliberations, but may not participate in the vote.

Written statements from consultants will be kept in the IRB records. Information provided by consultants at IRB meetings will be documented in the minutes.

Ad hoc or informal consultations requested by individual members (rather than the convened board) will be managed in a manner that protects the investigator's confidentiality and that complies with the IRB COI policy.

4.6 Reporting and Investigation of Allegations of Undue Influence

If an IRB Chair, member, or staff person feels that the IRB has been unduly influenced by any party, they shall make a confidential report to the IO. The IO will ensure that a thorough investigation is conducted and, if the allegation is determined valid, that corrective action is taken to prevent additional

occurrences. In the event that the allegation is regarding the IO, the matter will be referred to the KCU President for investigation and any necessary action.

Undue influence means attempting to interfere with the normal functioning and decision-making of the IRB, or to attempt to influence an IRB member or staff member or any other member of the research team, outside of the established processes or normal and accepted methods in order to obtain a particular result, decision, or action by the IRB or one of its members or staff.

5 Collaborative Research and IRB Reliance

When engaged in multi-site research (i.e., two or more sites following the same protocol), research involving external collaborators, or research that is otherwise under the jurisdiction of more than one IRB, KCU acknowledges that each organization is responsible for safeguarding the rights and welfare of human subjects and for complying with applicable federal regulations. KCU may choose to review the research in its entirety, only those components of the research KCU is engaged in, rely on the review of another qualified IRB, or make other arrangements for avoiding duplication of effort. When KCU is the prime awardee on an HHS grant, it will ensure that at least one IRB reviews the research in its entirety.

When relying upon another IRB or when serving as the reviewing IRB for an outside organization or external investigator, a formal relationship must be established between KCU and the outside organization or investigator through an IRB Authorization Agreement, Investigator Agreement, a Memorandum of Understanding, or other such written agreement. The written agreement must be executed before KCU will accept any human research proposals from the outside organization or investigator or rely on the review of an external IRB.

IRB reliance agreements establish the authorities, roles, and responsibilities of the reviewing IRB and the relying organization. The procedures for reliance, including for communication, information-sharing, and reports, may be outlined in the reliance agreement, in SOPs, or other written materials.

To support compliance, KCU will make every effort to ensure as much consistency as possible across reliance agreements.

Requests for the KCU to either rely upon another IRB or to serve as the IRB of record for an external organization or investigator should be submitted as early as possible in the grant/contract or other approval process.

5.1 KCU Serving as Reviewing IRB

Generally, KCU IRB does not serve as the IRB of record for an external organization unless KCU is also engaged in the research or has another agreement in place with the external organization. The IO evaluates the following factors, and others as appropriate, when considering a request for the KCU IRB to serve as the IRB of record for a particular study or studies:

1. The terms of the external organization's FWA;
2. Prior experience with the external organization and investigators;
3. The compliance history of the external organization and investigators (e.g., outcomes of prior audits or inspections, corrective actions);
4. The research activities conducted by or at the external organization;
5. The willingness of the external organization to accept KCU's reliance terms and procedures;
6. The ability of the organizations to collaboratively provide meaningful oversight of the proposed research, taking into account factors such as:
    a. The risks and procedures of the research;
    b. The resources available at each organization and ability to accommodate or collaborate with each other in observing the consent process, performing compliance reviews, investigations of potential noncompliance, and similar matters;

c. The expertise and experience of the KCU IRB with the proposed research, subject population, and applicable regulations;
d. The familiarity of the KCU IRB with the relevant local context considerations of the external organization; and/or
e. The willingness or ability of the external organization to provide information and respond to questions regarding investigator qualifications, conflicts of interest, organizational requirements, local context, and other matters that may inform the IRB review.

When the KCU IRB serves as the reviewing IRB for another organization, the requirements and procedures outlined throughout this manual apply unless an alternative procedure has been agreed to in the reliance agreement or outlined in a companion document.

For example, alternative procedures may be used for any of the following:

1. Management and documentation of scientific review, other ancillary reviews, and institutional permissions for research;
2. Training requirements and verification of qualifications and credentials for external investigators and staff;
3. For-cause and not-for-cause compliance reviews;
4. The disclosure and management of conflicts of interest. In all cases, any COIs and CMPs identified and developed by the relying organization will be communicated to the reviewing IRB. The reviewing IRB will determine the acceptability of the plan in accordance with their policies and procedures.
5. Review and management of matters such as site-specific consent language, HIPAA (e.g., authorizations, waivers, alterations), noncompliance, unanticipated problems, and federal reports;
6. Procedures for and type of IRB review (e.g., expedited, convened) of additional sites after the research protocol is IRB-approved;
7. Procedures for submission and review of interim reports and continuing review materials; and/or
8. The communication of IRB determinations and other information to external investigators and organizations.

5.2 External IRB Review of KCU Research

All non-exempt human subject research (or exempt research for which limited IRB review takes place pursuant to § __.104(d)(2)(iii), (d)(3)(i)(C), or (d)(7) or (8)) that KCU is engaged in must be reviewed and approved by the KCU IRB or an external IRB that KCU has agreed to rely upon prior to the initiation of the research. See Section 1.7 for information regarding engagement.

KCU may also choose to enter into an agreement to rely upon another external IRB, most commonly when required as a condition of a grant or contract. Investigators should submit reliance requests as early in the grant/contract process as possible.

IRB Staff, the IO, and/or the IRB Chair evaluates the following factors, and others as appropriate, when considering a request to rely upon an external IRB:

1. The research activities that will be conducted at or by KCU;

2. The risks and complexities of the proposed research;
3. The federal IRB registration and organizational FWA, as applicable;
4. The expertise and experience of the proposed IRB (e.g., with reviewing the type of research, research procedures, and subject population(s));
5. The accreditation status, if any, of the proposed IRB;
6. The compliance history of the IRB (e.g., outcomes of prior audits or inspections, corrective actions);
7. Prior experience with the IRB;
8. The proposed reliance terms and procedures including the procedures for collaborative management of matters such as conflicts of interest, noncompliance, unanticipated problems, and federal reports;
9. The plan for review and allowance of the incorporation of site-specific consent language; and
10. The plan for incorporation of other relevant local requirements or context information in the review process.

The evaluation may also take into consideration one or more of the following based upon the risks of the research, the research activities that KCU will be involved in, and KCU's familiarity with the IRB:

1. When the research is minimal risk (or the activities that KCU is involved with are minimal risk), a statement of assurance from the proposed IRB that its review will be consistent with applicable ethical and regulatory standards, and that it will report any regulatory investigations, citations, or actions taken regarding the reviewing IRB, and, when applicable, to the organization's federal oversight entity (e.g., OHRP, FDA, etc.);
2. An attestation about, or summary of, any quality assessment of the reviewing IRB such as evaluation by an external consultant or internal evaluation of compliance;
3. The willingness of the external IRB to accommodate requests for relevant minutes and other records of the proposed study and/or to copy KCU's IRB office on correspondence such as determination letters and notices of suspensions or terminations of IRB approval;
4. The willingness of the external IRB to accommodate a request for someone from the relying organization to serve as a consultant to the IRB or to observe the review of the proposed study; and/or
5. An assessment of the external IRB's policies and procedures.

The external IRBs that serve as the IRB of record for KCU research have the same authority as the KCU IRB and all determinations and requirements of the external IRBs are equally binding. Investigators must be familiar with and comply with the external IRB's policies and procedures and any additional requirements or procedures outlined in the IRB reliance agreement or companion materials (e.g., reliance SOPs). KCU will support compliance with the terms of reliance agreements by providing investigators with information relevant to their responsibilities, such as a copy or summary of the agreement, an information sheet, or reliance SOPs.

Regardless of which IRB is designated to review a research project and to serve as the IRB of record, KCU is responsible for the conduct of the research in which it engages. Research reviewed by external IRBs remains subject to review, approval, and oversight by KCU and must adhere to all applicable policies, procedures, and requirements, including those of the KCU IRB.

5.2.1 Registration of Studies Reviewed by External IRBs [KCU is not currently involved in any studies that need Registration so this section is RESERVED]

5.2.2 NIH Single IRB (sIRB) for Multi-Site Research [KCU is not currently involved in any NIH-funded research so this section is RESERVED]

In June 2016, the National Institutes of Health (NIH) released a final policy requiring domestic awardees and domestic sites of NIH-funded multi-site research to use a single IRB (sIRB) for review of non-exempt human subject research unless there is justification for an exception. This policy is intended to streamline the IRB review process and reduce inefficiencies and redundancies while maintaining and enhancing subject protections. The policy **does not** apply to career development, research training, or fellowship awards, nor to sites that are not conducting the same protocol as the other sites (e.g., sites providing statistical support or laboratory analysis only) or to foreign sites.

Exceptions to the policy are automatic when local IRB review is required by federal, tribal, or state law/regulation/policy and when the proposed research is the "child" of a grant that predates the requirement for sIRB review. Such exceptions and the basis (and information regarding the "parent" study, when applicable) should be cited in the proposed sIRB plan and, when the exception is based on law/regulation/policy, apply only to the site(s) to which the law/regulation/policy applies. Other exceptions will be considered when there is compelling justification. The site(s) and justification for why the site(s) cannot rely on the single IRB of record should be included in the proposed sIRB plan. The NIH will consider the exception request and inform the applicant of the outcome.

5.2.3 Selection and Designation of a sIRB [KCU is not currently involved in any NIH-funded research so this section is RESERVED]

5.2.4 Reliance Agreements for sIRB Studies [KCU is not currently involved in such research so this section is RESERVED]

5.2.5 Responsibilities [KCU is not currently involved in such research so this section is RESERVED]

6 Research Previously Approved by Another IRB

When an investigator transfers human subjects research to KCU that was previously approved by another IRB, the investigator must:

- Submit the research for review by the IRB or determination of exemption; or
- Submit a request for KCU to rely upon the existing IRB of record (such requests must be approved by both organizations)

Research determined to be exempt at the previous institution will be reviewed according to the procedures in Section 9. All other research must be submitted as if it were undergoing initial review and will be reviewed under expedited review or by the convened IRB. Research activities under the auspices of KCU cannot commence until all necessary approvals are in place including approval by the internal IRB or an IRB reliance agreement is executed (and the transferred activities are approved by the IRB of record).

For research transfers where stopping research interventions or procedures might harm subjects, the investigator can request permission from both organizations to continue the research under the oversight of the prior organization's IRB until final KCU IRB approval is obtained.

7 Documentation and Records

KCU prepares and maintains adequate documentation of the IRB's activities. All records are accessible for inspection and copying by authorized representatives of the FDA, OHRP, sponsors, and other authorized entities at reasonable times and in a reasonable manner.

7.1 IRB Records

IRB records include, but are not limited to:

1. Written operating procedures;
2. IRB membership rosters;
3. IRB member files including documentation of appointments, experience, education/training, and expertise;
4. IRB correspondence including reports to regulatory agencies;
5. IRB Study Files (See Section 7.2);
6. Documentation of exemptions, including those exemptions with limited IRB review;
7. Convened IRB meeting minutes;
8. Documentation of review by an external IRB, when appropriate;
9. Documentation of IRB reliance and cooperative review agreements;
    a. For nonexempt research involving human subjects covered by the Common Rule (or exempt research for which limited IRB review takes place as described in Section 9) that takes place at an institution in which IRB oversight is conducted by an IRB that is not operated by the institution, the institution and the organization operating the IRB shall document the institution's reliance on the IRB for oversight of the research and the responsibilities that each entity will undertake to ensure compliance with the requirements of this policy (e.g., in a written agreement between the institution and the IRB, by implementation of an institution-wide policy directive providing the allocation of responsibilities between the institution and an IRB that is not affiliated with the institution, or as set forth in a research protocol);
10. Documentation of independent or external investigator agreements;
11. Federal Wide Assurances;
12. Federal IRB Registrations; and
13. Documentation of complaints and any related findings and/or resolution.

7.2 IRB Study Files

The IRB maintains a separate file for each study it receives for review in the IRB electronic system under a unique identification number assigned by the system. As applicable, study files include, but are not limited to the following:

1. The initial application and all associated documents and materials;
2. Modification requests and all associated documents and materials;
3. Continuing review/progress reports and all associated documents and materials including the rationale for conducting continuing review of research that otherwise would not require continuing review as described in Section 10.5;
4. Closure reports and all associated documents and materials;
5. Reports submitted after study approval including reports of significant new findings, data and safety monitoring reports, protocol violation reports, complaints, noncompliance, and reports of injuries to subjects and unanticipated problems involving risks to subjects or others;
6. IRB-approved consent, parental permission, and assent forms;
7. IRB reviewer notes;
8. Documentation of scientific or scholarly review (if available);
9. Documentation of the type of IRB review. For exempt determinations and expedited review, this will include the category under which the review is allowed;
10. For expedited review, documentation of any findings and determinations required by the regulations and study-specific findings supporting those determinations, including, but not limited to, waiver or alteration of consent, waiver of documentation of consent, research involving pregnant women, fetuses, and neonates, research involving prisoners, and research involving children. For research reviewed by the convened board these findings and determinations are recorded in the minutes;
11. For expedited review, documentation of the risk determination and period of approval (when continuing review is required). For research reviewed by the convened board these determinations are recorded in the minutes;
12. For expedited review, the rationale for an expedited reviewer's determination under 45 CFR 46.110(b)(1)(i) that research appearing on the expedited review list described in 45 CFR 46.110(a) is more than minimal risk.
13. Documentation of all IRB review actions;
14. Notification of expiration of IRB approval to the investigator;
15. Notification of suspension or termination of research;
16. Letters to investigator informing them of IRB review outcomes;
17. IRB correspondence to and from investigators related to the study;
18. All other IRB correspondence related to the research;
19. Reports of unanticipated problems involving risk to subjects or others; and
20. Any statements of significant new findings provided to subjects.

7.3 The IRB Minutes

Draft minutes of IRB meeting proceedings are written and available for review by the next regularly scheduled IRB meeting. Changes may not be made to finalized minutes without re-review by the IRB to verify accuracy.

Minutes of IRB meetings must contain sufficient detail to show the following, as applicable:

1. Attendance
    a. Names of members or alternates present;
    b. Names of members or alternate members who are participating through videoconference or teleconference and documentation that those attending remotely received all pertinent material prior to the meeting and were able to actively and equally participate in all discussions;
    c. Names of alternates attending in lieu of specified (named) absent members. (Alternates may substitute for specific absent members or categories of members only as designated on the official IRB membership roster);
    d. Names of any consultants present;
    e. Names of any investigators present;
    f. Ex-Officio Members ;and
    g. The names of non-members and guests in attendance, such as investigators, and study administrators.

    Note: The minutes will indicate, by name, those members who enter or leave the meeting. The vote on each action will reflect the numbers of members present for the vote on that item.
2. The presence of a quorum throughout the meeting, including the presence of one member whose primary concern is in a non-scientific area;
3. When both a member and an alternate are present, the minutes will reflect if and when the alternate substituted for the member. Generally, the member votes, but an alternate may substitute when appropriate (e.g., the member has a conflict of interest, the alternate has needed expertise, etc.);
4. Business Items discussed and any education provided;
5. Actions taken, including separate deliberations, actions, and votes for each submission undergoing review by the convened IRB;
6. Vote counts on these actions (Total Number Voting; Number voting for; Number voting against; Number abstaining; Number of those recused). When a member is recused due to conflict of interest, the name of the member and reason for the recusal will be noted;
7. Basis or justification for actions disapproving or requiring changes in research;
8. Summary of controverted issues and their resolution;

9. Approval period for initial and continuing reviews, including identification of research that warrants review more often than annually and the basis for that determination;
10. The rationale for requiring continuing review of research that otherwise would not require continuing review as described in Section 10.5;
11. Risk determination for initial and continuing reviews, and modifications when the modification alters the prior risk determination;
12. Justification for deletion or substantive modification of information concerning risks or alternative procedures contained in the DHHS-approved sample consent document;
13. Study-specific findings supporting that the research meets each of the required criteria when approving a consent procedure that does not include or that alters some or all of the required elements of informed consent, or when waiving the requirement to obtain informed consent altogether;
14. Study-specific findings supporting that that the research meets each of the required criteria when the requirements for documentation of consent are waived;
15. Study-specific findings supporting that the research meets each of the criteria for approval for vulnerable populations under any applicable Subparts;
16. Determinations related to conflicts of interest and acceptance or modification of conflict management plans;
17. Identification of any research for which there is need for verification from sources other than the investigator that no material changes are made in the research;
18. Review and determinations related to interim reports (e.g., unanticipated problems or safety reports, serious or continuing noncompliance, suspensions or terminations, etc.);
19. A list of research approved under expedited review procedures including limited IRB reviews conducted using expedited procedures, since the time of the last such report;
20. An indication that, when an IRB member or alternate has a conflicting interest (see Section 22.2) with the research under review, the IRB member or alternate was not present during the final deliberations or voting; and
21. Key information provided by consultants will be documented in the minutes or in a report provided by the consultant.

7.4 IRB Membership Roster

A membership list of IRB members will be maintained; it will identify members sufficiently to describe each member's chief anticipated contributions to IRB deliberations. The list will contain the following information about members:

1. Name;
2. Earned degrees;

3. Employment or other relationship between each member and the organization (i.e., affiliated or non-affiliated). To be categorized as non-affiliated, neither the member nor an immediate family member of the member may be affiliated with KCU.
4. Status as scientist or non-scientist. Members whose training, background, and occupation would incline them to view scientific activities from the standpoint of someone within a behavioral or biomedical research discipline are considered a scientist for the purposes of the roster. Members whose training, background, and occupation would incline them to view research activities from a standpoint outside of any biomedical or behavioral scientific discipline are considered a nonscientist. Physicians, nurses, and pharmacists are considered scientists;
5. Indications of experience, such as board certifications, licenses, and areas of practice sufficient to describe each member's chief anticipated contributions to IRB deliberations;
6. Representative capacities of each IRB member; including which IRB member(s) is a prisoner representative, and which IRB members are knowledgeable about or experienced in working with children, pregnant women, adults with impaired decision-making capacity, and other subjects vulnerable to coercion or undue influence commonly involved in KCU;
7. Role on the IRB (Chair, Vice-Chair, etc.);
8. Voting status; and
9. For alternate members, the primary member or class of members for whom the member could substitute.

The IRB Office must keep the IRB membership list current. Changes in IRB membership are reported to OHRP and/or FDA on the federal IRB registration on an annual basis.

7.5 Documentation of Exemptions

Documentation of verified exemptions consists of the reviewer's citation of a specific exempt category and written concurrence that the activity described in the investigator's request satisfies the conditions of the cited exempt category as detailed in Section 9 and any additional protections for subjects required by the reviewer. When an exemption includes limited IRB review, the documentation will include this fact and the IRB action taken on those aspects of the research subject to limited IRB review in accordance with the procedures described for the review procedures used (expedited or convened board) elsewhere in this manual.

7.6 Documentation of Expedited Reviews

IRB records for initial and continuing review by the expedited procedure must include the reviewer's verification that the study qualifies for expedited review including the specific permissible category(ies), or status as exempt but requiring limited IRB review, documentation that the activity satisfies the criteria for approval, the period of approval (when applicable), and any determinations required by the regulations including study-specific findings justifying the following determinations:

1. Approving a procedure which waives or alters the informed consent process;

2. Approving a procedure which waives the requirement for documentation of consent;
3. Approving research involving pregnant women, human fetuses, or neonates;
4. Approving research involving prisoners;
5. Approving research involving children.

7.7 Access to IRB Records

IRB study files are secured in the IRB electronic system with administrative access controlled by the IRB office. Likewise, investigators control access to investigator records in the electronic system. All other IRB records (e.g., membership rosters) are kept secure in a limited access file on KCU's servers, locked filing cabinets or locked storage rooms.

Ordinarily, access to IRB records is limited to the IO, IRB Staff, IRB members, and authorized organizational officials, and officials of federal and state regulatory agencies (e.g., OHRP and FDA). Research investigators are provided reasonable access to files related to their research. Appropriate accreditation bodies are provided access.

Records are accessible for inspection and copying by authorized representatives of federal regulatory agencies during regular business hours.

IRB member rosters are only provided to regulatory agencies, accreditation bodies, and persons or offices within KCU with a legitimate need (e.g., Compliance, Legal, Internal Audit). A memorandum documenting compliance with pertinent federal rules and regulations, IRB membership requirements, and with KCU's Federalwide Assurance is available and will be provided to sponsors and others upon request.

All other access to IRB records is limited to those who have legitimate need for them, as determined by the IO or IRB Chair.

7.8 Record Retention

In order to comply with the requirements of OHRP, FDA, and HIPAA, IRB records are maintained for at least six (6) years after completion of the research.

After the noted times, IRB records may be shredded or otherwise securely destroyed.

8 "Human Subjects" and "Research" Determinations

The responsibility for initial determination whether an activity constitutes "human subjects research" rests with the individual with primary responsibility for the activity. This individual should make this determination based on the definitions of "research" and "human subjects" as provided in Section 1.3. Consultation with the IRB Office is encouraged. Because the analysis can be complex, individuals with any questions regarding the applicability of these definitions to their activities are urged to request a determination that an activity does or does not involve research. Such requests should be submitted via the completion of a "Human Subjects Research Determination" application in the IRB electronic system, and/or by sending the request and (specified) materials via email to the IRB office.

Human Subjects Research Determinations must be submitted, and determined, prospectively (i.e., before the proposed activity or research begins). Conducting human subjects research without IRB approval or exemption is noncompliance and will be managed as described in Section 14.

Determinations whether an activity constitutes human subject research will be made by the IRB Chair, vice chair, or other experienced IRB members according to the definitions in Section 1.3, applicable federal regulations, and federal guidance. A determination letter will be issued by IRB staff to document the determination.

9 Exempt Determinations

All research using human subjects must be approved by KCU. Although certain categories of human subject research are exempt from IRB oversight, at KCU the determination of exempt status must be made by the IRB Chair, IRB Vice Chair, or other experienced IRB members. KCU may also choose to accept an exempt determination made by an external IRB, KCU will consider such requests on a case by case basis.

Individuals involved in making the determination of an IRB exempt status of a proposed research project cannot be involved in the proposed research. Reviewers must not have any apparent conflict of interest.

Unless otherwise required by law or by Federal department or agency heads, exempt studies are exempt from the requirements of the Common Rule (i.e., IRB approval and full research consent are not required) other than as specified within the regulations (e.g., the conditions that permit exemption, and when limited IRB review is required). Exempt research is not exempt from ethical considerations, such as honoring the principles described in the Belmont Report. The individual/s making the determination of exemption will determine whether to require additional protections for subjects in keeping with ethical principles (e.g., requiring disclosure/consent, etc.).

9.1 Limitations on Exemptions

The following limitations on exemptions apply to research conducted or supported by HHS:

Children: Exemption #2(i) and (ii) for research involving survey or interview procedures or observations of public behavior does NOT apply to research in children, except for research involving observations of public behavior when the investigator does not participate in the activities being observed. Exemption #2(iii), where identifiable information is obtained and the IRB conducts a limited IRB review, is NOT applicable to research in children. Exemption #3 does NOT apply to research involving children. [45 CFR 46.104(b)(3)]

Prisoners: Exemptions do not apply except for research aimed at involving a broader subject population that only incidentally includes prisoners.

9.2 Categories of Exempt Research

With the above-referenced limitations, research activities not regulated by the FDA (See Section 25.4 for FDA Exemptions) and any other limitations or restrictions due to applicable law, regulation, or agency policy, in which the only involvement of human subjects are determined to be in one or more of the following categories are exempt from IRB approval:

1. Research, conducted in established or commonly accepted educational settings that 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.

2. Research that only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior (including visual or auditory recording) if 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;
    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 to make the determination required by .111(a)(7): *When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data*.

3. (i) Research involving benign behavioral interventions in conjunction with the collection of information from an adult subject through verbal or written responses (including data entry) or audiovisual recording if the subject prospectively agrees to the intervention and information collection and at least one of the following criteria is met:

    A. 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;
    B. 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
    C. 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 to make the determination required by .111(a)(7): *When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data*.

    (ii) For the purpose of this provision, 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. Provided all such criteria are met, 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.

(iii) 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.

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;
    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;
    iii. The research involves only information collection and analysis involving the investigator's use of identifiable health information when that use is regulated under 45 CFR parts 160 and 164, subparts A and E, for the purposes of "health care operations" or "research" as those terms are defined at 45 CFR 164.501 or for "public health activities and purposes" as described under 45 CFR 164.512(b); or
    iv. The research is conducted by, or on behalf of, a Federal department or agency using government-generated or government-collected information obtained for nonresearch activities, if the research generates identifiable private information that is or will be maintained on information technology that is subject to and in compliance with section 208(b) of the E-Government Act of 2002, 44 U.S.C. 3501 note, if all of the identifiable private information collected, used, or generated as part of the activity will be maintained in systems of records subject to the Privacy Act of 1974, 5 U.S.C. 552a, and, if applicable, the information used in the research was collected subject to the Paperwork Reduction Act of 1995, 44 U.S.C. 3501 et seq.

5. Research and demonstration projects that are conducted or supported by a Federal department or agency, or otherwise subject to the approval of department or agency heads (or the approval of the heads of bureaus or other subordinate agencies that have been delegated authority to conduct the research and demonstration projects), and that are designed to study, evaluate, improve, 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. Such projects include, but are not limited to, internal studies by Federal employees, and studies under contracts or consulting arrangements, cooperative agreements, or grants. Exempt projects also include waivers of otherwise mandatory requirements using authorities such as sections 1115 and 1115A of the Social Security Act, as amended.

i. Each Federal department or agency conducting or supporting the research and demonstration projects must establish, on a publicly accessible Federal website or in such other manner as the department or agency head may determine, a list of the research and demonstration projects that the Federal department or agency conducts or supports under this provision. The research or demonstration project must be published on this list prior to commencing the research involving human subjects.

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.

Note: Exempt categories 7 & 8 always require limited IRB review and are only available when broad consent will be (or has been) obtained. Currently, these are non-applicable because KCU has not adopted Broad Consent, nor does it anticipate it will conduct any research where Broad Consent would be a consideration.

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 in Section 10.3, #8.

8. Secondary research for which broad consent is required: Research involving the 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 Section 13.1 and Section 13.13;
   ii. Documentation of informed consent or waiver of documentation of consent was obtained in accordance with Section 13.8 or Section 13.11;
   iii. An IRB conducts a limited IRB review and makes the determination required by .111(a)(7): *When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data* and makes the determination that the research to be conducted is within the scope of the broad consent referenced in 8.i above; 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.

9.3 Procedures for Exemption Determination

To request an exempt determination, investigators submit the following materials via the IRB electronic system]:

1. A completed **Exemption Request** form;
2. Any subject materials such as recruitment materials, information sheets, consent form, scripts, and questionnaires, diaries, or surveys;
3. Any internal approval(s) for the research]
4. Letter(s) of permission from any non-KCU sites; or, when applicable, documentation of IRB approval or exemption from the external site;
5. Verification of current CITI training for all members of the research team; and

The IRB Chair, IRB Vice Chair, experienced IRB members and/or IRB Staff reviews all requests for exemptions and determines whether the request meets the criteria for exempt research. The reviewer's determination is documented into the IRB electronic system. If the request does not appear to meet the definition of human subject research, the reviewer evaluates the proposal as described in Section 4.

When the research requires limited IRB review, the review may be conducted using expedited review procedures by the IRB Chair or an experienced Chair-designated members of the IRB. As with all other research subject to IRB review requirements, when conducting limited IRB review the IRB has the authority to approve, require modifications in (to secure approval), or disapprove all research activities; and to suspend or terminate IRB approval. Actions of disapproval may only be made by the convened IRB. [45 CFR 46.109(a), 45 CFR 46.110]

Proposed modifications to the aspects of research subject to limited IRB review must be submitted to and approved by the IRB prior to implementation, except when necessary to eliminate apparent immediate hazards to the subject(s), in which case the change must be promptly reported to the IRB (i.e., within 10 business days). [45 CFR 46.108(a)(3)(iii)]

Continuing review is generally not required for research determined to be exempt, even when that research is subject to limited IRB review. However, the IRB may determine that continuing review is required for a particular study subject to limited IRB review, in which case it shall document the reasons for its determination in the IRB record and communicate the requirement to the investigator in the IRB determination letter. [45 CFR 46.109(f)(ii), 45 CFR 46.115(a)(3)]

The individual making the determination of exemption will determine whether to require additional protections for subjects in keeping with the guidelines of the Belmont Report.

The IRB staff will publish a letter documenting the outcome of the review in the IRB electronic system. The exempt application, review documentation, and determination letter are maintained in the same manner and for the same length of time as other IRB review documentation.

Exempt determinations will include a termination date, with the maximum time allotted being two Year If the investigator wants the research to extend beyond the termination date, the investigator must request another exemption determination by submitting the Annual Exempt Status Report . This process

will allow the investigator and the organization the opportunity to review and update the research activity and determine whether it still qualifies for exemption.

Investigators must report any proposed additions to study personnel so that CITI training can be verified and COI evaluated prior to their involvement with the research. Proposed modifications to the research itself must be submitted for a determination of whether the research still qualifies for exemption. Finally, investigators must submit a closure report when an exempt research project is complete so that the organization can maintain an accurate database of research activities.

10 IRB Review Process

The KCU IRB will review and ensure that research under its oversight meets all required ethical and regulatory criteria for initial and continuing review and any modifications of approved research. The IRB may conduct their review using the following review methods:

- Expedited Review
- Review by Convened IRB

10.1 Expedited Review

An IRB may use the expedited review procedure to review either or both of the following:

- Some or all of the research appearing on the list of categories of research eligible for expedited review unless the reviewer determines that the research involves more than minimal risk.
- Minor changes in research previously approved by the convened IRB. Note: review of minor changes does not alter the end-date of study approval
- Research for which limited IRB review is a condition of exemption under 45 CFR 46.104(d)(2)(iii), (d)(3)(i)(C), and (d)(7) and (8).

The standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review--expedited or convened--used by the IRB.

10.1.1 Definitions

Minimal Risk. 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.

Minor Change. A minor change is one which, in the judgment of the IRB reviewer, makes no substantial alteration in:

1. The acceptability of the risk-to-benefit analysis (i.e., the change does not increase the level of risk);
2. The research design or methods (adding procedures that are not eligible for expedited review (See Section 12.1.2) would be considered more than a minor change);
3. The number of local subjects to be enrolled in the research (usually not greater than 10% of the total requested);
4. The qualifications of the research team (i.e., the change does not negatively impact the expertise available to conduct the research);
5. The facilities available to support safe conduct of the research; or
6. Any other factor which would warrant review of the proposed changes by the convened IRB.

Minor changes also include the addition of sites to a protocol approved by the convened IRB so long as the investigator(s)/site(s) do not have a conflict of interest, potential compliance concerns (e.g., a 483 that has not been adequately resolved), or any other investigator or site-specific concerns (e.g., qualifications, facilities, or resources to safely conduct the research).

10.1.2 Categories of Research Eligible for Expedited Review

KCU applies the categories of research eligible for expedited review, which were published in the Federal Register notice Federal Register notice 63 FR 60364-60367, November 9, 1998.

The categories in this list apply regardless of the age of subjects, except as noted in category 2.

The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

Expedited Categories one (1) through seven (7) may be used for both initial and continuing review:

1. Clinical studies of drugs and medical devices only when condition (a) or (b) is met.
    a. Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)
    b. Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.
2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:
    a. From healthy, 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
    b. 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. (Note: Children are defined as "persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.)
3. Prospective collection of biological specimens for research purposes by noninvasive means.

    Examples: (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 gum base or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization; (k) vaginal swabs that do not go beyond the cervical os; rectal swabs that do not go beyond the rectum; and nasal swabs that do not go beyond the nares.

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.)

   Examples: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, Doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

5. Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for non-research purposes (such as medical treatment or diagnosis). (NOTE: Some research in this category may be exempt from the DHHS regulations for the protection of human subjects. See Exempt Categories and 45 CFR 46 101(b)(2) and b(3). This listing refers only to research that is not exempt.)

6. Collection of data from voice, video, digital, or image recordings made for research purposes.

7. Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior); or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (NOTE: Some research in this category may be exempt from the DHHS regulations for the protection of human subjects. See Exempt Categories and 45 CFR 46.101(b)(2). This listing refers only to research that is not exempt.)

Categories 8 and 9 apply only to continuing review.

8. Continuing review of research previously approved by the convened IRB as follows:

   a. Where (i) the research at KCU 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 (Note: "Long-term follow-up" includes research *interactions* that involve no more than minimal risk to subjects (e.g., quality of life surveys); and collection *of follow-up* data from procedures or interventions that would have been done as part of routine clinical practice to monitor a subject for disease progression or recurrence, regardless of whether the procedures or interventions are described in the research study, but not *interventions* that would not have been performed for clinical purposes, even if the research interventions involve no more than minimal risk.); ***or***

b. Where no subjects have ever been enrolled at KCU and no additional risks have been identified (Note: "no additional risks have been identified" means that neither the investigator nor the IRB has identified any additional risks from any institution engaged in the research project or from any other relevant source since the IRB's most recent prior review.); ***or***

c. Where the remaining research activities at KCU are limited to data analysis. (Note: Simply maintaining individually identifiable private information without using, studying, or analyzing such information is not human subject research and thus does not require continuing review.

9. Continuing review of research previously approved by the IRB at a convened meeting that meets the following conditions:

    a. The research is not conducted under an investigational new drug application (IND) or an investigational device exemption (IDE); ***and***

    b. Expedited review categories (2) through (8) do not apply to the research; ***and***

    c. The IRB has determined and documented at a convened meeting that the research, or the remaining research activity involving human subjects, involves no greater than minimal risk to the subjects; ***and***

    d. No additional risks of the research have been identified. (Note: "no additional risks have been identified" means that neither the investigator nor the IRB has identified any additional risks from any institution engaged in the research project or from any other relevant source since the IRB's most recent prior review.)

10.1.3 Expedited Review Procedures

Under an expedited review procedure, IRB review is carried out by the IRB Chair or by one or more reviewers designated by the Chair from among members and alternate members of the IRB. Designated reviewers must be professionally competent (i.e., experienced with and having demonstrated knowledge of and the ability to apply IRB review requirements) to conduct expedited reviews.

IRB members do not participate in the review of research in which they have with a conflict of interest (see Section 25.2) but may answer questions about the research if requested.

When reviewing research under an expedited review procedure, the IRB Chair, or designated reviewer, will receive and review the same materials that would be reviewed if the research were to be reviewed

by the convened IRB, and for previously approved research, will have access to the study history. The reviewer evaluates and documents whether the research qualifies for expedited review. When a reviewer determines that research subject to the Common Rule and that does fall within the expedited categories involves more than minimal risk, the reviewer will document the rationale for that determination and refer the research for review by the convened IRB. If the research otherwise does not meet the criteria for expedited review, then the reviewer will indicate that the research requires review by the convened IRB and the submission is placed on the next available IRB meeting agenda.

In reviewing the research, expedited reviewers will apply the same criteria for review and approval of research described throughout this manual and may exercise all of the authorities of the IRB except that the reviewers may not disapprove the research. A research activity may only be disapproved by the convened IRB.

Reviewers may use the appropriate reviewer checklist (e.g., initial, modification, continuing) to assess the criteria for approval and to document their review. For initial and continuing reviews, the documentation will include the category (ies) under which the research qualifies for expedited review. The checklist is maintained in the IRB electronic system. When expedited review is carried out by more than one IRB member and the reviewers disagree, the IRB Chair may make a final determination or refer the submission to the convened IRB for review.

A letter documenting the outcome of the review will be prepared by the IRB staff and provided to the investigator.

10.1.4 Informing the IRB

Members of the IRB will be apprised of expedited review approvals, including limited IRB reviews conducted using expedited review procedures, by means of a list in the agenda, or attached to the agenda, for the next scheduled meeting. Any IRB member can request to review the materials for any study by contacting the IRB Office.

10.2 Convened IRB Meetings

Except when an expedited review procedure is used, the IRB will conduct initial and continuing reviews of all non-exempt research, and exempt research subject to limited IRB review, at convened meetings at which a quorum of the members is present.

10.2.1 IRB Meeting Schedule

The IRB meets on a regular basis throughout the year (usually once per month). The schedule for the IRB may vary due to holidays, lack of quorum, or other reasons. The schedule for IRB meetings is provided to its members from IRB Staff. Special meetings may be called at as needed by the Chair or IO.

10.2.2 Preliminary Review

The IRB Staff will perform a preliminary review of all submissions for determination of completeness and accuracy, when applicable. Only complete submissions will be placed on the IRB agenda for review. The investigator will be informed of missing materials and any recommended changes. If an investigator is

submitting for the first time or is not be well-versed in submission procedures, consultations can be arranged with IRB Staff.

10.2.3 Primary and Secondary Reviewers

After it has been determined that a submission is complete, IRB staff with the assistance of the IRB Chair as needed, will assign submissions for review paying close attention to the subject matter of the research, the potential reviewer's area(s) of expertise, and representation for any vulnerable populations involved in the research. A "primary reviewer" will be assigned to each submission and will receive and review the full submission materials. When the IRB is presented with a research study which may be outside of the knowledge base or representative capacity of the IRB members, an outside consultant will be sought (See Section 10.5). Research studies for which appropriate expertise cannot be obtained for a given meeting will be deferred to another meeting when appropriate expertise is available.

Primary reviewers are responsible for:

- Performing an in-depth review of the submission materials and having a thorough understanding of the details
- Leading the discussion at the IRB meeting, by providing a summary and leading the IRB through the regulatory criteria for approval and any required determinations

One or more "secondary" reviewers may be assigned in addition to the primary reviewer. A secondary reviewer may be assigned to review the full submission materials or may be asked to review specified sections of the submission (e.g., the consent process and form(s).

All IRB members receive and are expected to review all studies, not just those assigned as primary [or secondary] reviewer.

When it can be anticipated that the primary reviewer may be absent from the meeting, a new primary reviewer will be assigned if possible, providing that they have the necessary expertise and sufficient time to review the materials in advance of the meeting. Absent reviewers can submit their written comments for presentation and consideration at the convened meeting. If an absent reviewer submits comments, those can indicate a recommendation regarding approval, but such recommendation will not be counted as a vote.

10.2.4 Materials received by the IRB

All required materials need to be submitted to the IRB office via IRBNet for inclusion on the IRB agenda. On occasion, when a review is time-sensitive, the IRB office may make an exception to this rule provided that there is still sufficient time for all members to review the submission materials. The meeting agenda will be prepared by IRB staff in consultation as needed with the IRB Chair. All IRB members receive the IRB agenda, prior meeting minutes, applicable business items, and research submission materials at least 5 business days before the scheduled meeting to allow sufficient time for review. On occasion, a time-sensitive item may be added to the agenda less than 5 business days in advance if circumstances warrant and the IRB staff have contacted the IRB members and verified that they will have sufficient time for review.

All IRB members are provided or have access in the IRB electronic system to all materials submitted for all studies on the agenda, which include the following, as applicable:

- The application or submission form (e.g., initial, continuing review, modification request, interim report)
- The proposed and/or previously approved Consent/Parental Permission/Assent Form(s)
- Proposed recruitment materials, including advertisements intended to be seen or heard by potential study participants

If an IRB member requires additional information to complete the review, they may contact the IRB office or the investigator. Any additional information should be provided to the other members.

10.2.5 Quorum

A quorum of the IRB consists of a majority (more than half) of the voting membership, including at least one member whose primary concern is in a non-scientific area. At meetings of the IRB, a quorum must be established and maintained for the deliberation and vote on all matters requiring a vote.

The IRB Chair, with the assistance of the IRB staff, will confirm that quorum is present before calling the meeting to order. The IRB Chair, with the assistance of the IRB staff, will be responsible to ensure that the IRB meeting remains appropriately convened. If a quorum is not maintained, either by losing a majority of the members, or losing all non-scientific members or another required member, the IRB may not take votes until quorum is restored.

In addition to the required attendance of at least one scientific member and at least one "non-scientist" member, it is generally expected that at least one unaffiliated member will be present at all IRB meetings. The IRB may, on occasion, meet without this representation; however, this should be the exception.

When the IRB regularly reviews research that involves subjects vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons, one or more individuals (e.g., IRB members, alternate members, or consultants) who are knowledgeable about and experienced with such subjects should be present during the review of the research.

IRB members are considered present and participating at a duly convened IRB meeting when either physically present or participating through electronic means (e.g., teleconferencing or video conferencing) that permits them to listen to and speak during IRB deliberations and voting. When not physically present, the IRB member must have received all pertinent materials prior to the meeting and must be able to participate actively and equally in all discussions.

Opinions of absent members may be considered by the attending IRB members but may not be counted as votes or to satisfy quorum requirements for convened meetings.

10.2.6 Meeting Procedures

The IRB Chair will call the meeting to order, once it has been determined that a quorum is in place. The Chair will remind IRB members to recuse themselves from the discussion and votes by leaving the room

when they have a conflict. The IRB will review and discuss the minutes from the prior meeting and determine if there are any revisions/corrections to be made. If there are no changes to be made, the minutes will be accepted as presented and considered final. If major revisions/corrections are necessary, the minutes will be amended and presented at the following IRB meeting. Minor revisions/corrections may be verified by the IRB Chair or Vice Chair outside of the meeting.

The IRB reviews submissions for initial and continuing review, requests for modifications to previously approved research, and other business items, as applicable (e.g., potentially serious noncompliance). The Primary [and Secondary] Reviewer presents an overview of the submission and assists the Chair in leading the IRB through the evaluation of the regulatory criteria for approval or other required determinations.

For the research to be approved, or any motion on a business item of the agenda to pass, it must receive the approval of a majority of those voting members present at the meeting.

IRB Recorder with assistance of the IRB staff are responsible for taking minutes at each IRB meeting.

10.2.7 Guests

Investigators and research staff may be invited to the IRB meeting, at the discretion of the IRB, to make a brief presentation or to answer questions about proposed or ongoing research. The investigator/research staff may not be present for the deliberations or vote on the research.

Other guests may be permitted to attend IRB meetings at the discretion of the IRB Chair. Such guests may be asked to sign a confidentiality agreement and do not participate in discussion unless requested by the IRB; under no circumstances may they vote.

10.3 Criteria for IRB Approval of Research

For the IRB to approve human subjects research, either through expedited review or by the convened IRB, it must determine that the following requirements are, or remain, satisfied.

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.
2. Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.
3. Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving subjects vulnerable to

coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons.

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 [45 CFR 46.116/21 CFR 50].
5. Informed consent will be appropriately documented, in accordance with, and to the extent required by the Federal Regulations [45 CFR 46.117/21 CFR 50].
6. When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.
7. When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.
8. For purposes of conducting the limited IRB review required by 45 CFR 46.104(d)(7), the IRB need not make the determinations at paragraphs (1) through (7) of this section, and shall make the following determinations:
    a. Broad consent for storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens is obtained in accordance with the requirements in Section 13.1 and Section 13.13;
    b. Broad consent is appropriately documented or waiver of documentation is appropriate, in accordance with 45 CFR 46.117; and
    c. 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.

When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, 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.

10.3.1 Risk/Benefit Assessment

The goal of the assessment is to ensure that the risks to research subjects posed by participation in the research are justified by the anticipated benefits to the subjects or society. Toward that end, the IRB must:

- Judge whether the anticipated benefit, either of new knowledge or of improved health or other direct benefit for the research subjects, justifies asking any person to undertake the risks; and
- Disapprove research in which the risks are judged unreasonable in relation to the anticipated benefits.

The assessment of the risks and benefits of proposed research involves a series of steps:

1. **Identify the risks** associated with the research, as distinguished from the risks of activities, diagnostic tests, treatments, or therapies the subjects would receive or undergo even if not participating in the research;
2. **Determine whether the risks will be minimized** to the extent possible by evaluating the necessity of procedures that impart risk and whether the data could be gained by procedures that are already being performed for other purposes or by alternative procedures that impart less risk;
3. **Identify the anticipated benefits** to be derived from the research, both direct benefits to subjects and possible benefits to society, science and others;
4. **Determine whether the risks are reasonable in relation to the benefits**, if any, and assess the importance of the knowledge that can reasonably be expected to result from the research.

In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research - as distinguished from risks and benefits subjects would receive even if not participating in the research.

The IRB should not consider possible long-range effects of applying knowledge gained in the research (e.g., the possible effects of the research on public policy) as among those research risks and benefits that fall within the purview of its responsibility.

The IRB should not consider any compensation that subjects may receive to be a benefit of the research.

When research subjects are assigned to different arms or otherwise undergo differing interventions, procedures, or exposures, the evaluation of risk and benefit should be made for each subject group (i.e., a "component analysis"). This is especially important when a subset of subjects will have no possibility of direct benefit but will be exposed to greater than minimal risks.

In addition to evaluation of the risks in the research, the IRB determines, based on the materials submitted by the investigator, that research studies have the resources necessary to protect participants, such as adequate time for the researchers to conduct and complete the research, adequate number of qualified staff, adequate facilities, access to a population that will allow recruitment of the necessary number of participants, availability of medical or psychosocial resources that participants might need as a consequence of the research.

10.3.1.1 Scientific or Scholarly Review

In order to assess the risks and benefits of proposed research, the IRB must determine that:

- The research uses procedures consistent with sound research design; and
- The research design is sound enough to yield the expected knowledge.

In making this determination, the IRB may draw on its own knowledge and expertise, or the IRB may draw on the knowledge and expertise of others, such as reviews by a funding agency, a scientific review committee, or departmental review. When scientific or scholarly review is conducted by a KCU individual

or entity external to the IRB, documentation of the outcome and detains of that review must be provided to the IRB for review and consideration.

10.3.2 Equitable Selection of Subjects

The IRB evaluates whether the selection of subjects is equitable with respect to gender, age, class, etc. by reviewing the IRB application, protocol, and other materials and information. The IRB will not approve a study that does not provide adequately for the equitable selection of subjects or has not provided an appropriate scientific and ethical justification for excluding classes of persons who might benefit from the research. In making this determination, the IRB evaluates:

- The purposes of the research;
- The setting in which the research occurs;
- Scientific and ethical justification for including subjects vulnerable to coercion or undue influence such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons;
- The scientific and ethical justification for excluding classes of persons who might benefit from the research; and
- The inclusion/exclusion criteria, and the procedures/materials intended for use for the identification and recruitment of potential subjects.

At the time of the continuing review the IRB evaluates whether subject selection has been equitable.

10.3.2.1 Recruitment of Subjects

The investigator will provide the IRB with a plan for recruitment of potential subjects. All recruiting materials will be submitted to the IRB, including advertisements, flyers, scripts, information sheets and brochures. The IRB should ensure that the recruitment plan and materials appropriately protect the rights and welfare of the prospective subjects (e.g., do not present undue influence). See Section 12.4.9 for a discussion of IRB review of advertisements and Section 12.4.10 for a discussion of IRB review of payments.

10.3.3 Informed Consent

The IRB will ensure that informed consent will be sought from each prospective subject or the subject's legally authorized representative (LAR), in accordance with, and to the extent required by 45 CFR 46.116 and 21 CFR 50.20. In addition, the IRB will ensure that informed consent will be appropriately documented, in accordance with, and to the extent required by 45 CFR 46.117 and 21 CFR 50.27. The IRB will ensure, as part of its review, that the information in the consent document and process is consistent with the research plan, and, when applicable, the HIPAA authorization. See Section 15 for a detailed discussion on informed consent.

10.3.4 Data and Safety Monitoring

For research that is more than minimal risk, the investigator should submit a data and safety monitoring (DSM) plan. The initial plan submitted to the IRB should describe the procedures for safety monitoring, reporting of unanticipated problems involving risks to subjects or others, descriptions of interim safety reviews and the procedures planned for providing DSM findings to the IRB. DSM may be performed by a researcher, medical monitor, safety monitoring committee, or other means.

The IRB reviews the safety monitoring plan and determines if it makes adequate provision for monitoring data to ensure the safety of subjects and for addressing problems that may arise over the course of the study. If a plan was not submitted, the IRB determines whether a plan is required, and, depending on the circumstances, what the plan should include. The overall elements of the monitoring plan depend on the potential risks, complexity, and nature of the research study.

The principles the IRB applies in evaluating the adequacy of a proposed DSM plan include:

- Monitoring should be commensurate with the nature, complexity, size, and risks of the research
- Monitoring should be timely. Frequency should be commensurate with risk. Conclusions are reported to the IRB
- For low risk studies, continuous, close monitoring by the study investigator or an independent party may be an adequate and appropriate format for monitoring, with prompt reporting of problems to the IRB, sponsor, and regulatory bodies, as applicable
- For greater than minimal risk studies that do not include a plan for monitoring by a Data Safety Monitoring Board (DSMB) or Data Monitoring Committee (DMC), and that are blinded, multi-site, involve vulnerable populations, or involve high-risk interventions or procedures, the IRB will carefully evaluate the proposed DSM plan and may require establishment of a DSMB, DMC, or other methods to enhance the monitoring and management of safety

Data and Safety Monitoring plans should specify:

- The entity or person(s) who will perform the monitoring, and the independence or affiliation that the entity or person(s) has with the sponsor or investigator
- The safety information that will be collected and monitored, including serious adverse events and unanticipated problems
- The frequency or periodicity of review of safety data
- The procedures for analysis and interpretation of the data
- The procedures for review of scientific literature and data from other sources that may inform the safety or conduct of the study
- The conditions that trigger a suspension or termination of the research (i.e., stopping rules), when appropriate
- The procedures for reporting findings to the IRB, including a summary description of what information, or the types of information, that will be provided

For a Data Safety Monitoring Board (DSMB) or Data Monitoring Committee (DMC), the plan should also describe the composition of the board or committee. Generally, a DSMB or DMC should be composed of experts in all scientific disciplines needed to interpret the data and ensure subject safety. Clinical trial experts, biostatisticians, bioethicists, and clinicians knowledgeable about the disease/condition and treatment under study should be part of the monitoring group or be available if warranted.

The National Institutes of Health (NIH) requires the establishment of DSMBs for multi-site clinical trials involving interventions that entail potential risk to the participants.

When DSMBs or DMCs are used, IRBs conducting continuing review of research may rely on a current statement, or the most recent report, from the DSMB or DMC which indicates that it has and will continue to review study-wide adverse events, study wide interim findings, and any recent literature that may be relevant to the research, in lieu of requiring that this information be submitted directly to the IRB.

10.3.5 Privacy and Confidentiality

The IRB will determine whether adequate procedures are in place to **protect the privacy** of subjects and to **maintain the confidentiality of the data**.

10.3.5.1 Definitions

Privacy. Having control over the extent, timing, and circumstances of sharing oneself (physically, behaviorally, or intellectually) with others. It is the state or condition of being free from unauthorized intrusion, being observed or disturbed by other people.

Confidentiality. Methods used to ensure that information obtained by investigators about subjects is not improperly divulged.

Private information. Information 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).

Sensitive Information. Data or information, on any storage media or in any form or format, which requires protection due to the risk of harm that could result from inadvertent or deliberate disclosure, unauthorized access, misuse, alteration, or loss or destruction of the information (e.g., could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subject's financial standing, employability, or reputation).

Identifiable information. Information where the identity of the subject is or may readily be ascertained by the investigator or associated with the information.

10.3.5.2 Privacy

The IRB must determine whether the activities in the research appropriately protect the privacy of potential and enrolled subjects. In order to make that determination, the IRB must obtain information regarding how the investigators plan to access subjects or subjects' private, identifiable information, and

the subjects' expectations of privacy in the situation. Investigators must have appropriate authorization to access the subjects or the subjects' information.

In developing strategies for the protection of privacy, consideration is given to the:

- Methods used to identify and contact potential participants
- Settings where recruitment and research activities will occur
- Appropriateness of personnel and others present for research activities
- Methods to verify the identity of subjects prior to disclosing information (e.g., with phone calls)
- Methods used to obtain information about participants, and the nature of the requested information, including whether the data is the minimum necessary to achieve the aims of the research
- Information that is obtained about individuals other than the "target subjects", (e.g., a subject provides information about a family member for a survey) and whether such individuals meet the regulatory definition of "human subject"

10.3.5.3 Confidentiality

The IRB must determine if appropriate protections are in place to minimize the likelihood that information about subjects or their participation in research will be inappropriately accessed or divulged. Safeguards designed to protect confidentiality should be commensurate with the potential of harm from unauthorized, inappropriate or unintentional disclosure.

The IRB assesses whether there are adequate provisions to protect data confidentiality by evaluating the methods used to obtain, record, share, and store information about individuals who may be recruited to participate in studies and about subjects. The investigator will provide the IRB with a plan regarding the procedures to be taken to protect the confidentiality of research data and sensitive information. The investigator will provide information regarding information security procedures and plans to address the protection of paper documents, other physical media (e.g., audio or videotapes), and electronic data, and information regarding the use, maintenance, storage, and transmission of information. The IRB will review the information received from the investigator and determine whether the confidentiality of research data is sufficiently protected. In some cases, the IRB may also require that a Certificate of Confidentiality is obtained to protect data from compelled disclosure (See Section 28.2).

In reviewing confidentiality protections, the IRB shall consider whether or not the data or other information accessed or gathered for research purposes is sensitive, and the nature, probability, and magnitude of harms that would be likely to result from a disclosure of collected information outside the research. The IRB will evaluate the effectiveness of proposed de-identification techniques, coding systems, encryption methods, methods of transmission, storage facilities, access limitations, and other relevant factors in determining the adequacy of confidentiality protections. In reviewing confidentiality protections, the IRB will also consider regulations and organizational requirements and policies regarding the use of information and information security.

Research regulated by the FDA that involves the use of electronic data collection/storage systems must comply with the requirements of 21 CFR Part 11.

10.3.6 Vulnerable Populations

Certain individuals, by nature of their age or mental, physical, economic, educational, or other circumstances, may be more vulnerable to coercion or undue influence than others. At the time of initial review, and when a proposed modification includes the involvement of vulnerable subject populations, the IRB will consider the scientific and ethical reasons for including vulnerable subjects in research. When appropriate, the IRB may determine and require that additional safeguards be put into place for vulnerable subjects, such as those without decision-making capacity.

For an extensive discussion about the IRB's review process for specific populations of vulnerable subjects, please refer to Section 16.

10.4 Additional Considerations

10.4.1 Determination of Risk Level

At the time of initial review, the IRB will make a determination regarding the risks associated with the research. Risks associated with the research will generally be classified as either "minimal" or "greater than minimal" with additional classifications as required by the various subparts or FDA regulations. Risk determinations may vary over the life of a research study depending on the procedures and risks that subjects will be exposed to as the research progresses. Because of this, the IRB may reevaluate the risk determination with modifications to the research, at continuing review, and when new information becomes available. The level of risk associated with the research influences eligibility for expedited review. The meeting minutes will reflect the convened IRB's determination regarding risk levels; expedited reviewers will document the determination of risk level on the reviewer's checklist.

10.4.2 Period of Approval

At the time of initial review and at continuing review, the IRB will make a determination regarding the period of approval. All studies will be reviewed by the IRB at intervals appropriate to the degree of risk but no less than once per year. The IRB will conduct continuing review of research requiring review by the convened IRB at intervals appropriate to the degree of risk of the research, but not less than once per year, except as described in Section 10.5;

In some circumstances, a shorter review interval (e.g., semi-annually, quarterly, or after accrual of a specific number of participants) may be required (see below). The meeting minutes will reflect the convened IRB's determination regarding review frequency; when applicable, expedited reviewers will document the determination of risk level in their review.

IRB approval is considered to have lapsed at the end of the day of the expiration date of the approval (i.e., the expiration date is the last day research can be conducted). For a new study reviewed by the IRB, the approval commences on the date that the IRB conducts its final review of the study; that is, the date that the convened IRB or expedited reviewer approves the research **or** the date (effective date) when it has been verified that the requirements of the IRB have been satisfied following an action of "Conditions Required for Approval". The expiration date of the initial approval period, which is the date

by which the first continuing review must occur, may be as late as one year after the effective date of initial IRB approval.

The use of the effective date of IRB approval to determine the latest permissible date for continuing review *only applies to the first continuing review*. For all subsequent continuing reviews of a research study subject to convened board review, the date the convened IRB or the date that the expedited reviewer conducts continuing review and approves the study (with or without conditions) determines the latest permissible date of the next continuing review.

The approval date and approval expiration date are clearly noted on IRB determination letters and must be strictly adhered to. Investigators should allow sufficient time for development and review of continuing review submissions. As a courtesy, the IRB electronic system sends reminders to the investigator prior to the study's expiration date, notifying him or her that the study is due for a continuing review or when approval has expired.

IRB review of a proposed modification to research ordinarily does not alter the date by which continuing review must occur. This is because continuing review is review of the full research project, not simply a change to it.

The regulations make no provision for any grace period extending the conduct of research beyond the expiration date of IRB approval. Therefore, continuing review and re-approval of research must occur before midnight of the date when IRB approval expires. If the IRB performs continuing review within 30 days before the IRB approval period expires, the IRB may retain the anniversary date as the date by which the continuing review must occur.

10.4.3 Review More Often Than Annually

The following factors will be considered when determining which studies require review more frequently than on an annual basis:

1. The probability and magnitude of anticipated risks to subjects;
2. The likely medical/psychological/social/legal/educational condition of the proposed subjects;
3. The overall qualifications of the investigator and other members of the research team;
4. The specific experience of the investigator and other members of the research team in conducting similar research;
5. The nature and frequency of adverse events observed in similar research at this and other institutions;
6. The novelty of the research making unanticipated adverse events/unanticipated problems more likely;
7. The involvement of especially vulnerable populations likely to be subject to undue influence or coercion (e.g., terminally ill);
8. A history of serious or continuing noncompliance on the part of the investigator; and
9. Any other factors that the IRB deems relevant.

In specifying an approval period of less than one year, the IRB may define the period with either a time interval or a maximum number of enrolled subjects. If a maximum number of subjects is used to define the approval period, it is understood that the approval period in no case can exceed one year unless the study does not require continuing review.

Independent Verification That No Material Changes Have Occurred

The IRB recognizes that protecting the rights and welfare of subjects sometimes requires that the IRB use sources other than the investigator to independently verify that no material changes have occurred since previous IRB review.

The IRB will determine the need for verification from outside sources on a case-by-case basis. The following factors will be considered when determining which studies require independent verification:

1. The nature, probability, and magnitude of anticipated risks to subjects;
2. The degree of uncertainty regarding the risks involved;
3. Whether the research involves novel therapies or procedures;
4. The vulnerability(ies) of the subject population;
5. The projected rate of enrollment;
6. The experience and expertise of the investigators;
7. The IRB's previous experience with the investigators or the sponsor (e.g., compliance history, complaints from subjects, etc.);
8. The probable nature and frequency of changes that may ordinarily be expected in the type of research;
9. Whether the research undergoes routine independent monitoring;
10. Whether concerns about possible material changes occurring without IRB approval have been raised based on information provided in continuing review reports or from other sources; and
11. Any other factors that suggest independent verification is warranted.

In making determinations about independent verification, the IRB may prospectively require that such verification take place at predetermined intervals during the approval period, or may require such verification at the time of continuing review, review of modification requests, and/or unanticipated problems.

If any material changes have occurred without IRB review and approval, the IRB will decide the corrective action to be taken (see Section 19 on Noncompliance).

10.4.4 Consent Monitoring

In reviewing the adequacy of informed consent procedures for proposed research, the IRB may on occasion determine that monitoring of the consent process by an impartial observer (e.g., consent monitor) is required in order to reduce the possibility of coercion and undue influence, ensure that the approved consent process is being followed, or ensure that subjects are truly giving informed consent.

Such monitoring may be particularly warranted for:

1. High risk studies;
2. Studies that involve particularly complicated procedures or interventions;
3. Studies where recruitment will occur in situations or circumstances that may negatively impact the consent process (e.g., the Emergency Room);
4. Studies involving highly vulnerable populations (e.g., ICU patients, children who are wards);
5. Studies involving study staff with minimal experience in administering consent to potential study participants; or
6. Other situations when the IRB has concerns that consent process may not be/is not being conducted appropriately (e.g., prior investigator noncompliance, etc.).

Monitoring may also be appropriate as a corrective action where the IRB has identified problems associated with a particular investigator or a research project.

If the IRB determines that consent monitoring is required, the IRB may consult with the IO and IRB Chair, and others to develop an appropriate plan. The investigator will be notified of the IRB's determination and the reasons for the determination. Arrangements will be made with the investigator for the monitoring of the consent process, typically for a specified number of subjects. When warranted, the investigator may not be notified until after the observation has occurred. When observing the consent process, the monitor will evaluate whether:

1. The informed consent process was appropriately conducted and documented;
2. The participant had sufficient time to consider study participation, and to ask questions and have them answered;
3. The consent process involved coercion or undue influence;
4. The information was accurate and conveyed in understandable language; and
5. The subject appeared to understand the information and provided their voluntary consent.

Following the monitoring, a report of the findings will be submitted to the IRB, which will determine the appropriate action to be taken, if any.

10.4.5 Investigator Qualifications

The IRB reviews credentials, curriculum vitae, resumes, or other relevant materials to determine whether investigators and members of the research team are appropriately qualified to conduct the research. The IRB may rely upon other KCU processes (e.g., credentialing) to inform this determination.

10.4.6 Significant New Findings

During the course of research, significant new knowledge or findings about the research, the test article, and/or the condition under study may develop. The investigator must report any significant new findings to the IRB and the IRB will review them and evaluate the impact on the subjects' rights and welfare. When the new knowledge or findings may affect the risks or benefits to subjects or subjects' willingness

to continue in the research, the IRB may require that the investigator contact subjects to inform them of the new information. The IRB will communicate this requirement to the investigator. If the study is still enrolling subjects, the consent document should be updated. The IRB may require that the currently enrolled subjects be re-consented or otherwise provided with the new information. When appropriate, the IRB may also require that former subjects be provided with the new information (e.g., late emerging safety information).

10.4.7 Conflicts of Interest (COI)

As part of its review process, the IRB will make a final determination as to whether any COI is adequately addressed and protects the human subjects in the research. Likewise, when there is an institutional COI, the IRB has final authority to determine whether the conflict and the management plan, if any, allow the study to be approved. (See Section 25 for a more detailed discussion of COI).

The IRB also receives information regarding any Institutional Conflict of Interest exists and has final authority to determine whether the Institutional Conflict, the Financial Interest, and the management plan, if any, allow the study to be approved. See Section 21.3 for a more detailed discussion of Institutional COI.

10.4.8 Advertisements and Recruitment Materials

The IRB must review and approve all advertisements and recruitment materials prior to posting, use, or distribution. The IRB will review:

1. The information contained in the advertisement/recruitment material
2. The mode/method of its communication;
3. The final copy of printed advertisement/recruitment material
4. The proposed script and final version of any audio/video advertisements/recruitment materials

This information must be submitted to the IRB with the initial application, or, if proposed after study approval, as a modification request.

The IRB reviews the material to assure that the material is accurate and is not coercive or unduly optimistic, creating undue influence to the subject to participate. This includes, but is not limited to the following (as applicable):

1. Statements implying a certainty of favorable outcome or other benefits beyond what was outlined in the consent form and the research plan;
2. Emphasis on payment or the amount to be paid, such as bold type or larger font on printed media;
3. The inclusion of exculpatory language.

Recruitment materials should be limited to the information prospective subjects need to determine their eligibility and interest. When appropriately worded, the following items may be included:

1. The name and address of the investigator and/or research facility;
2. The condition being studied and/or the purpose of the research;

3. In summary form, the criteria that will be used to determine eligibility for the study;
4. The time or other commitment required of the subjects;
5. The location of the research and the person or office to contact for further information;
6. A clear statement that the activity is research and not treatment;
7. A brief list of potential benefits.

Once approved by the IRB, advertisements and recruitment materials cannot be altered or manipulated in any way without prior IRB approval.

The first contact prospective study subjects make is often with a person who follows a script to determine basic eligibility for the specific study. The IRB should review the script and procedures to ensure that the screening procedures adequately protect the rights and welfare of the prospective subjects.

10.4.9 Payments and Reimbursement

Payments to research subjects are commonly proposed as an incentive for participation in recognition of the time, effort, inconveniences, and discomforts that participation in the proposed research may entail. In contrast to payments, reimbursement is provided to cover actual costs incurred by subjects as a result of participation (e.g., travel, parking, lodging, etc.). Payment arrangements should be managed separately from reimbursement whenever possible because the ethical considerations differ (as well as the potential tax implications). Reimbursement offsets costs and may decrease financial risks associated with participation and in doing so may facilitate equitable selection of subjects. In contrast, the amount, timing, and nature of payments may unduly influence potential subjects' decision-making, influencing them to accept discomforts or risks that they otherwise would find unacceptable and interfering with truly voluntary informed consent. Payment arrangements may also create issues with equitable selection of subjects, including the societal distribution of research risks and benefits and the generalizability of the research results.

The IRB must consider the proposed amount of payment, the method and timing of disbursement, the subject population, the recruitment methods and materials, and the information provided within the proposed consent form in order to evaluate the acceptability of a proposed payment plan. The IRB does not consider payment as a benefit when weighing the risks and benefits of the research, payment is an incentive not a benefit of the research.

Investigators who wish to pay research subjects must include in their application to the IRB the amount and schedule of all payments and the justification or basis for payment. Such justification should substantiate that proposed payments are reasonable and commensurate with the expected contributions of the subject and do not constitute (or appear to constitute) undue pressure on the potential subject to volunteer for the research study.

When research involves multiple visits or interactions, payment should be prorated and not be contingent upon the participant completing the entire study. The IRB does not allow the entire payment to be contingent upon completion of the entire study. Further, any amount paid as bonus for completion

of the entire study should not be so great that it could unduly induce subjects to remain in the study when they otherwise would have withdrawn.

The consent form must describe the terms of payment including the amount and schedule of payments and any conditions under which subjects would receive partial payment (e.g., if they withdraw from the study before their participation is completed) or no payment.

Plans to reimburse subjects for incurred expenses must also be outlined in the application to the IRB and described within the consent.

KCU has policies in place to address how and what information is collected and reported for subjects who receive the amount of compensation required to be reported to the Internal Revenue Service (IRS). When applicable, the consent form must disclose the information that will be collected (e.g., Social Security Number), who will be provided or have access to the information, and the circumstances that necessitate IRS reporting.

10.4.10 Non-Monetary Gifts and Incentives

Similar to financial incentives, non-monetary gifts or incentives can also present problems of undue influence or coercion that impact a potential subject's ability to fully and freely consider participation in research.

If subjects will be provided with non-monetary gifts or tokens of appreciation, such as course credit, totes, books, toys, or other non-monetary gifts or incentives, the approximate retail value must be described to the IRB and the IRB will be provided with a description, photo, or sample product to review.

The IRB will review all gifts and incentives being particularly sensitive to the influence of power or authority, whether perceived or actual, over free decision-making. Overt coercion (e.g., threatening loss of credit, or access to services or programs, to which the potential subjects are otherwise entitled) is never appropriate. Moreover, it must be clear that choosing to not participate will not adversely affect an individual's relationship with the organization or its staff or the provision of services in any way (e.g., loss of credits or access to programs).

Investigators should carefully structure incentives and methods of disbursement so that while the incentives may serve as a factor in a subject's decision to participate, that they have not served to unduly influence or coerce participation.

10.4.11 State and Local Laws

The IRB considers and adheres to all applicable state and local laws in the jurisdictions where the research is taking place. KCU and its IRB rely on KCU Counsel for the interpretation and application of Missouri law and the laws of any other jurisdiction where research is conducted as they apply to human subjects research. The IRB will ensure that consent forms are consistent with applicable state and local laws.

10.5 Continuing Review

The IRB will conduct continuing review of ongoing research at intervals that are appropriate to the level of risk of the research, but not less than once per year. The date by which continuing review must occur will be recorded in the IRB electronic system and on initial and continuing review approval letters. Continuing review must occur as long as the research remains active, including when the remaining research activities are limited to the analysis of private identifiable information.

10.5.1 Continuing Review Process

As a courtesy to investigators, the IRB electronic system will send out reminder notices to investigators in advance of the expiration date; however, it is the investigator's responsibility to ensure that the continuing review of ongoing research is approved prior to the expiration date. By federal regulation, no extension to that date can be granted.

Investigators must submit the following for continuing review, as applicable to the research:

1. The Continuing Review Application (this serves as the progress report);
2. CITI training certificates for each member of the research team;
3. Other relevant documentation, as applicable.

IRB office staff attend the convened meetings and has access to the complete study files for each study on the agenda. IRB members can request the study file or any additional materials from the IRB staff prior to the meeting.

10.5.2 IRB Considerations for Continuing Review

In order to re-approve research at the time of continuing review, the IRB must determine that the regulatory criteria for approval continue to be satisfied. Because the research was previously found to satisfy the criteria for approval, the IRB focuses its considerations at the time of continuing review on whether any new information is available that would affect the IRB's prior determination that the criteria for approval are satisfied. The IRB pays particular attention to four aspects of the research:

1. Risk assessment and monitoring;
2. Adequacy of the informed consent process;
3. Local investigator and organizational issues; and
4. Research progress.

10.5.3 Convened Board Review

In conducting continuing review of research not eligible for expedited review, IRB members are provided all of the materials listed in Section 12.2.4 and are responsible for reviewing, at a minimum, the Continuing Review Application, the current IRB-approved consent form(s) (when applicable), and any proposed modifications to the research or consent form(s).

The Primary Reviewer is responsible for reviewing the complete materials submitted for continuing review to facilitate the review and discussion at the meeting. At the meeting, the Primary and Secondary Reviewers assist the Chair in leading the IRB through the discussion of the submission and the regulatory criteria for approval.

10.5.4 Expedited Review

In conducting continuing review under expedited procedures, the IRB Chair or designated reviewer(s) receive all of the previously noted materials. The reviewer(s) determine whether the research meets the criteria allowing continuing review using the expedited procedure, and if so, whether the research continues to meet the regulatory criteria for approval. If the research no longer requires continuing review under the Common Rule (See Section 10.5) and the IRB reviewer determines that continuing review is required, the reviewer shall document the rationale.

Generally, if research did not qualify for expedited review at the time of initial review, it does not qualify for expedited review at the time of continuing review, unless it has progressed to the point that it involves only one or both of the following:

- Data analysis, including analysis of identifiable private information or identifiable biospecimens, or
- Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care;

and in limited circumstances described by expedited review categories (8) and (9) (see Expedited Review Categories in Section 10.1.2). It is also possible that research activities that previously qualified for expedited review, have changed or will change, such that expedited continuing review would no longer be permitted.

10.5.5 Possible IRB Actions after Continuing Review

As with Initial Review, at the time of Continuing Review, the convened IRB or IRB Member(s) conducting expedited review may take any of the actions described in Section 11.

If an IRB member conducting expedited review believes that continuation of the research should be disapproved, they will refer the proposed modification to the convened board for review. If the proposed changes raise significant concerns on the part of the IRB, the IRB may vote to suspend or terminate the research (See Section 13 for a detailed discussion of suspensions and terminations).

If a research study receives Conditions Required for Approval at the time of the continuing review, the IRB will specify whether any conditions need to be satisfied before an investigator can continue particular research activities related to those conditions or requirements that must be adhered to until the conditions of approval have been satisfied. For example, if at the time of continuing review, the IRB requires the investigator to change the research protocol to include a specific new procedure for screening prospective subjects, the IRB could approve the research with the following condition: "*Research activities involving currently enrolled subjects may continue, but no new subjects may be enrolled until a designated IRB member reviews a revised protocol and verifies that the protocol includes the new screening procedure"*. Additionally, the IRB may specify a time period, such as 1, 2, or 3 months,

for the condition(s) to be satisfied as long as the activity with conditions is not begun or restarted until final approval is granted.

10.5.6 Lapses in Continuing Review

The regulations permit no grace period or approval extension after expiration of approval. Research that continues after the approval period has expired is research conducted without IRB approval. If re-approval does not occur within the time set by the IRB, all research activities must stop, including recruitment (media advertisements must be withdrawn), enrollment, consent, interventions, interactions, and data collection. **This will occur even if the investigator has submitted the continuing review materials before the expiration date. Therefore, investigators must submit their continuing review materials enough in advance of expiration to allow sufficient time for IRB review before the expiration date**.

When the IRB approves research with conditions at the time of continuing review before the expiration date of the preceding IRB approval period, IRB approval does not lapse if the investigator needs additional time – beyond the date on which the preceding IRB approval would have expired – to satisfy some or all of the IRB's conditions. However, the investigator and the IRB should make every effort to resolve any conditions and finalize approval in as timely a manner as possible.

In the event that study approval does expire, the IRB staff sends a notification to the investigator noting the expiration of approval and instructions that all research activities must stop. If the investigator fails to respond to the notification, and does not submit continuing review materials or a closure report within 30 days, the IRB staff will refer the matter to the IRB Chair to evaluate as possible noncompliance (See Section 19).

The lapse of IRB approval due to a failure to complete continuing review and obtain re-approval prior to expiration of the prior approval does not ordinarily constitute a suspension or termination of IRB approval, for federal reporting purposes; however, the failure to meet continuing review obligations may be grounds for suspension or termination of the research. If the IRB notes a pattern of noncompliance with the requirements for continuing review (e.g., an investigator repeatedly or deliberately neglects to submit materials for continuing review in a timely fashion or the IRB itself is not meeting the continuing review dates), the IRB should determine the reasons for the non-compliance and take appropriate corrective actions. When research is subject to federal reporting mandates, the IRB must report to FDA/OHRP any instance of serious or continuing noncompliance with FDA regulations or IRB requirements or determinations.

10.5.6.1 Management of Enrolled Subjects During Lapse

While enrollment of new subjects cannot occur after the expiration of IRB approval, the IRB recognizes that temporarily continuing participation of already enrolled subjects may be necessary or appropriate, for example, when the research interventions hold out the prospect of direct benefit to the subjects, or when withholding those interventions or safety monitoring procedures would place subjects at increased risk. In these instances, the investigator must, at the earliest opportunity, contact the IRB office and submit a request to continue those research activities that are in the best interests of subjects. Such a request should specifically list the research activities that should continue, provide justification,

and indicate whether the request applies to all or only certain subjects. The IRB Chair or designee will review the request and provide a determination regarding what activities, if any, may continue during the lapse. Such a determination may include a time limit or other conditions or restrictions. If the IRB decides that already enrolled subjects should continue to receive the interventions that were being administered to subjects under the research project, data collection (especially safety information) should also continue for such subjects.

When there is insufficient time to obtain an IRB determination (e.g., the study regimen includes daily administration of an investigational agent), the investigator may make an initial determination in consultation with the subjects' treating physician, if appropriate. In such cases, the investigator must, as soon as possible, contact the IRB office and submit a request for confirmation that the IRB agrees with the determination. The IRB Chair or designee will review the request and provide a determination. In the event that the IRB does not agree with the investigator's determination, or only agrees in part (e.g., agrees that some but not all of the activities are in the best interests of subjects), the IRB will notify the investigator who must then comply with the IRB's requirements or request a re-review of the determination by providing additional justification or information that the IRB may not have considered.

10.6 Modification of an Approved Protocol

Investigators may wish to modify or amend approved research. **Investigators must seek IRB approval before making any changes, no matter how minor, in approved research** unless the change is necessary to eliminate an immediate hazards to the subject (in which case the IRB must then be notified at once).

Investigators should consider whether the proposed changes to the research alter the original scope, purpose, or intent of the research. When the research itself is fundamentally changed, the IRB will typically require a new study application rather than allow such changes to be made through a modification to the existing research plan.

10.6.1 Procedures

Investigators proposing to modify a study must submit a Modification/Amendment Request Form and all supporting documents identified in the form via the IRB electronic system for review. The modifications may not be implemented until the IRB has reviewed and approved the proposed changes. When the modification involves the addition of investigators or study personnel, the investigators/personnel may not assume any study responsibilities involving human subjects or their identifiable data until the IRB has approved their participation.

IRB office staff will review the submission and make an initial determination whether the proposed changes may be approved through an expedited review process (i.e., changes to expedited research that do not alter the eligibility of the research for expedited review or minor changes to convened board studies) or whether the modification warrants convened board review. The IRB reviewer(s) using the expedited procedure has the ultimate responsibility to determine that the proposed changes may be approved through the expedited review procedure and, if not, must refer the research study for convened board review.

10.6.2 Convened Board Review of Modifications

When a proposed change in a convened board research study is not minor, or when a proposed change to an expedited study renders it no longer eligible for expedited review, the IRB must review and approve the proposed change at a convened meeting before the change can be implemented. The only exception is implementation of a change necessary to eliminate apparent immediate hazards to the research subjects. In such a case, the IRB must be promptly informed of the change following its implementation and will review the change to determine whether it was consistent with ensuring the subjects' continued welfare.

All IRB members are provided and review all documents provided by the investigator. The complete IRB file and relevant IRB meeting minutes are available to IRB members upon request

The Primary Reviewer is responsible for reviewing the complete materials submitted for a modification to facilitate the review and discussion at the meeting. At the meeting, the Primary and Secondary Reviewers assist the Chair in leading the IRB through the discussion of the submission and the regulatory criteria for approval.

When the IRB reviews modifications to previously approved research, the IRB considers whether information about those modifications might relate to subjects' welfare or willingness to continue to take part in the research, and, if so, whether to provide that information to future, current, or past subjects.

10.6.3 Expedited review of Modifications

An IRB may use expedited review procedures to review changes to expedited research (as long as the proposed changes would not make the research no longer eligible for expedited review) and for minor changes to studies normally subject to convened IRB review. An expedited review may be carried out by the IRB Chair or the experienced members that have been designated by the Chair to conduct expedited reviews.

Expedited reviewer(s) determine whether the modifications meet the criteria allowing review using the expedited procedure, and, if so, whether the research with the proposed modifications continues to meet the regulatory criteria for approval. The reviewer(s) will also evaluate whether the modification alters any previous determinations (e.g., a Subpart determination), or necessitates any additional determinations (e.g., for vulnerable populations).

The reviewer will also consider whether information about the modifications might relate to future, current, or past subjects' welfare or willingness to continue to take part in the research, and, if so, whether to provide that information to subjects.

10.6.4 Possible IRB Actions after Modification Review

As with initial review, the convened IRB or IRB Member(s) conducting expedited review may take any of the actions described in Section 11. (see Section 11 for a detailed description of these actions):

If an IRB member conducting expedited review believes that the proposed modifications should be disapproved, they will refer the proposed modification to the convened board for review. If the

proposed changes raise significant concerns on the part of the IRB, the IRB may vote to suspend or terminate the research (See Section 13 for a detailed discussion of suspensions and terminations).

10.7 Closure of Research Studies

The completion or early termination of the study, is a change in research activity and must be reported to the IRB. Although subjects will no longer be "at risk" under the study, a final report to the IRB allows it to close its files as well as providing information that may be used by the IRB in the evaluation and approval of related studies.

Studies may be closed when the involvement of human subjects ceases (interventions, interactions, observations, and the gathering, use, study, and analysis of identifiable private information, including specimens, are all complete).

Investigators may maintain the data that they collected, including identifiable private data, if this is consistent with the IRB-approved research plan. However, investigators may not conduct any additional analysis of identified data without applying for IRB approval or exemption. Investigators must continue to protect the confidentiality of the data as described to the IRB and honor any other commitments that were agreed to as part of the approved research including, for example, future use of data or specimens, provision of research results to subjects, and provision of any outstanding payments or compensation.

The IRB will review study closure reports, typically by expedited review, and either approve the closure of the study or request additional information or confirmation of facts from the investigator.

11 IRB Actions, Failure to Respond, Appeals

11.1 IRB Actions

In conducting its review of research, the IRB may take any of the following actions. With the exception of disapproval, the actions listed below may be used for either expedited or convened board review including limited IRB review. . Disapproval can only be decided at a convened IRB meeting. An expedited reviewer cannot disapprove a study.

Approval. The research, continuing review of the research, proposed modification to previously approved research, or another item is approved. The IRB has made all of the determinations required for approval (i.e., approval criteria and any applicable special determinations (e.g., waivers, alterations, vulnerable population determinations, etc.)). No further action is needed.

Conditions Required for Approval.

The research, continuing review of the research, proposed modification to the previously approved research, or other item is approved but conditions must be satisfied before the approval becomes effective.

The IRB may approve research with conditions if, given scope and nature of the conditions, the IRB is able, based on the assumption that the conditions are satisfied, to make all of the determinations required for approval (i.e., approval criteria and any applicable special determinations (e.g., waivers, alterations, vulnerable population determinations, etc.)). Any time the IRB cannot make one or more of the determinations required for approval, the IRB may not approve the study with conditions.

The IRB may require the following as conditions of approval of research:

1. Confirmation of specific assumptions or understanding on the part of the IRB regarding how the research will be conducted (e.g., confirmation that research excludes children);
2. Submission of additional documentation (e.g., certificate of training);
3. Precise language changes to the study, consent, or other study documents; or
4. Substantive changes to the study, consent, or other study documents along with clearly stated parameters that the changes must satisfy.

When the IRB approves research with conditions, the conditions will be documented in the IRB minutes for research reviewed at a convened meeting for research reviewed under an expedited review procedure.

When the convened IRB approves research with conditions, the IRB may designate the IRB Chair (and/or other qualified individual(s)) to review responsive materials from the investigator and determine that the conditions have been satisfied. If the conditions have not been satisfied, or are only partially satisfied, the responsive materials must be referred to the convened IRB for review. When an expedited reviewer approves research with conditions, the original expedited reviewer (and/or other qualified individual(s)) will receive the response materials.

After verification, the following will be documented in IRB records and written communication to the investigator:

1. The date when the IRB determined that the criteria for approval were satisfied (i.e., the "approval date");
2. The date when verification was made that all IRB conditions have been satisfied (i.e., the “effective date”), and;
3. For initial approval and continuing reviews, the date by which continuing review must occur (i.e., the “expiration date”)

The IRB will be informed of the outcome of the review of the investigator’s response.

Partial Approval or Approval with Limitations or Restrictions.

This action may be taken when the IRB only approves some but not all components of the research while other components of the research that require modification or clarification cannot begin or continue until approved by the IRB. For example, the IRB could determine that a study may begin but that children cannot be enrolled until the investigator submits, and the IRB approves, a plan for assent; the IRB could stipulate that the approval for the local site only includes adult subjects; the IRB could approve one phase of the research but require that a modification is submitted before future phases begin; or the IRB could limit the research responsibilities of an investigator due to a COI.

Defer. *(This action is sometimes referred to tabled.)* This action is taken by the IRB when modifications are required of the nature or amount that the full IRB cannot make or specify exact changes or parameters, or additional information or clarification is needed in order to determine that one or more criteria for approval are satisfied (e.g., the risks and benefits cannot be assessed until additional information is provided.).

The deferral is documented in the IRB minutes (for convened review) or reviewer checklist (for expedited review) and is communicated to the investigator in writing.

When the convened IRB defers approval, the responsive materials from the investigator will be provided to the convened IRB for review at a subsequent meeting. When an expedited reviewer defers approval, the original expedited reviewer will review the response materials whenever possible. When the original expedited reviewer is unavailable, the response will be reviewed by the IRB Chair or other qualified IRB member who has been designated to conduct expedited review.

Disapprove. This action is taken when the convened IRB determines that the proposed research activity does not satisfy the criteria for approval and that it cannot be modified to render it approvable (or the sponsor or investigator will not make necessary modifications that would render the research approvable).

Approval in Principle. Per HHS regulations at 45 CFR 46.118, there are circumstances in which a sponsoring department or agency may require certification of IRB approval as a condition of submitting for or releasing funds but before definitive plans for the involvement of human subjects have been developed (e.g., grants in which the procedures involving human subjects are dependent on preliminary activities such as the completion of animal studies or development of instruments). In these circumstances, the IRB may grant “approval in principle” without having reviewed the as yet undeveloped procedures or materials. The IRB Chair or designee will review the available information (i.e., the grant or proposal and any supplemental information provided by the investigator) and, if

appropriate, will provide certification of IRB approval in principal. Any approvals in principle will note that IRB approval must be obtained before any activities involving human subjects may commence.

Acknowledgment. In addition to the above actions, the IRB may **acknowledge** reports and other items that don't involve prospective changes to already approved research. For example, the IRB may acknowledge the report of a protocol deviation but approve, require modifications in, or disapprove any associated corrective action plan. Further, the IRB may approve an item but include **comments** noting certain requirements, restrictions, or understandings. For example, with collaborative research, the IRB may note that approval must also be obtained from another IRB with jurisdiction and that the letter documenting that approval must submitted to the KCU IRB before human research activities involving the collaborating organization or personnel may commence.

11.2 Failure to Respond

Upon review of a research study, the IRB may require changes or request certain information from an investigator. Failure to respond to IRB required changes or requests for information within 60 days (or less if the IRB determines that the information must be submitted earlier to ensure protection of the research subjects) may result in suspension or termination of IRB approval for the study. For studies that have not yet been approved, the study submission may be administratively withdrawn. At its discretion, the IRB may grant an extension beyond 60 days if the investigator contacts the IRB office prior to the deadline and presents sufficient cause for delay.

11.3 Reporting IRB Actions

All IRB actions are communicated to the investigator, and/or designated contact person for the research study, via the publication of a letter in the IRB electronic system within ten (10) working days, whenever possible, of the review. When applicable, a stamped copy of the approved consent form, parental permission form, and/or assent form will also be published. For IRB actions of conditions required for approval or deferral, the notification will include a listing of the conditions or requirements that must be satisfied or responded to. For a disapproval, suspension, or termination, the notification will include the basis for the action and will offer the investigator an opportunity to respond in person or in writing.

The IRB reports its findings and actions to the organization in the form of its minutes, which are distributed by IRB staff to the KCU IO.

11.4 Appeal of IRB Decisions

When the IRB suspends, terminates, or disapproves research, the IRB letter communicating the decision will include the basis for the action and will offer the investigator the opportunity to respond in person or in writing. Additionally, whenever an investigator disagrees with an IRB requirement or decision, or believes that providing the IRB with additional information may result in a different outcome, they may request that the IRB reconsider its decision by submitting a memo and other supportive materials via the IRB electronic system. The investigator may be invited to attend the IRB meeting to discuss the request and provide information, but will be asked to leave prior to the IRB's final deliberations and vote.

Where there is disagreement between the IRB and the investigator regarding the nature and extent of the requested changes or the necessity of or basis for a suspension or termination, and these disagreements cannot be resolved, the investigator and/or the IRB may make an appeal to the IO for a resolution of the matter. The IO may organize a meeting to help facilitate discussion between the IRB and the investigator. While the IO may provide input and make recommendations to the investigator and IRB for expeditious resolution of the matter, final determinations for approval/disapproval remain under the purview of the IRB.

Because the IO is responsible for policies and procedures followed by the IRB, the IO may review IRB decisions to ensure that the decision-making process is appropriate. If the IO has concerns regarding the process that the IRB followed in making a decision, the IO may ask the IRB to reconsider the decision. However, the IO cannot overrule an IRB decision.

12 Suspensions, Terminations, and Investigator Holds

12.1 Suspension/Termination

IRB approval may be suspended or terminated if research is not being conducted in accordance with IRB or regulatory requirements or has been associated with unexpected problems or serious harm to subjects. (See Section 18 for a discussion of unanticipated problems and Section 19 for a discussion of noncompliance.) The IRB's authority to suspend or terminate research applies to all research subject to IRB approval, including exempt research with limited IRB review and research for which continuing review is no longer required.

The IO has the authority to suspend or terminate the organization's approval for research. Such actions will be promptly reported to the IRB so that the IRB can review the circumstances and take any necessary actions relevant to IRB review and oversight.

Suspension of IRB approval is a directive of the convened IRB or IRB Chair or Vice Chair to temporarily stop some or all previously approved research activities. The IRB Chair may temporarily suspend IRB approval, in part or in full, when the available information suggests that actions must be taken to protect human subjects or the integrity of the research, prior to the next convened meeting of the IRB. Temporary suspensions by the Chair or Vice Chair will be reported to the convened IRB at the next scheduled meeting at which time the convened IRB will determine if the suspension should continue, be lifted, or be modified. Suspended research studies remain open and require continuing review. Investigators must continue to provide reports to both the IRB and sponsors just as if there had never been a suspension (i.e., all events that need to be reported during a study need to continue to be reported during the suspension period).

When approval of some or all research activities is suspended by the IRB, the IRB will consider whether subjects should be notified and any actions necessary to ensure that the rights, safety, and welfare of subjects are appropriately protected.

The IRB will notify the investigator of suspensions in writing; a call or email may precede the written notice when appropriate. Written notices of suspensions will include a statement of the reason(s) for

the IRB's action and any requirements or conditions associated with the suspension (e.g., notification of subjects). The investigator will be provided with an opportunity to respond in person or in writing.

Suspensions of IRB approval must be reported promptly to the IO, sponsors including federal department or agency heads, and federal oversight agencies as applicable. See Section 22 for a detailed discussion of reporting requirements.

Termination of IRB approval is a directive of the convened IRB to permanently stop all activities in a previously approved research study. Terminated research studies are closed and no longer require continuing review. Terminations of IRB approval of research studies must be made by the convened IRB.

When study approval is terminated by the IRB, in addition to stopping all research activities, the IRB will consider notification of subjects and any actions necessary to ensure that the rights, safety, and welfare of subjects are appropriately protected.

The IRB will notify the investigator of terminations in writing; a call or email may precede the written notice when appropriate. Written notices of terminations will include a statement of the reasons for the IRB's action and any requirements associated with the termination (e.g., notification of subjects). The investigator shall be provided with an opportunity to respond in person or in writing.

Terminations of IRB approval must be reported promptly to the IO, sponsors including federal department or agency heads, and federal oversight agencies as applicable. See Section 22 for a detailed discussion of reporting requirements.

12.2 Investigator Hold

An investigator may request an investigator hold when the investigator wishes to temporarily or permanently stop some or all approved research activities. Such a hold is initiated by an investigator, but must be immediately reported to the IRB so that the IRB can consider whether any additional actions are necessary to protect subjects. Investigator holds are not equivalent to IRB suspensions or terminations.

12.2.1 Procedures

Investigators must submit a memo and any supporting materials via the IRB electronic system to inform the IRB of the hold. The memo and materials should include:

1. A statement that the investigator is voluntarily placing a study on hold;
    a. The reason(s) for the hold;
    b. A description of the research activities that will be stopped;
    c. Proposed actions to be taken to protect current participants; and
    d. Any actions that will be taken prior to IRB approval of proposed changes in order to eliminate apparent immediate risk of harm.
2. Upon receipt, IRB staff notify the IRB Chair or designee and place the research on the next available agenda for review;

3. For greater than minimal risk studies, the IRB Chair or designee, in consultation with the investigator, determines whether any additional procedures need to be followed to protect the rights and welfare of current participants as described in Section 13.3;
4. For greater than minimal risk studies, the IRB Chair or designee, in consultation with the investigator, determines whether and how currently enrolled subjects will be notified of the hold;
5. Investigators may request a revision of the research on hold by submitting a request for revisions to previously approved research.
6. Prior to lifting the hold, the investigator must seek approval from the IRB so that the IRB may consider whether subjects are appropriately protected and if the research remains approvable.

12.3 Protection of Currently Enrolled Participants

Before a study hold, termination, or suspension, is put into effect the IRB Chair/Vice Chair or convened IRB considers whether any additional procedures need to be followed to protect the rights and welfare of current participants. Such procedures might include:

- Transferring subjects to another investigator/site
- Allowing continuation of some research activities under the supervision of an independent monitor
- Requiring or permitting follow-up of subjects for safety reasons
- Requiring adverse events or outcomes to be reported to the IRB and the sponsor
- Notification of current subjects
- Notification of former subjects

13 Unanticipated Problems Involving Risks to Subjects or Others

Regulations require an organization to have written procedures for ensuring prompt reporting of "unanticipated problems involving risk to subjects or others" (also referred to as UPs, UAPs, and UPIRTSOs).

This section provides definitions and procedures for the reporting of UAPs to the KCU IRB. Investigators conducting research under the oversight of an external IRB must comply with the reporting requirements of the external IRB and the internal reporting requirements outlined in Section 8.2.

In conducting its review of protocol deviations, noncompliance, subject complaints, and other reportable events, the IRB will also consider whether the event or issue was caused by, contributed to, or otherwise related to an UAP.

13.1 Definitions

Unanticipated problems involving risk to participants or others. Unanticipated problems involving risks to subjects or others (UAPs) refer to any incident, experience, outcome, or new information that:

1. Is unexpected; **and**
2. Is at least possibly related to participation in the research; **and**
3. Indicates that subjects or others are at a greater risk of harm (including physical, psychological, economic, legal or social harm) than was previously known or recognized

UAPs also encompass Unanticipated Adverse Device Effects, as defined below.

Unexpected. The incident, experience or outcome is not expected (in terms of nature, severity, or frequency) given the research procedures that are described in the study-related documents, such as the IRB-approved research protocol/research plan and informed consent documents; and the characteristics of the subject population being studied.

Related. There is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research.

Adverse Event. For the purposes of these policies and procedures, an adverse event (AE) is any untoward or unfavorable occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject's participation in the research, whether or not considered related to the subject's participation in the research. Adverse events encompass both physical and psychological harms. They occur most commonly in the context of biomedical research, although on occasion, they can occur in the context of social and behavioral research.

13.2 Procedures

13.2.1 Reporting

Investigators must report the following events or issues to the IRB as soon as possible but within **7 working days** after the investigator first learns of the event using the "Event Report" form in the IRB electronic system.

If investigators are uncertain but believe that the event might represent an UAP, a report should be submitted.

Examples of UAPs include:

1. A single occurrence of a serious, unexpected event that is uncommon and strongly associated with the intervention (such as acute emotional reactions);
2. A single occurrence, or more often a small number of occurrences, of a serious, unexpected event that is not commonly associated with intervention, but uncommon in the study population (e.g., panic attacks or severe depression);
3. Multiple occurrences of an AE that, based on an aggregate analysis, is determined to be an unanticipated problem. There should be a determination that the series of AEs represents a signal that the AEs were not just isolated occurrences and involve risk to human subjects (e.g., a comparison of rates across treatment groups reveals higher rate in the intervention arm versus a control). A summary and analyses supporting the determination should accompany the report;
4. An AE that is described or addressed in the protocol, or informed consent documents, but occurs at a specificity or severity that is inconsistent with prior observations. For example, if suicide in depressed subject occurs at a higher rate than would be anticipated based on the intervention). A discussion of the divergence from the expected specificity or severity should accompany the report;
5. AEs involving direct harm to subjects enrolled by the local investigator which in the opinion of the investigator or sponsor, may represent an UAP;
6. Reports (including reports from DSMBs/DMCs) that indicate that risks are greater than previously known or that indicate that the research should be modified, suspended, or halted.
7. Sponsor or lead investigator/coordinating center imposed suspension or termination of some or all research activities;
8. An unanticipated event related to the research that exposes subjects to potential risk but that does not involve direct harm to subjects;
9. A breach of confidentiality or loss of research data (e.g., a laptop or thumb drive is lost or stolen);

10. An unanticipated event related to the research that results in actual harm or exposes individuals other than the research subjects (e.g., investigators, research assistants, students, the public, etc.) to potential risk;
11. New information that indicates increased risk, new risk(s), or decrease to potential benefit from what was previously understood. Examples include:
    a. An interim analysis or safety monitoring report indicates that the frequency or magnitude of harms or benefits may be different than initially presented to the IRB;
    b. A report or publication that indicates the risks, benefits, or merit of the research are different from what was previously understood.

13.2.2 Review Procedures

1. Upon receipt of the Event Report, the IRB staff pre-reviews the submission and, if needed, contacts the investigator for corrections or additional information.
2. The IRB Chair or designated reviewer receives and reviews the report and makes an initial determination as to whether the event represents an UAP. If needed, the Chair or designee may request additional information from the investigator, sponsor, or others (including study committees, such as data monitoring committees, data safety monitoring boards, or steering committees).
3. If the reviewer determines that the problem does not meet the definition of an UAP, they will determine whether any additional actions are necessary to ensure the protection of human subjects. As warranted, the reviewer may refer the matter to the convened IRB for review. The results of the review will be recorded in review notes in the electronic system and communicated to the investigator.
4. If the reviewer determines that the event may be an UAP, the report will be referred for review by the convened IRB. The convened IRB will determine whether the event is a UAP and whether any additional actions, such as those outlined below, are necessary to ensure the protection of human subjects. If needed, the IRB may request additional information from the investigator, sponsor, or others (including study committees, such as data monitoring committees, data safety monitoring boards, or steering committees). The results of the review will be recorded in the IRB minutes and communicated to the investigator.
5. Based upon the circumstances, the IRB may take any of the following actions, or others, to ensure the protection of human subjects:
    a. Requiring modifications to the protocol or plan or procedures for implantation of the research (Research Plan) as described in the application and other materials submitted to the IRB;
    b. Revising the continuing review timetable;
    c. Modifying the consent process;

d. Modifying the consent document;

e. Providing additional information to current participants (e.g., whenever the information may relate to the subject's rights, welfare, or willingness to continue participation);

f. Providing additional information to past participants;

g. Requiring additional training of the investigator and/or study staff;

h. Requiring that current subjects re-consent to participation;

i. Monitoring the research;

j. Monitoring consent;

k. Reporting or referral to appropriate parties (e.g., the IO);

l. Suspending IRB approval;

m. Terminating IRB approval;

n. Other actions as appropriate given the specific circumstances.

When the IRB determines that an event is an UAP, the IRB staff will follow the procedures for reporting to regulatory agencies, sponsors, and organizational officials in Section 22. When appropriate, a preliminary report may be submitted while more information is obtained to inform the determination or actions.

14 Noncompliance

This section provides definitions and procedures for the reporting and review of known or suspected noncompliance for research under the oversight of the KCU IRB. Research under the oversight of an external IRB must comply with the reporting requirements of the external IRB and the internal reporting requirements outlined in Section 8.2.

In conducting its review of protocol deviations, unanticipated problems, subject complaints, and other reportable events, the IRB will also consider whether the event or issue was caused by, contributed to, or otherwise related to noncompliance.

14.1 Definitions

Noncompliance is defined as the failure to follow federal, state, or local regulations governing human subject research, institutional policies related to human subject research, or the requirements or determinations of the IRB. Noncompliance may be minor or sporadic or it may be serious or continuing.

Serious Noncompliance is defined as noncompliance that, in the judgment of the convened IRB, creates an increase in risks to subjects, adversely affects the rights, welfare, or safety of subjects, or adversely affects the scientific integrity of the study. Willful violation of policies and/or federal regulations may also constitute serious noncompliance.

Continuing Noncompliance is defined as a pattern of noncompliance that, in the judgment of the convened IRB, suggests a likelihood that instances of noncompliance will continue unless the IRB or institution intervenes.

Allegation of Noncompliance. Allegation of Noncompliance is defined as an unproved assertion of noncompliance.

14.2 Reporting

Investigators and their study staff are required to report instances of possible noncompliance to the IRB within **7 working days** of discovery using the Event Report form in the IRB electronic system. Additionally, anyone may report concerns of possible noncompliance to the ORSPORSPor IRB verbally, by email, or other means. In such cases, the reporting party is responsible for making these reports in good faith, maintaining confidentiality and, unless reporting anonymously, cooperating with any subsequent fact-finding in relation to the report.

If an individual, whether investigator, study staff or other, is uncertain whether there is cause to report noncompliance, he or she may contact the IO or IRB Chair directly to discuss the situation informally.

14.3 Review Procedures

1. Upon receipt of the Event Report, the IRB staff pre-reviews the submission and, if needed, contacts the investigator for corrections or additional information. If the report came from someone other than the investigator verbally, by email, or by other means, IRB staff

will develop a written report summarizing the available information and will upload the report into the IRB electronic system. If the information provided suggests that subjects may be at risk of harm without immediate intervention or that research misconduct may have occurred, the IRB Chair, and, when appropriate, the IO, will be notified so that they can take any necessary steps to ensure the safety of subjects or investigate the matter.

2. The IRB Chair or designated reviewer receives and reviews the report and makes an initial determination as to whether the event represents noncompliance, and, if so, if the noncompliance may be serious or continuing. If needed, the reviewer may request additional information from the investigator or others. When circumstances warrant, the IO and The IRB Chair may bypass this step and assign the report for convened board review.
3. If the reviewer determines that the event or issue is not noncompliance, or is noncompliance but not serious or continuing, they will review any proposed corrective and preventative action plans and determine if the plan is acceptable as proposed or if modifications to the plan or additional actions are required. As warranted, the reviewer may refer the matter to the convened IRB for review. The results of the review will be recorded in the electronic system and communicated to the investigator.
4. If the reviewer determines that the event or issue may be serious or continuing noncompliance, the report will be referred for review by the convened IRB. The convened IRB will determine whether the event is serious or continuing noncompliance. The IRB will review any proposed corrective and preventative action plans and determine if the plan is acceptable as proposed or if modifications to the plan or additional actions, such as those outline below, are necessary to ensure the protection of human subjects. If needed, the IRB may request additional information from the investigator or others. The results of the review will be recorded in the IRB minutes and communicated to the investigator.
5. When the IRB determines that an event is serious or continuing noncompliance, the IRB may take any of the following actions, or others, to ensure the protection of human subjects:
    a. Requiring modifications to the protocol or research plan
    b. Revising the continuing review timetable
    c. Modifying the consent process
    d. Modifying the consent document
    e. Providing additional information to current participants (e.g., whenever the information may relate to the subject's willingness to continue participation)
    f. Providing additional information to past participants
    g. Requiring additional training of the investigator and/or study staff
    h. Requiring that current subjects re-consent to participation

i. Monitoring the research

j. Monitoring consent

k. Reporting or referral to appropriate parties (e.g., the IO)

l. Suspending IRB approval

m. Terminating IRB approval

n. Other actions as appropriate given the specific circumstances

6. When the IRB determines that an event is serious or continuing noncompliance, the IRB staff will follow the procedures for reporting to regulatory agencies, sponsors, and organizational officials in Section 22. When appropriate, a preliminary report may be submitted while more information is obtained to inform the determination or actions.
7. Investigators may request that the IRB reconsider its determination by following the procedures in Section 11.4.

15 Complaints

The IRB will be responsive and sensitive to the complaints or concerns expressed by subjects or others and will respond to all complaints or concerns in a confidential and timely manner. The PI and all other research team members are responsible for the safety and welfare of all subjects enrolled in their studies. When investigators or team members hear complaints or concerns from subjects, he or she will try to resolve them.

Investigators conducting research under the auspices of KCU must report complaints to the KCU IRB regardless of who serves as the IRB of record. Investigators conducting research under the oversight of another IRB must comply with the reporting requirements of the other IRB and the internal reporting requirements outlined in Section 8.2. Investigators conducting research under the oversight of the KCU IRB report complaints using the Event Report form in the IRB electronic system. Investigators are encouraged to contact the IO or IRB Chair when they are having difficulty resolving a complaint or concern, and whenever circumstances warrant (e.g., immediate attention is needed).

When the IRB office is the direct recipient of complaints or concerns, the staff will do the following:

1. Immediately contact the IO and IRB Chair.
2. Document the complaint or allegation. When appropriate, the staff may request that the subject submit the complaint in writing.
3. Reassure the subject that the IRB will take all necessary measures to inquire into the circumstances and to address the issue.
4. Provide written confirmation of receipt of the complaint to the subject, if the subject is willing to provide contact information.
5. Convey the information to the IRB of record in a timely manner.

6. When appropriate, contact the investigator for additional information or to assist with resolution.
7. When appropriate, contact other resources (e.g., Risk Management) to assist with information-gathering or resolution.

For research under the oversight of the KCU IRB, the IRB Chair or designee will consider the complaint or concern and take any reasonable steps necessary to investigate and/or resolve the issue, if appropriate, prior to review and consideration by the IRB. A report will be provided to the IRB at the next available meeting if the research is subject to convened IRB review, or provided to the designated expedited reviewer if the research is eligible for expedited review. When reviewing complaints, the IRB will consider whether the complaint was the result of, or related to, an UAP or noncompliance, and, if so, will follow the relevant procedures. The IRB Chair or designated expedited reviewer may refer any complaint for review by the convened IRB. The IRB minutes, or reviewer comments for expedited reviews, will reflect the action(s) taken and, if necessary, notice to the appropriate officials and/or agencies.

The IRB will maintain written copies of complaints and concerns and will document the investigation and resolution. The complainant will be notified promptly following resolution of the complaint or concern, when appropriate, and if contact information has been provided. If the IRB receives a complaint, or identifies information while investigating a complaint, that is indicative of possible misconduct in research, KCU's IO will be notified immediately.

16 Other Reportable Information

When research is under the oversight of the KCU IRB, in addition to UAPs, noncompliance, and complaints, any change to the research implemented without IRB approval and any information that may impact the rights, safety, or welfare of subjects or inform the IRB's oversight of the research must be reported to the IRB within **7 working days** of discovery. Investigators conducting research under the oversight of an external IRB must comply with the reporting requirements of the external IRB and the internal reporting requirements outlined in Section 8.2.

Other reportable information includes, but is not limited to, the following:

1. Changes made to the research without prior IRB approval to eliminate apparent immediate hazards to the subject(s);
2. Protocol Deviations - any variation from the IRB approved research plan that happens without prior review and approval of the IRB and isn't necessary to eliminate apparent immediate hazards to the subject(s);
3. Monitoring, audit, and inspection reports in accordance with Section 2.1 of this manual;
4. Sponsor or coordinating center reports;
5. Data Safety Monitoring reports, including reports from DSMBs, DMCs, and others;
6. Enrollment or inclusion of vulnerable populations not previously approved by the IRB for the study (e.g., prisoner, pregnant woman, neonate, child, adult with impaired decision-making capacity);
7. When an existing subject becomes a member of a vulnerable population not previously approved by the IRB for inclusion in the study (e.g., incarceration, pregnancy, or change in decision-making capacity of an already enrolled subject);
8. Holds, suspensions, or terminations of a study, in part or in full, by an investigator, sponsor, or others;
9. Changes that impact the ability of the PI to conduct or supervise the study, temporarily or permanently;
10. Changes that impact the qualifications of investigators or research staff members such as actions taken by regulatory authorities, licensing boards, or credentialing committees;
11. New information that may impact the rights, welfare, or willingness of subjects to continue in the research.

16.1 Review Procedures

1. Upon receipt of the information, the IRB staff pre-reviews the submission and, if needed, contacts the investigator for corrections or additional information. If the information provided suggests that subjects may be at risk of harm without immediate intervention or that research misconduct may have occurred, the IRB Chair, and, when appropriate,

the IO, will be notified so that they can take any necessary steps to ensure the safety of subjects or investigate the matter.

2. The IRB Chair or designated reviewer receives and reviews the report and if the report may represent an UAP or noncompliance, reviews the report as described in Section 18 or 19. When circumstances warrant, the IRB Staff may bypass this step and assign the report for convened board review.
3. If the reviewer determines that the event or issue is not noncompliance or an UAP, they will review the event or issue, any proposed corrective and preventative action plans, and determine if any additional actions are needed to ensure the protection of human subjects. As warranted, the reviewer may refer the matter to the convened IRB for review. The results of the review will be recorded in the electronic system and communicated to the investigator.

17 Reporting to Federal Agencies, Departments, and Organizational Officials

Federal regulations require prompt reporting to appropriate institutional officials and, as applicable, the federal department or agency (e.g., OHRP, FDA), of (i) any unanticipated problems involving risks to subjects or others; (ii) any serious or continuing noncompliance with the applicable federal regulations or the requirements or determinations of the IRB; and (iii) any suspension or termination of IRB approval. KCU IRB complies with this requirement as follows. When research is under the oversight of an external IRB, the terms of the agreement with that IRB will guide reporting.

17.1 Procedures

IRB staff will initiate these procedures as soon as the IRB takes any of the following actions:

1. Determines that an event may be considered an unanticipated problem involving risks to participants or others
2. Determines that noncompliance was serious or continuing
3. Suspends or terminates approval of research

The IO or designee is responsible for preparing reports or letters which includes the following information:

1. Reason for the report (Unanticipated problem involving risks to subjects or others, serious or continuing noncompliance, suspension or termination of IRB approval)
2. Name of the involved institution(s)
3. Title of the research project and/or grant proposal in which the problem occurred
4. Name of the investigator on the project
5. Number of the research project assigned by the IRB and the number of any applicable federal award(s) (grant, contract, or cooperative agreement)
6. A detailed description of the problem including the findings of the organization and the reasons for the IRB's decision
7. Actions the institution is taking or plans to take to address the problem (e.g., revise the protocol, suspend subject enrollment, terminate the research, revise the informed consent document, inform enrolled subjects, increase monitoring, etc.)
8. Plans, if any, to send a follow-up or final report by the earlier of
    a. A specific date
    b. When an investigation has been completed or a corrective action plan has been implemented
9. The IRB Chair and the IO review the letter and recommend modifications as needed
10. The IO is the signatory

11. The IRB Staff sends a copy of the report to:
12. The IRB Chair
13. The IO
14. Federal agencies, as follows:
    a. OHRP, if the study is subject to DHHS regulations or subject to a DHHS FWA.
    b. If the study is conducted or supported by a Common Rule agency other than DHHS, the report is sent to OHRP or the head of the federal agency, as required by the agency.
    c. If the study is conducted or supported by a federal agency that has not adopted the Common Rule, and reporting is required, the report is sent to the party identified by the agency.
    d. FDA, if the study is subject to FDA regulations.

    Note: Reporting to a regulatory agency is not required if the event occurred at a site that was not subject to the direct oversight of the organization, and the agency has been notified of the event by another party (e.g., sponsor).
15. Sponsor, if the study is sponsored
16. Investigator
17. Others as deemed appropriate by the IO

The IO and IRB Staff ensures that all steps of this policy are completed within 30 working days of the determination. If additional time is needed to gather facts, or determine corrective actions, a preliminary report will be submitted within 30 days, to be followed by a final report as described above.

18 Obtaining Informed Consent from Research Subjects

No investigator conducting research under the auspices of KCU may involve a human being as a subject in research without obtaining the legally effective informed consent of the subject or the subject's legally authorized representative (LAR) (See Section 13.3) unless a waiver of consent has been approved by the IRB of record. Except as provided in Sections 15.10, 15.11, and 15.12 of these procedures, informed consent must be documented using a written consent form approved by the IRB.

The IRB will evaluate both the consent process and the procedures for documenting informed consent to ensure that adequate informed consent is obtained from participants.

The following procedures describe the requirements for obtaining consent from subjects in research conducted under the auspices of KCU. When the KCU IRB is serving as the IRB of record for external sites or personnel, the below requirements may be adapted as appropriate based upon the local context where the research will occur (e.g., who may serve as a LAR).

18.1 General Requirements

The requirement to obtain the legally effective informed consent of individuals before involving them in research is one of the central protections provided for by the federal regulations and KCU ORSP. Investigators are required to obtain legally effective informed consent from a subject or the subject's LAR unless the requirement has been waived by the IRB. When informed consent is required, it must be sought prospectively, and properly documented.

Except as provided elsewhere in these Standard Operating Procedures:

1. Before involving a human subject in research, an investigator shall obtain the legally effective informed consent of the subject or the subject's LAR
2. An investigator shall seek informed consent only under circumstances that provide the prospective subject or the LAR sufficient opportunity to discuss and consider whether or not to participate and that minimize the possibility of coercion or undue influence
3. The information that is given to the subject or the LAR shall be in language understandable to the subject or the LAR
4. The prospective subject or the LAR must be provided with the information that a reasonable person would want to have in order to make an informed decision about whether to participate, and an opportunity to discuss that information
5. Informed consent must begin with 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. This part of the informed consent must be organized and presented in a way that facilitates comprehension
6. Informed consent as a whole must present information in sufficient detail relating to the research, and must be organized and presented in a way that does not merely provide lists of isolated facts, but rather facilitates the prospective subject's or LAR's understanding of the reasons why one might or might not want to participate
7. No informed consent may include any exculpatory language through which the subject or the LAR is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence.

These informed consent requirements are not intended to preempt any applicable federal, state, or local laws (including tribal laws passed by the official governing body of an American Indian or Alaska Native tribe) that have additional requirements for informed consent to be legally effective.

The informed consent process involves three key features: (1) disclosing to the prospective human subject information needed to make an informed decision; (2) facilitating the understanding of what has been disclosed; and (3) promoting the voluntariness of the decision about whether or not to participate in the Research.

Informed consent is more than just a signature on a form. It is a process of information exchange to include reading, discussing, receiving answers to any questions, and signing the consent document. The informed consent process is the critical communication link between the prospective human subject and an investigator, beginning with the initial approach by an investigator and continuing through the completion of the research study. Investigators must have received the appropriate training and be knowledgeable about the study procedures, potential risks, anticipated benefits, and alternatives in order that they may appropriately describe the research and answer questions. The exchange of information between the investigator and study participant can occur via one or more of the following modes of communication, among others; face to face dialogue; mail; electronic interface, telephone, or fax; however, obtaining informed consent must allow for a dialogue so that the potential subject has the opportunity to ask questions and receive responses. Investigators must obtain consent prior to entering a subject into a study, gathering data about a subject, and/or conducting any procedures required by the research plan, unless consent is waived by the IRB. See Section 18.10.1 for an exclusion for certain screening and recruitment activities.

If someone other than the investigator conducts the interview and obtains consent, the investigator needs to formally delegate this responsibility, and the person so delegated must have received appropriate training to perform this activity. The person so delegated must be knowledgeable about the research to be conducted and the consenting process, and must have the expertise be able to answer questions about the study including those regarding risks, procedures, and alternatives.

The IRB of record is the final authority on the content of the consent documents that are presented to prospective subjects.

18.2 Additional Requirements

Informed consent must be obtained under the following circumstances:

1. Informed consent may only be obtained from subjects who have the legal and mental capacity to give consent. For subjects without that capacity, permission must be obtained from a legal guardian with appropriate authority to make decisions regarding the activities called for in the research or a legally authorized representative (LAR);
2. The informed consent information must be presented in language that is understandable to the subject (or LAR/guardian). To the extent possible, the language should be understandable by a person who is educated to 8th grade level and layman's terms shall be used in the description of the research. The IRB may require or allow different readability standards based upon the characteristics of the target subject population;
3. For subjects with Limited English Proficiency (LEP), informed consent must be obtained in a language that is understandable to the subject (or LAR/guardian). In accordance with this policy, the KCU IRB requires that informed consent discussions include a reliable interpreter when the prospective subject does not understand the language of the person who is obtaining consent, and, in most circumstances, that consent materials are translated;

4. The investigator is responsible for ensuring that each prospective subject is adequately informed about all aspects of the research and understands the information provided.

18.3 Legally Authorized Representative (LAR)

[If a KCU investigation wishes to conduct research where consent must be obtained from an LAR, please contact the IRB office for assistance. The section is currently RESERVED because KCU does not have any research in its research portfolio where consent needs to be obtained from an LAR]

18.4 Basic Elements of Informed Consent

To be valid, the consent process must provide the following basic elements of information to potential subjects:

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**;
2. A description of any reasonably foreseeable **risks or discomforts** to the subject;
3. A description of any **benefits** to the subject or to others which may reasonably be expected from the research;
4. A disclosure of appropriate **alternative procedures** or courses of treatment, if any, that might be advantageous to the subject;
5. A statement describing the extent, if any, to which **confidentiality** of records identifying the subject must be maintained;
6. **For research involving more than minimal risk**, an explanation as to whether any compensation **and** an explanation as to whether any medical treatments are available if injury occurs **and**, if so, what they consist of, or where further information may be obtained;
7. An **explanation of whom to contact** for answers to pertinent questions about the research **and** research subjects' rights, **and** whom to contact in the event of a research-related injury to the subject;
8. A statement that participation is **voluntary**, refusal to participate will involve **no penalty or loss of benefits** to which the subject is otherwise entitled, and the subject **may discontinue participation** at any time without penalty or loss of benefits to which the subject is otherwise entitled;
9. One of the following statements about any research that involves the **collection of identifiable private information or identifiable biospecimens**:
    a. A statement that **identifiers might be removed** from the identifiable private information or identifiable biospecimens **and that**, after such removal, the information or biospecimens **could be used** for future research studies or

distributed to another investigator for future research studies **without additional informed consent** from the subject or the legally authorized representative, if this might be a possibility; or

b. 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 studies.

10. For **FDA-regulated studies**, a statement that notes the possibility that the Food and Drug Administration may inspect the records;

18.5 Additional elements of informed consent to be applied, as appropriate:

1. A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable;
2. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;
3. Any additional costs to the subject that may result from participation in the research;
4. When applicable, the amount and schedule of all payments;
5. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;
6. 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;
7. The approximate number of subjects involved in the study.
8. 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;
9. A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions;
10. For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen).

18.6 KCU Requirements

[This section is reserved in the event KCU would mandate additional consent requirements]

18.7 Subject Withdrawal or Termination

A subject enrolled in a research study may decide to withdraw from the research, or an investigator may decide to terminate a subject's participation in research regardless of whether the subject wishes to continue participating. Investigators must plan for the possibility that subjects will withdraw from research and include a discussion of what withdrawal will mean and how it will be handled in their research plans and consent documents.

When seeking informed consent from subjects the investigator should inform subjects whether the investigator or study sponsor intends to either: (1) retain and analyze already collected data relating to the subject up to the time of subject withdrawal; or (2) honor a research subject's request that the investigator or study sponsor will destroy the subject's data or that the investigator or study sponsor will exclude the subject's data from any analysis.

When a subject's withdrawal request is limited to discontinuation of the primary interventional component of a research study, research activities involving other types of participation for which the subject previously gave consent may continue. Investigators should ask a subject who is withdrawing whether the subject wishes to participate in continued follow-up and further data collection following their withdrawal from the interventional portion of the study. Under this circumstance, the discussion with the subject would distinguish between study-related interventions and procedures and continued follow-up in person, by phone, or via records review.

If a subject withdraws from the interventional portion of the study, but agrees to continued follow-up as described in the previous paragraph, the investigator must obtain the subject's informed consent for this limited participation in the study (assuming such a situation was not described in the original consent document). IRB approval of consent documents for these purposes would be required.

If a subject withdraws from the interventional portion of a study and does not consent to continued follow-up, the investigator must not access or gather private information about the subject for purposes related to the study. However, an investigator may review study data related to the subject collected prior to the subject's withdrawal from the study, and may consult public records, such as those establishing survival status.

18.8 Documentation of Informed Consent

Except as provided in Sections 18.10, 18.11 and 18.12 of this document, informed consent must be documented by the use of a written consent form approved by the IRB.

1. Informed consent is documented by the use of a written consent form approved by the IRB and signed) and dated by the subject or the subject's LAR at the time of consent;
2. The name of the person who obtained consent and the date they did so is documented on the written consent form;
3. A written copy of the signed and dated consent form must be given to the person signing the form. The investigator should retain the signed original in the research records.

The consent form may be either of the following:

1. A written consent document that embodies the basic and required additional elements of informed consent. The investigator shall give either the subject or the subject's LAR adequate opportunity to read the informed consent form before it is signed; alternatively, this form may be read to the subject or the subject's legally authorized representative;

   or

2. A short form written consent document stating that the elements of informed consent have been presented orally to the subject or the subject's LAR and that the key information required by Section 18.1 #5.a was presented first to the subject, before other information, if any, was provided. . When this method is used:

   a. The oral presentation and the short form written document should be in a language understandable to the subject; and

   b. There must be a witness to the oral presentation; and

   c. The IRB must approve a written summary of what is to be said to the subject (the approved full consent document may serve as this summary); and

   d. The short form document is signed by the subject;

   e. The witness must sign both the short form and a copy of the summary; and

   f. The person actually obtaining consent must sign a copy of the summary; and

   g. A copy of the summary must be given to the subject or representative, in addition to a copy of the short form.

When the short form procedure is used with subjects who do not speak or read English, or have Limited English Proficiency (LEP), (i) the oral presentation and the short form written document should be in a language understandable to the subject; (ii) the IRB-approved English language informed consent document may serve as the summary; and (iii) the witness should be fluent in both English and the language of the subject. When the person obtaining consent is assisted by an interpreter, the interpreter may serve as the witness.

The IRB must receive all foreign language versions of the short form document as a condition of approval. Expedited review of these versions is acceptable if the protocol/research plan, the full English language informed consent document, and the English version of the short form document have already been approved by the convened IRB.

18.9 Special Consent Circumstances

18.9.1 Enrollment of persons with Limited English Proficiency

1. **Expected enrollment**: In some studies, the investigator may be able to anticipate enrollment of persons who do not speak or read, or have limited proficiency in, oral or written English. When the target subject population includes such persons or the investigator or the IRB otherwise anticipates that consent will be conducted in a language

other than English, the IRB requires a translated consent document and other subject materials, as applicable. Generally, translated consent forms should not be prepared until the final approved version of the English-language version is available. To ensure that translated documents are accurate, the IRB may choose to require a certified translation, to have an independent back-translation, or to have a review of the translated documents by an IRB member or other person who is fluent in the language.

2. **Unexpected enrollment:** If a person who does not speak or read, or has limited proficiency in, English unexpectedly presents for possible enrollment, an IRB-approved translated version of the written consent may not be available for use. Investigators should carefully consider the ethical and legal ramifications of enrolling subjects when a language barrier exists. If the subject does not clearly understand the information presented during the consent process or in subsequent discussions, his/her consent may not be informed or legally effective.

   If an investigator decides to enroll a subject into a study for which there is not an extant IRB-approved consent document in the prospective subject's language, the investigator must receive IRB approval to follow the procedures for a "short form" written consent in as described in Section 18.8.

3. **Use of interpreters in the consent process:** Unless the person obtaining consent is fluent in the prospective subject's language, an interpreter will be necessary to facilitate the consent discussion. Preferably someone who is independent of the subject (i.e., not a family member) should assist in presenting information and obtaining consent. Whenever possible, interpreters should be provided copies of the translated consent, or short form and the IRB-approved consent script (typically the English-language version of the consent document), well before (24 to 48 hours if possible) the consent discussion with the subject. If the interpreter also serves as the witness, s/he may sign the translated consent, or short form consent document and script, as the witness and should note "Interpreter" under the signature line. The person obtaining consent must document that the "short form" process was used in the subject's research record, including the name of the interpreter.

18.9.2 Braille consent

For blind subjects who read Braille, the IRB may approve a consent document prepared in Braille. To ensure that a Braille consent document is accurate, the IRB may require a transcription into print text or review of the document by an IRB member or other person who reads Braille. If possible, the subject will sign the Braille consent; otherwise oral consent will be obtained, witnessed and documented as described under "Oral Consent" (see Section 18.9.4).

18.9.3 Consenting in American Sign Language (ASL)

For deaf subjects who are fluent in ASL, the IRB may approve a consent process using ASL and the IRB-approved written consent form. When this process is approved, the individual authorized to consent prospective subjects must use a certified interpreter fluent in ASL to

conduct the consent process and the documentation of the consent process must conform to the requirements set forth in Section 18.8.

18.9.4 Oral Consent

When subjects are unable to read a written consent form (such as blind or illiterate subjects), the IRB may approve an oral consent process, provided the subject (1) retains the ability to understand the concepts of the study and evaluate the risk and benefit of being in the study when it is explained orally and (2) is able to indicate approval or disapproval to study entry.

For research that is no more than minimal risk, documentation of consent may be waived according to the criteria in Section 18.11.

For greater than minimal risk research, the consent form must be read to the subjects and the subjects must be given an opportunity to ask questions. An audiotape approved by the IRB may also be used. If capable of doing so, the subject signs, or marks an X to signify consent. If that is not possible, the subject will provide oral consent. The person obtaining consent and a witness will sign the written study consent form with a statement that documents that an oral process was used and that the subject gave oral consent or made their mark. The consent process will also be documented in the subject's research record. Signed copies of the consent form are given to the subject and, whenever possible, these documents should be provided to the subject on audio or video-tape.

18.9.5 Physically-Challenged Subjects

A person who is physically challenged (e.g., physically unable to talk or write) can enroll in research if competent and able to indicate voluntary consent to participate. Whenever possible, the subjects should sign the consent form or make their mark by initialing or making an X. As with oral consent, a witness to the consent process is recommended and the circumstances and consent process should be carefully documented in the research records.

18.10 Waiver or Alteration of Informed Consent

An IRB may waive the requirement to obtain informed consent, provided the IRB finds and documents that the below criteria are satisfied. An IRB **may not** waive or alter broad consent (See Section 18.12), nor may it waive consent for the storage, maintenance, or secondary research use of identifiable biospecimens if an individual was asked to provide broad consent in accordance with Section 18.12 and refused.

1. The research or clinical investigation involves no more than minimal risk to the subjects;
2. The research or clinical investigation could not practicably be carried out without requested waiver or alteration;
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;

4. The waiver or alteration will not adversely affect the rights and welfare of the subjects; and
5. Whenever appropriate, the subjects or LARs will be provided with additional pertinent information after participation.

This option applies to both FDA-regulated and DHHS-conducted or supported research.

Likewise, an IRB may approve a consent procedure that omits some, or alters some or all, of the basic and additional elements of informed consent (an "alteration") (See Sections 18.4 and 18.5), provided that the IRB finds and documents that the below criteria are satisfied. An IRB **may not** omit or alter any of the general requirements for informed consent (See Section 18.1).

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:
    a. Public benefit or service programs;
    b. Procedures for obtaining benefits or services under those programs;
    c. Possible changes in or alternatives to those programs or procedures; or
    d. Possible changes in methods or levels of payment for benefits or services under those programs; and,
2. The research could not practicably be carried out without the waiver or alteration.

This option **does not** apply to FDA-regulated research.

18.10.1 Screening, recruiting, or determining eligibility

An IRB may approve a research proposal in which an investigator will obtain information or biospecimens for the purpose of screening, recruiting, or determining the eligibility of prospective subjects without the informed consent of the prospective subject or the subject's legally authorized representative, if either of the following conditions are met:

1. The investigator will obtain information through oral or written communication with the prospective subject or legally authorized representative, or
2. The investigator will obtain identifiable private information or identifiable biospecimens by accessing records or stored identifiable biospecimens.

18.11 Waiver of Documentation of Informed Consent

The IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds **any** of the following:

1. The only record linking the subject and the research would be the consent document and the principal risk would be potential harm from a breach of confidentiality (e.g., domestic violence research where the primary risk is discovery by the abuser). Subjects must be

asked whether they want documentation linking them with the research, and their wishes must govern.

This option **does not** apply to FDA-regulated research.

OR

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. Procedures such as non-sensitive surveys, questionnaires and interviews generally do not require written consent when conducted by non-investigators (e.g., marketing surveys, telemarketing).

   This option **does** apply to FDA-regulated research (most commonly in the context of minimal risk screening activities that are necessary to determine eligibility for enrollment in a clinical trial.

3. If the subjects or LARs are members of a distinct cultural group or community in which signing forms is not the norm, that the research presents no more than minimal risk of harm to subjects and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained.

   This option **does not** apply to FDA-regulated research.

Unless the IRB has granted a full waiver of the requirement to obtain informed consent, investigators who seek and receive approval for a waiver of documentation of consent still must perform an appropriate consent process.

In cases in which the documentation requirement is waived, the IRB requires the investigator to provide in the application materials a written summary of the information to be communicated to the subject, and the IRB will consider whether to require the investigator to provide subjects with a written statement regarding the research.

18.12 Elements of broad consent [This section is RESERVED, as KCU has no research where this currently applies.]

18.13 Posting of Clinical Trial Consent Forms [This section is RESERVED, as KCU is not involved in any federally funded clinical trials]

19 Vulnerable Subjects in Research

When participants in research conducted under the auspices of KCU are likely to be vulnerable to coercion or undue influence or have diminished decision-making capacity, the research must include additional safeguards to protect the rights and welfare of these participants. The IRB must ensure that all of the regulatory requirements for the protection of subjects are met and that appropriate additional protections for vulnerable subjects are in place.

19.1 Definitions

Children. Children are 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 [45 CFR 46.402(a)].

NOTE: For research conducted in jurisdictions other than Missouri, the research must comply with the laws regarding the legal age of consent in the relevant jurisdictions. Legal counsel will be consulted with regard to the laws in other jurisdictions or such "local context" information will be sought through other mean (e.g., according to the terms of a reliance agreement).

Guardian. A guardian is an individual who is authorized under applicable state or local law to consent on behalf of a child to general medical care [45 CFR 46.402(e)].

NOTE: For research conducted in jurisdictions other than Missouri, the research must comply with the laws regarding guardianship in all relevant jurisdictions. Legal counsel will be consulted with regard to the laws in other jurisdictions or such "local context" information will be sought through other mean (e.g., according to the terms of a reliance agreement).

Pregnancy. Pregnancy encompasses the period of time from implantation until delivery. A woman shall be assumed to be pregnant if she exhibits any of the pertinent presumptive signs of pregnancy, such as missed menses, until the results of a pregnancy test are negative or until delivery [45 CFR 46.202(f)].

Prisoner. Prisoner means 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 [45 CFR 303(c)].

19.2 Involvement of Vulnerable Populations in Research

When the IRB reviews research that involves categories of participants vulnerable to coercion or undue influence, the review process should include one or more individuals who are knowledgeable about or experienced in working with these participants. When the IRB does not have the relevant expertise among its membership, expertise may be sought through the use of consultants.

45 CFR 46 has additional subparts designed to provide extra protections for certain defined vulnerable populations which also have additional requirements for IRBs.

Subpart B - Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research

Subpart C - Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects

Subpart D - Additional Protections for Children Involved as Subjects in Research

DHHS-conducted or supported research that involves any of these populations must comply with the requirements of the relevant subparts. Research regulated by the FDA includes equivalent protections and obligations when **research** involves children (Subpart D). Research conducted, supported, or otherwise regulated by other federal agencies may or may not be covered by the subparts.

19.3 Procedures

The following policies and procedures apply to all research involving subjects vulnerable to coercion or undue influence under the oversight of the KCU IRB. Subsequent sections address additional procedures and requirements that apply to specific populations.

Initial Review of Research Proposal:

1. The investigator identifies the potential to enroll vulnerable subjects in the proposed research at initial review and provides the justification for their inclusion in the study;
2. The investigator describes safeguards to protect the subject's rights and welfare in the research proposal;
3. IRB staff, in collaboration with the IRB Chair as needed, ensure that the IRB has the relevant expertise with the vulnerable population, and, if necessary, arrange for consultation. When the research involves no more that minimal risk and is eligible for expedited review, the designated reviewer may determine the need for additional expertise to ensure the protection of the vulnerable population(s);
4. The IRB evaluates the proposed inclusion of vulnerable population(s) in the research and the safeguards proposed by the investigator, taking into consideration the following factors, as applicable to the research:
    a. Whether inclusion of vulnerable populations is ethically and scientifically appropriate;
    b. Whether the proposed plans, including the settings and circumstances, for the identification and recruitment of subjects, and for obtaining consent or parental permission, ensure equitable selection of subjects and promote voluntariness;
    c. Whether the proposed research confers any direct benefit, whether the benefit is available outside of the research, and whether access to the benefit may unduly influence participation by vulnerable populations;
    d. Whether any costs or plans for subject reimbursement or compensation, may exclude or unduly influence participation by vulnerable populations;

e. Whether the provisions for privacy and confidentiality adequately protect vulnerable populations; and
f. Other relevant considerations as appropriate for the population(s) and the circumstances of the research

5. When applicable, the IRB considers any costs associated with participation in the proposed research and any plans for reimbursement of expenses or provision of compensation, and the potential impact of such on the vulnerable population(s);
6. The IRB evaluates the research to determine whether the proposed plan is adequate or if additional protections are needed such as interim monitoring, review more than annually, or the use of a data and safety monitoring board, consent monitor, or research subject advocate.

Modifications to Research

1. When an investigator proposes to add inclusion of a vulnerable population after research has already been approved by the IRB, the investigator must submit a modification request to the IRB identifying the population they would like to add, justification for inclusion of the population, and any modifications to the research plan to ensure protection of the subjects' rights and welfare;
2. The IRB staff and IRB will follow the procedures outlined for initial review above.

19.4 Research Involving Pregnant Women, Human Fetuses and Neonates

The following applies to all research involving pregnant women, human fetuses, and neonates reviewed by the KCU IRB.

If a woman becomes pregnant while participating in a study that has not been approved for inclusion of pregnant women, the IRB must be notified immediately so that the IRB can determine whether the subject may continue in the research, whether additional safeguards are needed, and to make the determinations required by the regulations and these policies.

19.4.1 Research Involving Pregnant Women or Fetuses

19.4.1.1 Research Not Conducted or Supported by DHHS

For research not conducted or supported by DHHS, where the risk to the pregnant women and fetus is no more than minimal, no additional safeguards are required by policy and there are no restrictions on the involvement of pregnant women in research. However, the IRB may determine that additional safeguards or restrictions are warranted for a specific study.

Pregnant women or fetuses may be involved in research not funded by DHHS **involving more than minimal risk** to pregnant women and/or fetuses if all of the following conditions are met:

1. Where scientifically appropriate, pre-clinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;

2. The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus;
3. Any risk is the least possible for achieving the objectives of the research;
4. If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, then the consent of the pregnant woman is obtained in accord with the provisions for informed consent;
5. If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accord with the provisions for informed consent, except that 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.
6. Each individual providing consent under paragraph 4 or 5 of this section is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;
7. For children (as defined in Section 19.1) who are pregnant, assent and permission are obtained in accord with the requirements of state law and the IRB;
8. No inducements, monetary or otherwise, will be offered to terminate a pregnancy;
9. Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and

19.4.1.2 Research Conducted or Supported by DHHS

For DHHS-conducted or supported research, 45 CFR Subpart B applies to all non-exempt human subject research involving pregnant women, fetuses, and neonates.

Pregnant women or fetuses may be involved in research if all of the following conditions are met:

1. Where scientifically appropriate, pre-clinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses.
2. The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means;
3. Any risk is the least possible for achieving the objectives of the research;
4. If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or 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, then the consent of the pregnant woman is obtained in accord with the provisions for informed consent.

5. If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accord with the provisions for informed consent, except that 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.
6. Each individual providing consent under paragraph 4 or 5 of this section is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;
7. For children (as defined in Section 19.1) who are pregnant, assent and permission are obtained in accord with the provisions of permission and assent in Section 19.6.2;
8. No inducements, monetary or otherwise, will be offered to terminate a pregnancy;
9. Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and

19.4.2 Research involving Neonates of Uncertain Viability or Nonviable Neonates [This section is RESERVED as KCU currently does not anticipate being involved in research involving neonates.]

19.4.2.1 Research Not Conducted or Supported by DHHS

19.4.2.2 Research Conducted or Supported by DHHS

19.4.3 Viable Neonates

19.4.4 Research Involving, After Delivery, the Placenta, the Dead Fetus or Fetal Material

19.4.5 Research Not Otherwise Approvable

19.4.5.1 Research Not Conducted or Supported by DHHS

19.4.5.2 Research Conducted or Supported by DHHS

19.5 Research Involving Prisoners

19.5.1 Applicability

For research not conducted or supported by DHHS, where the risk to prisoners is no more than minimal (as defined in Section 19.5.2), no additional safeguards are required under these policies and procedures. However, the IRB may determine that additional safeguards or restrictions are warranted for a specific study.

For research involving more than minimal risk, and for research conducted or supported by DHHS unless the research qualifies for exemption and only incidentally includes prisoners (See Section 9), the requirements outlined in this section apply.

As applicable, investigators must obtain permission from and abide by the requirements of correctional authorities and state or local law.

19.5.2 Minimal Risk

Minimal risk, in studies involving prisoners, means 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.

19.5.3 Composition of the IRB

In addition to satisfying the general membership requirements detailed in other sections of these policies and procedures, when reviewing research involving prisoners, the IRB must also meet the following requirements:

1. A majority of the IRB (exclusive of prisoner members) must have no association with the prison(s) involved, apart from their membership on the IRB;
2. At least one member of the IRB must be a prisoner, or a prisoner representative with appropriate background and experience to serve in that capacity, except that where a particular research project is reviewed by more than one IRB, only one IRB need satisfy this requirement; and
3. The prisoner representative must be a voting member of the IRB. A comment may be added to the roster indicating that the prisoner representative will only count towards quorum when s/he is in attendance and reviewing studies involving prisoners.

19.5.4 Review of Research Involving Prisoners

Initial Review of Research Proposal

1. The prisoner representative must review research involving prisoners, focusing on the requirements outlined in Subpart C and these policies;
2. The prisoner representative must receive all review materials pertaining to the research (same as primary reviewer); and
3. The prisoner representative must be present at a convened meeting when the research involving prisoners is reviewed. If the prisoner representative is not present, research involving prisoners cannot be reviewed or approved. The prisoner representative may attend the meeting by phone, video-conference, or webinar, so long as the representative is able to participate in the meeting as if they were present in person at the meeting.
4. The IRB must be familiar with the specific conditions in the local prison(s) or jail site(s) that are pertinent to subject protections, before approving the proposal for the local site (45 CFR 46.107(a)).

Modifications to Research

1. Minor modifications to research involving prisoners may be reviewed using the expedited procedure described below;
2. Modifications reviewed by the convened IRB must use the same procedures for initial review including the responsibility of the prisoner representative to review the modification and participate in the meeting (as described above).

Continuing Review

1. Continuing review will follow the same procedures as initial review including the responsibility of the prisoner representative to review the continuing review materials and participate in the meeting (as described above).

Expedited Review

1. Research **involving interaction** with prisoners may be reviewed by the expedited procedure if a determination is made that the research involves no greater than minimal risk for the prison population being studied and the research falls within the categories of research eligible for expedited review. Whenever possible, the prisoner representative will be consulted to verify that they agree that the research is minimal risk and to conduct (if designated by the IRB Chair as an expedited reviewer) or participate in the expedited review as a consultant. Review of modifications and continuing review will follow these same procedures;
2. Research **that does not involve interaction** with prisoners (e.g., records review) may be reviewed by the expedited procedure if a determination is made that the research involves no greater than minimal risk for the prison population being studied. Review by a prisoner representative is not required. The prisoner representative may review the research as a reviewer (if designated by the IRB Chair as an expedited reviewer) or consultant. Review of modifications and continuing review will follow these same procedures.

19.5.5 Incarceration of Enrolled Subjects

1. If a subject becomes a prisoner while enrolled in a research study that was not reviewed according to these procedures, the investigator must promptly notify the IRB and the IRB shall:
    a. Confirm that the subject meets the definition of a prisoner;
    b. Consult with the investigator to determine if it is in the best interests of the subject to continue participation in the study, in part or in full, and if so, if there are specific study activities which are in the best interests of the subject that should continue until the IRB is able to review the research applying the standards and requirements for research involving prisoners.
2. If the subject should continue, one of two options are available:
    a. Keep the subject enrolled in the study and review the research applying the standards and requirements for research involving prisoners. If some of the

requirements cannot be met or are not applicable (e.g., procedures for the selection of subjects within the prison), but it is in the best interests of the subject to remain in the study, keep the subject enrolled and, if the research is DHHS-conducted or supported, inform OHRP of the decision along with the justification; or

b. Remove the subject from the study and keep the subject on the study intervention under an alternate mechanism such as compassionate use or off-label use.

3. If a subject is incarcerated temporarily while enrolled in a study:

   a. If the temporary incarceration has no effect on the study (i.e., there is no need for study activities involving the prisoner subject to take place during the temporary incarceration), keep the subject enrolled.

   b. If the temporary incarceration has an effect on the study, follow the guidance outlined above.

19.5.6 Additional Duties of the IRB

In addition to the responsibilities of the IRB described in other sections of this manual, the IRB will review research involving prisoners and approve such research only if it finds that:

1. The research falls into one of the following **permitted categories** [45 CFR 46.306(a)(2)]:

   a. 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;

   b. 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;

   c. Research on conditions particularly affecting prisoners as a class (for example, research on diseases or social and psychological problems much more prevalent in prisons) provided that the study may proceed only after the DHHS Secretary has consulted with appropriate experts in penology, medicine, and ethics, and published notice in the Federal Register of his/her intent to approve the research;

   d. Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subject. In cases in which those studies require the assignment of prisoners in a manner consistent with protocols/research plans approved by the IRB to control groups which may not benefit from the research, the study may proceed only after the DHHS Secretary has consulted with appropriate experts in penology, medicine, and ethics, and published notice in the Federal Register of his/her intent to approve the research; or

   e. The research qualifies under the HHS Secretarial waiver that applies to certain epidemiological research (68 FR 36929, June 20, 2003). The criteria for this

category are that the research must have as its sole purpose (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.

2. Any possible advantages accruing 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;
3. The risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers;
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 investigator provides to the IRB justification in writing for following some other procedures, control subjects must be selected randomly from the group of available prisoners who meet the characteristics needed for that particular research proposal;
5. The information is presented in language which is understandable to the subject population;
6. Adequate assurance exists that parole boards will not take into account a prisoner's participation in the 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; and
7. Where the IRB finds there may be a need for follow-up examination or care of subjects 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 subjects of this fact.

19.5.7 Certification to DHHS

Under 45 CFR 46.305(c), the institution responsible for conducting research involving prisoners that is conducted or supported by DHHS shall certify to the Secretary (through OHRP) that the IRB has made the seven findings required under 45 CFR 46.305(a) and receive OHRP authorization prior to initiating any research involving prisoners. Certifications, and requests for DHHS Secretarial consultation, do not need to be submitted to OHRP for research not conducted or supported by DHHS.

For all DHHS-conducted or supported research, KCU will send to OHRP a certification letter to this effect, which will also include the name and address of the institution and specifically identify the research study in question and any relevant DHHS grant application or protocol/research plan. DHHS-conducted or supported research involving prisoners as subjects may not proceed until OHRP issues its authorization in writing to KCU on behalf of the Secretary.

Under its authority at 45 CFR 46.115(b), OHRP requires that the institution responsible for the conduct of the proposed research also submit to OHRP a copy of the research proposal so that

OHRP can determine whether the proposed research involves one of the categories of research permissible under 45 CFR 46.306(a)(2), and if so, which one.

The term "research proposal" includes:

1. The IRB-approved protocol; any relevant DHHS grant application or proposal;
2. Any IRB application forms required by the IRB; and
3. And any other information requested or required by the IRB to be considered during initial IRB review.

OHRP also encourages the organization to include the following information in its prisoner research certification letter to facilitate processing:

1. The OHRP Federalwide Assurance (FWA) number;
2. The IRB registration number for the designated IRB; and
3. The date(s) of IRB meeting(s) in which the study was considered, including a brief chronology that encompasses:
    a. The date of initial IRB review; and
    b. The date of subpart C review, if not done at the time of initial IRB review.

19.6 Research Involving Children

The following applies to all research involving children, regardless of funding source. The requirements in this section are consistent with Subpart D of 45 CFR 46, which applies to DHHS-funded research and Subpart D of 21 CFR 50, which applies to FDA-regulated research involving children.

19.6.1 Allowable Categories

In addition to the IRB's normal duties, research involving children must be reviewed by the IRB to determine if it fits within and is permissible under one or more federally-defined categories (OHRP/FDA). Each procedure or intervention that the child will undergo for the research must be taken into consideration, and, if the research includes more than one study group assignment (e.g., placebo vs. active, investigational agent vs. comparator) the category determination must be made for each group assignment. In other words, a component analysis must be conducted by the IRB. The categories are as follows:

1. **Research not involving greater than minimal risk** [45 CFR 46.404/21 CFR 50.51]. Research determined to not involve greater than minimal risk to child subjects may be approved by the IRB only if the IRB finds and documents that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians as set forth in Section 19.6.2.
2. Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects [45 CFR 46.405/21 CFR 50.52]. Research in which the IRB finds

that more than minimal risk to children is presented by an intervention or procedure that holds out the prospect of direct benefit for the individual subject, or by a monitoring procedure that is likely to contribute to the subject's well-being, may be approved by the IRB only if the IRB finds and documents that:

a. The risk is justified by the anticipated benefit to the subjects;

b. The relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative options; and

c. Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians as set forth in Section 19.6.2**.**

3. Research involving greater than minimal risk and no prospect of direct benefit to the individual subject, but likely to yield generalizable knowledge about the subject's disorder or condition [45 CFR 46.406/21 CFR 50.53]. Research in which the IRB finds 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, may be approved by the IRB only if the IRB finds and documents that:

   a. The risk represents a minor increase over minimal risk;

   b. 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;

   c. 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

   d. Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians as set forth in Section 19.6.2.

4. Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate serious problems affecting the health or welfare of children [45 CFR 46.407/21 CFR 50.54]. When the IRB does not believe that the research meets the requirements of any of the above categories, and the IRB finds and documents that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children, the IRB shall refer the research for further review as follows:

   a. DHHS-conducted or supported research in this category will be referred for review by the Secretary of Health and Human Services. However, before doing so the IRB must determine that the proposed research also meets all of the requirements of the Common Rule.

   b. FDA-regulated research in this category will be referred for review by the Commissioner of Food and Drugs.

c. For research that is not DHHS conducted or supported and not FDA-regulated, the IRB will consult with a panel of experts in pertinent disciplines (for example: science, medicine, ethics, law). Based on the recommendation of the panel, the IRB may approve the research based on either:

   i. That the research in fact satisfies the conditions of the previous categories, as applicable; or

   ii. The following:

      1. The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;

      2. The research will be conducted in accord with sound ethical principles; and

      3. Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians as set forth in Section 19.6.2.

19.6.2 Parental Permission and Assent

19.6.2.1 Parental Permission

The IRB must determine that adequate provisions have been made for soliciting the permission of each child's parent or guardian.

Parents or guardians must be provided with the basic elements of consent and any additional elements the IRB deems necessary, as described in Section 18.

The IRB may find that the permission of one parent is sufficient for research to be conducted under Categories 1 [45 CFR 46.404/21 CFR 50.51] & 2 [45 CFR 46.405/21 CFR 50.52] above. The IRB's determination of whether permission must be obtained from one or both parents will be documented in the reviewer's notes when a study receives expedited review, and in meeting minutes when reviewed by the convened committee.

Permission from both parents is required for research to be conducted under Categories 3 [45 CFR 46.406/21 CFR 50.53] & 4 [45 CFR 46.407/21 CFR 50.54] above unless:

1. One parent is deceased, unknown, incompetent, or not reasonably available; or
2. When only one parent has legal responsibility for the care and custody of the child.

The IRB may waive the requirement for obtaining permission from a parent or legal guardian if:

1. The research meets the provisions for waiver in Section 18.10; or
2. For research that is not FDA-regulated, if the IRB determines that the research is designed to study conditions in children or a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children) provided that an appropriate mechanism for protecting the

children who will participate as subjects in the research is substituted, and that the waiver is not inconsistent with Federal, State, or local law. The choice of an appropriate mechanism would depend upon the nature and purpose of the activities described in the protocol/research plan, the risk and anticipated benefit to the research subjects, and the child's age, maturity, status, and condition.

Permission from parents or legal guardians must be documented in accordance with and to the extent required by Section 18.8.

19.6.2.2 Assent from Children

The IRB is responsible for determining 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. This judgment may be made for all children to be involved in the study, or for each child, as the IRB deems appropriate.

If the IRB determines that the capability of some or all of the children 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 children and is available only in the context of the research, the assent of the children is not a necessary condition for proceeding with the research. Even where the IRB determines that the subjects are capable of assenting, the IRB may still waive the assent requirement under circumstances in which consent may be waived in accordance with the applicable regulations. It is important to note that the FDA regulations do permit the IRB to waive the assent requirement if it finds and documents that:

1. The clinical investigation involves no more than minimal risk to the subjects;
2. The waiver will not adversely affect the rights and welfare of the subjects;
3. The clinical investigation could not practicably be carried out without the waiver; and
4. Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

Because "assent" means a child's affirmative agreement to participate in research, the child must actively show his or her willingness to participate in the research, rather than just complying with directions to participate and not resisting in any way.

The IRB should take into account the nature of the proposed research activity and the ages, maturity, and psychological state of the children involved when reviewing the proposed assent procedure and the form and content of the information conveyed to the prospective subjects. For research activities involving adolescents whose capacity to understand resembles that of adults, the assent procedure should likewise include information similar to what would be provided for informed consent by adults or for parental permission. For children whose age and maturity level limits their ability to fully comprehend the nature of the research activity, but who are still capable of being consulted about participation in research, it may be appropriate to focus on conveying an accurate picture of what the actual experience of participation in research is likely to be (for example, what the experience will be, how long it will take, whether it might

involve any pain or discomfort). The assent procedure should reflect a reasonable effort to enable the child to understand, to the degree they are capable, what their participation in research would involve.

Parents and children will not always agree on whether the child should participate in research. Where the IRB has indicated that the assent of the child is required in order for him or her to be enrolled in the study, dissent from the child overrides permission from a parent. Similarly, a child typically cannot decide to be in research over the objections of a parent. There are individual exceptions to these guidelines but in general, children should not be forced to be research subjects, even when permission has been given by their parents.

Documentation of Assent

When the IRB determines that assent is required, it is also responsible for determining whether and how assent must be documented. When the research targets the very young child or children unable or with limited capacity to read or write, an oral presentation accompanied perhaps by some pictures with documentation of assent by the person obtaining assent in a research note is likely more appropriate than providing the child a form to sign. In this case, the investigator should provide the IRB with a proposed script and any materials that they intend to use in explaining the research.

When the research targets children who are likely able to read and write, investigators should propose a process and form that is age appropriate and study specific, taking into account the typical child's experience and level of understanding, and composing a document that treats the child respectfully and conveys the essential information about the study. The assent form should:

1. Tell why the research is being conducted;
2. Describe what will happen and for how long or how often;
3. Say it's up to the child to participate and that it's okay to say no;
4. Explain if it will hurt and if so for how long and how often;
5. Say what the child's other choices are;
6. Describe any good things that might happen;
7. Say whether there is any compensation for participating; and
8. Ask for questions.

Whenever possible, the document should be limited to one page. Illustrations might be helpful, and larger type and other age appropriate improvements are encouraged when they have the potential to enhance comprehension. Studies involving older children or adolescents should include more information and may use more complex language.

19.6.2.3 Children Who are Wards

[This section is RESERVED as KCU does not conduct research with children who are wards. If such research is proposed, this section may become become applicable.]

Children who are wards of the State or any other agency, institution, or entity can be included in research approved under 45 CFR 46.406/21 CFR 50.53 or 45 CFR 46.407/21 CFR 50.54 (Categories 3 & 4 in Section 19.6.1), **only if such research** is:

1. Related to their status as wards; or
2. Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.

If the research meets the condition(s) above, an advocate must be appointed for each child who is a ward (one individual may serve as advocate for more than one child), in addition to any other individual acting on behalf of the child as legal guardian or in *loco parentis.*

The advocate must be an individual who has the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child's participation in the research and who is not associated in any way (except in the role as advocate or member of the IRB) with the research, the investigator(s), or the guardian organization.

19.7 Adults with Impaired Decision-Making Capacity

When vulnerable populations are included in research, regulations require that additional safeguards are put in place to protect the rights and welfare of these subjects. [45 CFR 46.111(b)/21 CFR 56.111(b)] Adults who lack or who have impaired, fluctuating, or diminishing decision-making capacity (collectively referred to as "adults with impaired decision-making capacity" in this section) are particularly vulnerable. Investigators and IRBs must carefully consider whether inclusion of such subjects in a research study is appropriate; and when it is, must consider how best to ensure that these subjects are adequately protected. The principals and procedures outlined in this section are intended to assist KCU investigators and the IRB with the development and review of research involving adults with impaired decision-making capacity.

19.7.1 Informed Consent

Obtaining legally effective informed consent before involving human subjects in research is one of the central ethical principles described in the Belmont Report and provided for by federal regulations governing research.

As discussed previously, the informed consent process involves three key features: (1) providing the prospective subject the information needed to make an informed decision (in language understandable to him or her); (2) facilitating the understanding of what has been disclosed; and (3) promoting the voluntariness of the decision about whether to participate in the research.

Among other requirements, for consent to be legally effective, the potential subject or their LAR must have the necessary decision-making capacity to make a rational and meaningful choice about whether to participate (or continue participating) in a study.

19.7.2 Decision-Making Capacity

"Decision-making capacity" refers to a potential subject's ability to make a rationale and meaningful decision about whether or not to participate in a research study. This ability is generally thought to include at least the following four elements:

1. Understanding, i.e., the ability to comprehend the disclosed information about the nature and purpose of the study, the procedures involved, the risks and benefits of participating versus not participating, and the voluntary nature of participating;
2. Appreciation, i.e., the ability to appreciate the significance of the disclosed information and the potential risks and benefits for one's own situation and condition;
3. Reasoning, i.e., the ability to engage in a reasoning process about the risks and benefits of participating versus alternatives, and;
4. Choice, i.e., the ability to express a choice about whether or not to participate.

"Decision-making capacity" should not be confused with the legal concept of "competence." While the court may consider information about a person's decision-making capacity in making a competency determination, the terms are not synonymous. Incompetence is a legal determination made by a court of law. For example, someone who is judged legally incompetent to manage their financial affairs may retain sufficient decision- making capacity to make meaningful decisions about participating in a research protocol. Likewise, people who have normal cognitive functioning and are considered legally competent may be put into circumstances where their decision-making capacity is temporarily impaired by a physical or mental condition or by alcohol or drugs.

Decision-making capacity is protocol and situation-specific. Thus, a person may have capacity to consent to participate in low risk research in usual circumstances, but not have the capacity to consent to a higher risk protocol when s/he is under significant stress or faced with unfamiliar circumstances.

19.7.3 Inclusion of Adults with Impaired Decision-Making Capacity in Research

Research involving adult subjects without the ability to provide consent or with impaired decision-making capacity should only be conducted when the aims of the research cannot reasonably be achieved without their participation.

Investigators must disclose to the IRB both plans and justification for including adults with impaired decision-making capacity in a given research proposal. If adults with questionable or fluctuating capacity will be included, investigators must specify procedures for assessing capacity prior to providing informed consent and, if appropriate, for re-evaluating capacity during study participation. If a prospective subject's capacity to consent is expected to diminish, the investigator should consider requesting that the subject designate a future LAR prior to enrollment in the research, including the future LAR in the initial consent process, and obtaining written documentation of the subject's wishes regarding participation in the research. When the study includes subjects likely to regain capacity to consent while the research is ongoing, the

investigator should include provisions to inform them of their participation and seek consent for ongoing participation.

Plans for evaluation of capacity should be tailored to the subject population and the risks and nature of the research. In some instances, assessment by a qualified investigator may be appropriate. However, an independent, qualified assessor should evaluate subjects' capacity when the risks of the research are more than a minor increase over minimal or the investigator is in a position of authority over a prospective subject. In all cases, the person(s) evaluating capacity must be qualified to do so and use appropriate, validated tools and methods (e.g., University of California, San Diego Brief Assessment of Capacity to Consent [UBACC], MacArthur Competence Assessment Tool for Clinical Research [MacCAT-CR]). Assessments of capacity should be documented in the research record, and when appropriate, in the medical record.

Under some circumstances, it may be possible for investigators to enable adults with a degree of decisional impairment to make voluntary and informed decisions to consent, assent, or refuse participation in research. Potential measures include repetitive teaching, audiovisual presentations, and oral or written recall tests. Other measures might include follow-up questions to assess subject understanding, videotaping or audio-taping of consent discussions, use of waiting periods to allow more time for the potential subject to consider the information that has been presented, or involvement of a trusted family member or friend in the disclosure and decision making process. Audio or videotapes, electronic presentations, or written materials used to promote understanding must be provided to the IRB for review and approval prior to use.

When a prospective subject is deemed to lack capacity to consent to participate in research, investigators may obtain informed consent from the individuals' surrogate or LAR (See Section 18.3). Under these circumstances, the prospective subject should still be informed about the research in a manner compatible with the subjects' likely understanding and, if possible, be asked to assent to participate. Potential subjects who express resistance or dissent (by word, gesture, or action) to either participation or use of surrogate consent, should be excluded from the study. Some subjects may initially assent but later resist participation. Under no circumstances may an investigator or caregiver override a subject's dissent or resistance. When assent is possible for some or all subjects, the investigator should provide the IRB with an assent plan that describes when and how assent will be obtained, provisions that will be taken to promote understanding and voluntariness, how assent will be documented, and a copy of the assent form. If the investigator intends to use audio or video recordings to document assent, provisions to ensure the security of the recordings should be described to the IRB.

When inclusion of adults with impaired decision-making capacity is **not anticipated** and a plan for inclusion of such subjects **has not been** reviewed and approved by the IRB, and an enrolled subject becomes unable to provide consent or impaired in decision-making capacity, the investigator is responsible for promptly notifying the IRB (as soon as possible but within 5 business days). The investigator should consider whether continuing participation is appropriate and, if so, present a plan for surrogate consent from a LAR and, if appropriate, a plan to periodically evaluate capacity and re-obtain consent if possible.

19.7.4 IRB Review

The IRB review process will include at least one member, or a consultant, who is experienced with or otherwise knowledgeable about the population when the research involves greater than minimal risk, or the research is minimal risk but includes interactions with subjects, and the proposed subject population includes adults with impaired decision-making capacity.

In evaluating research, the IRB must be able to determine that the risks to subjects are reasonable not only in relation to any benefits, but also in relation to the importance of the knowledge that may reasonably be expected to result. In considering the risks of research involving adults with impaired decision-making capacity, the IRB should consider whether any components of the research involve risks that are greater for participants with diminished capacity. For example, whether subjects might experience increased sensitivity or discomfort to certain stimuli or may not be able to verbalize or otherwise demonstrate when they are experiencing discomfort or pain.

As appropriate to the research, the IRB will consider the following in evaluating research involving adults with impaired decision-making capacity:

1. Whether the aims of the research cannot reasonably be achieved without inclusion of the population;
2. Whether the research is likely to improve the understanding of the condition, disease, or issue affecting the subject population;
3. Whether any experimental procedure or interventions have undergone pre-clinical testing or human testing on other populations and whether the data from that testing supports its use in the proposed research;
4. Whether the procedures or interventions that the subject will undergo in the research place them at increased risk and whether appropriate mechanisms are in place to minimize risks, when possible;
5. Whether the data and safety monitoring plan, including any stopping rules, is appropriate given the risks of the research and the vulnerability of the population;
6. Whether the procedures for withdrawing individual subjects from the research are appropriate;
7. Whether the recruitment procedures, consent process, and any plans for financial compensation support voluntariness and minimize the likelihood of undue influence or coercion;
8. Whether the subjects will be exposed to financial or other risks that they might not consider acceptable if they had the capacity to provide consent, and whether appropriate mechanisms have been put into place to minimize these risks;
9. Whether the procedures for determining capacity to provide consent, and for evaluating capacity on an ongoing basis, if applicable, are appropriate;

10. Whether the procedures for informing subjects who regain capacity about their involvement in the research, and for obtaining consent for on-going participation, if applicable, are appropriate;
11. Whether assent should be required when possible, and, if so, if the proposed procedures to obtain and document assent are appropriate;
12. Whether periodic re-evaluation of capacity and/or periodic re-consent should be required; and
13. Whether a research subject advocate or consent monitor should be required, for some or all subjects.

In general, the IRB will only approve research involving subjects unable to provide consent or with impaired decision-making capacity when the aims of the research cannot reasonably be achieved without inclusion of the population, and there are appropriate provisions to: (1) evaluate capacity, (2) obtain consent (and assent if possible), and (3) otherwise protect subjects.

19.8 RESERVED

This section is RESERVED as a placeholder to describe procedures for research involving other vulnerable populations that the IRB may review on a regular basis. For example, research involving employees, students, refugees, undocumented workers, mental health patients under involuntary holds, etc.

20 Investigator Responsibilities

Principal Investigators (PIs) are ultimately responsible for the conduct of research. PIs may delegate tasks to appropriately trained and qualified members of their research team. However, PIs must maintain oversight and retain ultimate responsibility for the proper conduct of the research.

Within the regulations, the term 'investigator' refers to individuals involved in the design, conduct, or reporting of the research. Such involvement could include one or more of the following:

- Designing the research
- Obtaining information about living individuals by intervening or interacting with them for research purposes
- Obtaining identifiable private information about living individuals for research purposes
- Obtaining the voluntary informed consent of individuals to be subjects in research
- Studying, interpreting, or analyzing identifiable private information or data for research purposes.

20.1 Responsibilities

Investigators who conduct research involving human subjects must:

1. Develop and conduct research that is in accordance with the ethical principles in the Belmont Report;
2. Develop a research plan that is scientifically sound and minimizes risk to the subjects;
3. Develop a research plan that ensures the just, fair, and equitable recruitment and selection of subjects;
4. When some or all of the subjects are likely to be vulnerable to coercion or undue influence, include additional safeguards in the study to protect the rights and welfare of these subjects;
5. Ensure that the research plan includes adequate provisions for the monitoring of subjects and data to ensure the safety of subjects;
6. Ensure that there are adequate provisions to protect the privacy interests of subjects;
7. Ensure that there are adequate provisions to protect the confidentiality of data;
8. Have sufficient resources necessary to protect human subjects, including:
    a. Access to a population that would allow recruitment of the required number of subjects;
    b. Sufficient time to conduct and complete the research;
    c. Adequate numbers of qualified staff;

d. Adequate facilities;

e. Necessary equipment;

f. A plan to ensure proper supervision of the research including a plan for periods of absence or decreased availability; and

g. When appropriate, a plan to ensure the availability of medical, psychological, or other services that subjects might require as a result of their participation.

9. Ensure that all procedures in a study are performed with the appropriate level of supervision and only by individuals who are qualified to perform such pursuant to the policies of KCU;
10. Ensure that all study personnel are educated in the regulatory requirements regarding the conduct of research and the ethical principles upon which they are based;
11. Ensure that all persons assisting with the research are adequately trained and informed about the protocol and research implementation plan and their specific duties and functions;
12. Promptly report any changes in, addition to, or departure of investigators or research staff to the IRB for evaluation and approval (note that investigators and staff may not begin work on the research until IRB-approved);
13. Protect the rights, safety, and welfare of participants;
14. Ensure that the language in the consent form is consistent with that in the protocol, and any associated grant or contract.
15. Obtain and document informed consent and ensure that no human subject is involved in the research prior to obtaining consent or consent/permission from their LAR, unless a waiver of the requirement has been approved by the IRB;
16. Have a procedure to receive questions, complaints, or requests for additional information from subjects and respond appropriately;
17. Ensure that all information provided to the IRB is accurate and complete so that the IRB may fulfill its responsibilities to review the research and make the required determinations;
18. Ensure that all research involving human subjects receives IRB review and approval in writing or a determination of exemption before the research begins;
19. Ensure that all required reviews and approvals (e.g., COI) are in place before initiating the research;
20. Comply with all IRB decisions, conditions, and requirements;
21. Ensure that studies receive timely continuing IRB review and approval;
22. Report unanticipated problems, deviations, complaints, noncompliance, suspensions, terminations, and any other reportable events to the IRB and the organization, as required by regulations and policy;

23. Notify the IRB if information becomes available that suggests a change to the potential risks, benefits, merit, or feasibility of the research;
24. Obtain IRB review and approval before changes are made to the research unless a change is necessary eliminate apparent immediate hazards to the subject(s);
25. Seek IRB assistance when in doubt about whether proposed research requires IRB review;
26. Retain records for the time-period and in the manner described to and approved by the IRB and as required by required by regulations, agreements, and policies;

Additional investigator responsibilities, including specific responsibilities for investigators engaged in FDA-regulated research are described throughout this manual.

20.1.1 Record Retention

Investigator research records, including, but not limited to, signed consent forms and HIPAA authorizations, subject records and data, test article records, IRB records (submission materials, IRB determinations and associated documentation, correspondence to and from the IRB, etc.), and sponsor/grant records must be retained in accordance with regulatory, organizational, IRB, sponsor or grantor, and journal or publication standards. Records must be maintained securely with limited access. Disposal of investigator records must be done in such a manner that no identifying information can be linked to research data. When research is sponsored or grant-supported, consult the contract, grant terms, or other relevant agreements prior to destroying or transferring any records. If there are questions or allegations about the validity of the data or the appropriate conduct of the research, all records must be retained until such questions or allegations have been completely resolved.

The following summarizes a few of the more common regulatory requirements:

1. **OHRP** – research records must be retained for at least 3 years after the completion of the research.
2. **HIPAA** – Research authorizations, or documentation of waivers or alterations of authorization, must be held for a minimum of 6 years after the authorization or waiver/alterations was last obtained or in effect, whichever is later. At this time, KCU is not a covered entity that conducts research involving PHI.

20.2 Investigator Concerns

Investigators who have concerns or regarding the conduct of research at KCU, KCU ’s IRB or, or other IRBs that KCU relies upon should convey them to IRB Staff, the IO or other responsible parties (e.g., IRB Chair), when appropriate. The recipient of the concern will consider the issue, and when deemed necessary, seek additional information and convene the parties involved to form a response for the investigator or make necessary procedural or policy modifications, as warranted.

Consistent with KCU policies, there will be no retaliation against employees, faculty, students, staff, etc. who report concerns in good faith.

21 Sponsored Research

It is KCU policy that any sponsored research conducted under the auspices of the KCU is conducted in accordance with federal guidelines and ethical standards.

The following describe the procedures required to ensure that all sponsored research meets this requirement.

21.1 Definitions

Sponsor. Sponsor means the company, institution, individual donor, or organization responsible for the initiation, management or financing of a research study.

Sponsored research. Sponsored research means research funded by external entities (public, industry, or private) through a grant or contract that involves a specified statement of work (e.g., the research proposal), including clinical trials involving investigational drugs, devices or biologics.

21.2 Responsibility

Sponsor grants, contracts, and other written agreements will be reviewed for the following by the KCU's Grants and Contracts Office, with consultation with the IRB, as necessary:

1. All sponsor contracts have a written agreement with the Sponsor that addresses medical care for research participants with a research-related injury, when appropriate.
2. In studies where Sponsors conduct research site monitoring visits or conduct monitoring activities remotely, the sponsor contracts have a written agreement with the Sponsor that the Sponsor promptly reports to the KCU findings that could affect the safety of participants or influence the conduct of the study.
3. When the Sponsor has the responsibility to conduct data and safety monitoring, the sponsor contracts have a written agreement with the Sponsor that addresses provisions for monitoring the data to ensure the safety of participants and for providing data and safety monitoring reports to the KCU.
4. Sponsor contracts have a written agreement with the Sponsor about plans for disseminating findings from the research and the roles that investigators and Sponsors will play in the publication or disclosure of results.
5. When participant safety could be directly affected by study results after the study has ended, the sponsor contracts have a written agreement with the Sponsor that the investigator or KCU will be notified of the results in order to consider informing participants

22 Conflict of Interest in Research It is KCU policy to preserve public trust in the integrity and quality of research by reducing actual or perceived conflict of interest in the conduct of research.

Conflicts of interest (COI) in research can be broadly described as any interest that competes with an organization's or individual's obligation to protect the rights and welfare of research subjects, the integrity of a research study, or the credibility of the research program. Conflicts of interest can be financial or non-financial.

In the environment of research, openness and honesty are indicators of integrity and responsibility, characteristics that promote quality research and strengthen the research process. Therefore, conflicts of interest should be eliminated when possible and effectively managed and disclosed when they cannot be eliminated.

22.1 Researcher Conflicts of Interest

Pursuant to the KCU Conflict of Interest policy, KCU IRB will collaborate with the Vice Provost of Research to ensure that COI of investigators and research team members (investigators) are identified and managed before the IRB completes its review of any research application.

22.1.1 Procedures

22.1.1.1 Disclosure of Researcher COI

For IRB purposes, investigator conflict review occurs at the time of new study submission, continuing review, status report, with the addition of a new investigator, and whenever an investigator updates their KCU COI disclosure indicating a new or changed interest.

In the event a conflict that requires disclosure or management is identified, the KCU IRB will defer the research study review or prohibit participation by the researcher with a potential COI until the Research Compliance Office and Vice Provost of Research review process is completed and the results are made available to the IRB. When the research is under an external IRB, any conflicts identified as the result of COI review and any CMP are provided to the external IRB in accordance with any IRB reliance agreement.

22.1.1.2 Evaluation of COI

The IRB will review COIs and CMPs to determine:

1. Whether the COI affects the rights or welfare of research subjects;
2. Whether the COI might adversely affect the integrity or credibility of the research or the research program; and
3. Whether the CMP effectively protects research subjects and the integrity and credibility of the research and the research program.

In evaluating COIs and CMPs, among other factors the IRB will consider:

1. How the research is supported or financed;
2. The nature and extent of the conflict;
3. The role and responsibilities of the conflicted individual in the design, conduct, and reporting of the research; and
4. The ability of the conflicted individual to influence the outcome of the research.

22.1.1.3 Management of COI

The IRB has final authority to determine whether the research, the COI, and the CMP, if any, allow the research to be approved. With regard to the CMP issued by the RCOI Committee, the IRB shall either affirm or request changes to strengthen it. The IRB can require additional measures to manage a COI so that the research may be approved. However, the IRB cannot weaken a CMP approved by the RCOI Committee.

For example, in addition to the CMP, the IRB may require:

1. Disclosure of the COI to subjects through the consent process;
2. Modification of the research plan or safety monitoring plan;
3. Monitoring of research by a third party;
4. Disqualification of the conflicted party from participation in all or a portion of the research;
5. Appointment of a non-conflicted PI;
6. Divestiture of significant financial interests; and/or
7. Severance of relationships that create actual or potential conflicts.

In the event the conflict cannot be effectively managed, the IRB may disapprove the research.

22.2 IRB Member Conflict of Interest

No IRB member or alternate may participate in the review of any research project in which the member has a COI, except to provide information as requested. It is the responsibility of each IRB member to disclose any COI related to a study submitted for review and recuse himself or herself from the deliberations and vote by leaving the room.

All members and alternate members of the IRB complete a conflict disclosure when first appointed and annually thereafter or sooner when their circumstances change. These forms are submitted to IRB Staff, who reviews the disclosure and determines if a COI exists. To protect the privacy of members, the specific details of the conflict will not be given to other members; however, the type of research where a COI exists will be provided (e.g., studies from X sponsor; studies involving X investigator). The IRB staff, in turn, ensures that IRB members and alternates are not assigned to conduct reviews of studies for which the member has a conflict and reminds members of conflicts at convened meetings as needed to ensure recusal. IRB staff may consult with the IO to clarify whether a specific study involves a member COI.

IRB members, alternates, or consultants may be considered to have a conflicting interest requiring recusal when they, or an immediate member of their family, have any of the following:

1. Involvement in the design, conduct, and reporting of the research;
2. Significant financial interests (See *[research COI policy]* for a definition of significant financial interests) related to the research being reviewed; or
3. Any other situation where an IRB member believes that another interest conflicts with his or her ability to deliberate objectively on a study.

The IRB Chair will ask IRB members at the beginning of each convened meeting if any members have a COI regarding any of the items to be reviewed and reminds members that they must recuse themselves by leaving the room during the discussion and vote of the specific research study. If a conflicted member is participating by conference call, videoconference or web meeting, the member's participation (connection) is terminated for discussion and voting.

IRB members with a conflicting interest are excluded from being counted towards quorum. Recusals of members with COIs are recorded in the minutes.

22.3 Institutional Conflict of Interest

Pursuant to the KCU Policy on Institutional Conflicts of Interest, KCU will not participate in a human subjects' research project when it has an institutional financial interest. An exception to this policy may be made only when the Provost, Vice Provost of Research and The IO determines that circumstances exist to merit an exception and a conflict management plan is adopted to maintain research integrity and serve the best interests of participants enrolled in the research. KCU's IRB collaborates with the COI Committee to ensure that institutional COI is identified and managed before the IRB completes its review of any research application.

23 Participant Outreach

KCU is committed to ensuring that educational opportunities are offered to research participants, prospective research participants, and community members which will enhance their understanding of human subjects research at KCU and provide them the opportunity to provide input, seek information, and express concerns.

The following procedures describe how KCU fulfils that responsibility.

23.1 Outreach Resources and Educational Materials

1. KCU holds an annual "Research Day" to which members of the public are invited.

23.2 Evaluation [This section is RESERVED for further elaboration.]

24 Student Research

24.1.1 Human Subject Research and Course Projects

Learning how to conduct ethical human subject research is an important part of a student's educational experience. Research activities that are designed as part of a course requirement for purposes of learning experience only and are **not "**designed to develop or contribute to generalizable knowledge" **may** not require IRB review and approval if all of the following conditions are true:

1. Results of the research are viewed only by the course instructor for teaching purposes and discussed within the classroom for teaching and learning purposes;
2. Results of the research are not made public through presentation (outside of the classroom) and are not published in paper or electronic format (e.g., cannot be made available on the internet, cannot be published in a journal, etc.);
3. Research procedures are no more than minimal risk;
4. Permissions are obtained from any facilities or organizations where research activities, including recruitment, will take place;
5. Vulnerable populations are not targeted (e.g., children under age 18, prisoners, persons who are cognitively impaired, etc.);
6. Data collected are recorded in such a manner that the subjects are not identifiable (images in videotapes and photographs and voices on audiotape are identifiable); and
7. When appropriate, an informed consent process is in place.

24.1.1.1 Responsibility of the Course Instructor:

The course instructor is responsible for ensuring the protection of human subjects (including a process for obtaining voluntary informed consent from research subjects when appropriate), and for monitoring the students' progress.

When designing a project, students should be instructed on the ethical conduct of research and on the preparation of the IRB application when such is required. In particular, instructors and students should:

1. Understand the principles of the Belmont Report and their application;
2. Develop appropriate consent documents;
3. Plan appropriate strategies for recruitment;
4. Identify and minimize potential risks to subjects or others;
5. Assess the risk-benefit ratio for the project;
6. Establish and maintain strict guidelines for protecting privacy and confidentiality; and
7. Allow sufficient time for IRB review, if applicable, and completion of the project.

In making a determination of whether or not a class research project requires IRB review, the instructor is encouraged to contact the IRB office for assistance or to submit a for a determination following the procedures outlined in Section 8.

24.1.1.2 Individual Research Projects Conducted by Students

When students conduct, or participate as a research team member, in human subjects research other than class work as described above, they must follow the standard procedures for research described throughout this manual, as applicable to the research. As described in Section 1.10.7, students may not serve as PI on human subjects research conducted under the auspices of KCU but may serve as a sub-investigator or member of the research team. When students of KCU conduct, or participate as a research team member, in research at or with another organization, they must contact the KCU ORSP/IRB office to determine if review by the KCU IRB is required, or if a reliance agreement is needed, prior to engaging in the activity. It is important to keep in mind that any human subject research activity that will ultimately contribute to part or all of a thesis, dissertation, or other type of publication or presentation must go through the IRB review process prior to enrolling subjects and collecting data. IRB review/approval cannot occur after a study has begun.

Students and advisors should contact the IRB Office with any questions.

25 Special Topics

(This section contains discussion of additional topics that KCU may want to have included in future SOP's. Some content in this section is currently deleted or "[RESERVED]" to allow for future expansion.)

25.1 Medical Records Research and HIPAA

KCU is NOT currently a covered entity, and does not produce any medical records. The language is being kept here for educational purposes for those who may be applying for IRB approval at facilities that are covered entities (e.g., hospitals and clinics). As always, consult the SOPs at those entities for specific requirements.

The use of medical records or protected health information (PHI) usually requires IRB review. Even studies which involve only chart /medical record review sometimes pose significant risk to subjects. The most common risk is a breach of confidentiality with the exposure of potentially embarrassing information without the knowledge or consent of the subject. Such studies may also lead to recruitment of subjects into future non-therapeutic studies in a manner which may provoke the subject to ask how his/her record was revealed to someone not part of his/her therapeutic team.

The Health Insurance Portability and Accountability Act of 1996 (HIPAA) required the creation of a Privacy Rule for identifiable health information. The resulting Privacy Rule was finalized in August 2002. While the main impact of the Privacy Rule is on the routine provision of and billing for health care by covered entities, the Rule also affects the conduct and oversight of research.

KCU is not a covered entity under HIPAA, but research involving PHI obtained from a covered entity must comply with the requirements of HIPAA.

25.1.1 Definitions

Authorization. An individual's written permission to allow a covered entity to use or disclose specified PHI for a particular purpose. Except as otherwise permitted by the Privacy Rule, a covered entity may not use or disclose PHI for research purposes without a valid Authorization that includes all of the required elements under the Privacy Rule.

Covered entity. A health plan, a health care clearinghouse, or a health care provider who or that transmits health information in electronic form in connection with a transaction for which DHHS has adopted a standard.

Data Use Agreement. An agreement into which the covered entity enters with the intended recipient of a limited data set that establishes the ways in which the information in the limited data set may be used and disclosed and how it will be protected.

De-identified. Data is considered de-identified under HIPAA when they do not identify an individual, and there is no reasonable basis to believe that the data can be used to identify an individual. The Privacy Rule defines two methods for de-identifying PHI: (1) when the PHI is stripped of all 18 HIPAA-defined identifying elements and the covered entity does not have actual knowledge that the information could be used alone or in combination with other information to identify an individual who is a subject of the information (Safe Harbor method); or (2) when an appropriate expert 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 (Expert Determination method).

Disclosure. The release, transfer, provision of access to, or divulging in any manner, of information outside the entity holding the information.

Health Information. Health Information means any information, including genetic information, whether oral or recorded in any form or medium, that (1) is created or received by a health care provider, health plan, public health authority, employer, life insurer, school or university, or health care clearinghouse; 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.

Individually Identifiable Health Information. Information that is a subset of health information, including demographic information collected from an individual, and (1) is created or received by a health care provider, health plan, employer, or health care clearinghouse; 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; and (a) that identifies the individual; or (b) with respect to which there is a reasonable basis to believe the information can be used to identify the individual.

Limited Data Set. Refers to data sets that exclude 16 categories of direct identifiers that are specified in the Privacy Rule. Limited Data Sets may be used or disclosed, for purposes of research, public health, or health care operations, without obtaining either an individual's Authorization or a waiver or an alteration of Authorization for its use and disclosure, only if the covered entity obtains satisfactory assurances in the form of a Data Use Agreement. Limited Data Sets are not de-identified information under the Privacy Rule.

Minimum Necessary. The least PHI reasonably necessary to accomplish the intended purpose of the use, disclosure, or request. Unless an exception applies, this standard applies to a covered entity when using or disclosing PHI or when requesting PHI from another covered entity. A covered entity that is using or disclosing PHI for research without Authorization must make reasonable efforts to limit PHI to the minimum necessary. A covered entity may rely, if reasonable under the circumstances, on documentation of IRB or Privacy Board approval or other appropriate representations and documentation under section 164.512(i) as establishing that the request for PHI for the research meets the minimum necessary requirements.

Privacy Board. A board that is established to review and approve requests for waivers or alterations of Authorization in connection with a use or disclosure of PHI as an alternative to obtaining such waivers or alterations from an IRB. A Privacy Board consists of members with varying backgrounds and appropriate professional competencies as necessary to review the effect of the research protocol on an individual's privacy rights and related interests. The board must include at least one member who is not affiliated with the covered entity, is not affiliated with any entity conducting or sponsoring the research, and is not related to any person who is affiliated with any such entities. A Privacy Board cannot have any member participating in a review of any project in which the member has a conflict of interest.

Protected Health Information. Protected Health Information (PHI) means individually identifiable health information that is transmitted by electronic media; maintained in electronic media; or transmitted or maintained in any other form or medium. PHI excludes individually

identifiable health information in education records covered by the Family Educational Rights and Privacy Act (FERPA), as amended, 20 U.S.C. 1232g; in records described at 20 U.S.C. 1232g(a)(4)(B)(iv); in employment records held by a covered entity in its role as employer; and regarding a person who has been deceased for more than 50 years.

Waiver or Alteration of Authorization. The documentation that the covered entity obtains from a researcher or an IRB or a Privacy Board that states that the IRB or Privacy Board has waived or altered the Privacy Rule's requirement that an individual must authorize a covered entity to use or disclose the individual's PHI for research purposes.

25.1.2 Effects of HIPAA on Research

There are several provisions under which investigators may utilize PHI from a covered entity. The following is based on the NIH HIPAA Privacy Rule Booklet for Research.

25.1.2.1 Authorized Use

Except as otherwise permitted, the Privacy Rule requires that a research subject "authorize" the use or disclosure of his/her PHI to be utilized in the research. This authorization is distinct from the subject's consent to participate in research, which is required under the Common Rule and FDA regulations. Just as a valid consent under Common Rule and FDA regulations must meet certain requirements, a valid authorization must contain certain core elements (45 CFR 164.508(c)). The subject must authorize specifically what research information may be shared and who will receive the information, must acknowledge the expiration of the authorization and have the right to revoke the authorization, and must be informed that further disclosure by recipients of the information may not be covered by the federal privacy rules. The subject's right to revoke authorization is limited. The investigator and the institution may continue to use and disclose PHI that was obtained before the subject revoked authorization to the extent that the investigator or institution has acted in reliance on the authorization, such as to use or disclose PHI in order to maintain the integrity of the research (45 CFR 164.508(b)(5)(i)).

25.1.2.2 Waiver of Authorization

For research uses and disclosures of PHI, a covered entity IRB or Privacy Board may approve a waiver or an alteration of the Authorization requirement in whole or in part. The criteria for a waiver of authorization are similar to the criteria for a waiver of informed consent in the Common Rule. In most cased, the investigator must request a waiver of authorization from the covered entity's IRB or Privacy Board.

25.1.2.3 De-Identified PHI

Covered entities may disclose health information that is de-identified without restriction under the Privacy Rule. Covered entities seeking to release this health information must determine that the information has been de-identified using either statistical verification of de-identification or by removing certain pieces of information from each record as specified in the Rule.

The Privacy Rule allows a covered entity to de-identify data by removing all 18 elements that could be used to identify the individual or the individual's relatives, employers, or household members; these elements are enumerated in the Privacy Rule. The covered entity also must have no actual knowledge that the remaining information could be used alone or in combination with other information to identify the individual who is the subject of the information. Under this method, the identifiers that must be removed are the following:

1. Names.
2. All geographic subdivisions smaller than a state, including street address, city, county, precinct, ZIP Code, and their equivalent geographical codes, except for the initial three digits of a ZIP Code if, according to the current publicly available data from the Bureau of the Census:
    a. The geographic unit formed by combining all ZIP Codes with the same three initial digits contains more than 20,000 people.
    b. The initial three digits of a ZIP Code for all such geographic units containing 20,000 or fewer people are changed to 000.
3. All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death; and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older.
4. Telephone numbers.
5. Facsimile numbers.
6. Electronic mail addresses.
7. Social security numbers.
8. Medical record numbers.
9. Health plan beneficiary numbers.
10. Account numbers.
11. Certificate/license numbers.
12. Vehicle identifiers and serial numbers, including license plate numbers.
13. Device identifiers and serial numbers.
14. Web universal resource locators (URLs).
15. Internet protocol (IP) address numbers.
16. Biometric identifiers, including fingerprints and voiceprints.
17. Full-face photographic images and any comparable images.
18. Any other unique identifying number, characteristic, or code, unless otherwise permitted by the Privacy Rule for re-identification.

Covered entities may also use statistical methods to establish de-identification instead of removing all 18 identifiers. The covered entity may obtain certification by "a person with appropriate knowledge of and experience with generally accepted statistical and scientific principles and methods for rendering information not individually identifiable" that there is a "very small" risk that the information could be used by the recipient to identify the individual who is the subject of the information, alone or in combination with other reasonably available information. The person certifying statistical de-identification must document the methods used as well as the result of the analysis that justifies the determination. A covered entity is required to keep such certification, in written or electronic format, for at least 6 years from the date of its creation or the date when it was last in effect, whichever is later.

25.1.2.4 Limited Data Set

The Privacy Rule permits a covered entity, without obtaining an Authorization or documentation of a waiver or an alteration of Authorization, to use and disclose PHI included in a limited data set. A covered entity may use and disclose a limited data set for research if the disclosing covered entity and the limited data set recipient enter into a data use agreement. Because limited data sets may contain identifiable information, they are still PHI.

A limited data set is described as health information that excludes certain, listed direct identifiers (see below) but that may include city; state; ZIP Code; elements of date; and other numbers, characteristics, or codes not listed as direct identifiers. The direct identifiers listed in the Privacy Rule's limited data set provisions apply both to information about the individual and to information about the individual's relatives, employers, or household members. The following identifiers must be removed from health information if the data are to qualify as a limited data set:

1. Names.
2. Postal address information, other than town or city, state, and ZIP Code.
3. Telephone numbers.
4. Fax numbers.
5. Electronic mail addresses.
6. Social security numbers.
7. Medical record numbers.
8. Health plan beneficiary numbers.
9. Account numbers.
10. Certificate/license numbers.
11. Vehicle identifiers and serial numbers, including license plate numbers.
12. Device identifiers and serial numbers.
13. Web universal resource locators (URLs).
14. Internet protocol (IP) address numbers.
15. Biometric identifiers, including fingerprints and voiceprints.
16. Full-face photographic images and any comparable images.

A data use agreement is the means by which covered entities obtain satisfactory assurances that the recipient of the limited data set will use or disclose the PHI in the data set only for specified purposes.

25.1.2.5 Activities Preparatory to Research

For activities involved in preparing for research, covered entities may use or disclose PHI to a researcher without an individual's Authorization, a waiver or an alteration of Authorization, or a data use agreement. However, the covered entity must obtain from a researcher representations that (1) the use or disclosure is requested solely to review PHI as necessary to prepare a research protocol or for similar purposes preparatory to research, (2) the PHI will not be removed from the covered entity in the course of review, and (3) the PHI for which use or access is requested is necessary for the research. The covered entity may permit the researcher to make these representations in written or oral form.

25.1.2.6 Research on Decedents' Protected Health Information

To use or disclose PHI of the deceased for research, covered entities are not required to obtain Authorizations from the personal representative or next of kin, a waiver or an alteration of the Authorization, or a data use agreement. However, the covered entity must obtain from the researcher who is seeking access to decedents' PHI (1) oral or written representations that the use and disclosure is sought solely for research on the PHI of decedents, (2) oral or written representations that the PHI for which use or disclosure is sought is necessary for the research purposes, and (3) documentation, at the request of the covered entity, of the death of the individuals whose PHI is sought by the researchers.

25.1.3 IRB Review of Medical Records Research

25.1.3.1 Exempt Research

Research involving medical records is exempt provided the records utilized in the research are existing and the data are recorded in such a manner that participants cannot be identified (e.g., either all 18 HIPAA specified identifiers are removed or a bio-statistical consult indicated there is only a “small risk” of re-identification of a participant).

25.1.3.2 Non-Exempt Research

For research that is not exempt (expedited or full review required) the IRB will require documentation that the investigator is authorized by the covered entity to receive PHI under one of the above HIPAA provisions described above.

25.2 Databases, Registries, & Repositories

Databases, registries, and biospecimens repositories (all referred to as repositories throughout this section) are used to store data and/or biospecimens for future use.

There are two type of repositories:

- Non-research repositories created and maintained for purposes that are unrelated to research. Such purposes may include diagnosis, treatment, billing, marketing, quality control, and public health surveillance.
- Research repositories created and maintained specifically for research purposes. Such purposes may include databases to identify prospective subjects, patient outcome information to evaluate treatment effectiveness, and tissues samples for future research. Non-research repositories that are altered to facilitate research (e.g., through the addition of data fields not necessary for the core purpose of the repository) are considered research repositories.

25.2.1 Non-research Repositories

Even though repositories were not created for research purposes, they may contain information that is of great interest to researchers. The creation (or operation) of non-research databases or repositories does not involve human subject research and does not require IRB oversight. However, IRB approval is required for the research use of identifiable private information or identifiable human specimens from non-research repositories, and, regardless of identifiability, when specimens will be used to evaluate the safety or effectiveness of a medical device. Research under the auspices of KCU that includes the use of coded private information or specimens, must either be submitted for IRB review or for a "Human Subjects Research Determination" (See Section 8).

Researchers submitting an application for research using data or specimens from non-research repositories must describe the source of the data/specimens and any terms, conditions, or restrictions on use. Data/specimens cannot be used for research if the person from whom the data/specimens originated objected to its use for research. Informed consent and HIPAA authorization (when applicable) must be obtained unless the IRB determines that the criteria for a waiver are satisfied.

25.2.2 Research Repositories

Research repositories involve three distinct activities:

1. Collection of data/specimens;
2. Storage and management of data/specimens; and
3. Distribution of data/specimens.

Collection

Informed consent and HIPAA authorization (when applicable) must be obtained unless the IRB determines that the criteria for a waiver are satisfied.

Informed Consent information should include:

- A clear description of
    - What data/specimens will be collected;
    - Where the data/specimens will be stored, who will have access, and how the data/specimens will be secured;
    - Whether the data/specimens will be identifiable, coded, or de-identified;
    - The types of research to be conducted and any limitations or restrictions on such; and
    - The conditions under which data/specimens will be released to recipient-investigators

- A statement regarding future withdrawal of the data from the study (i.e., state whether subjects may, in the future, request that their data be destroyed or that all personal identifiers be removed from data and how to make such a request)
- When appropriate, the plan for management of incidental findings and sharing of results

Storage and Management

Repositories should have written policies describing:

- The conditions under which data/specimens will be accepted (e.g., inclusion criteria)
- Informed consent
- IRB review
- The sources of data/specimens
- Whether data/specimens will be identifiable, coded, or de-identified, and, if coded, management of the linkage key; and
- Physical and procedural mechanisms for the secure receipt, storage, and distribution of data/specimens

Distribution

Repositories should have written policies describing:

- How data/specimens may be requested and by whom
- Any requirements associated with a request for data/specimens (e.g., verification of IRB approval or that approval is not required)
- Any limitations or restrictions on how data/specimens may be used
- Whether released data/specimens will be identifiable, coded, or de-identified, and, if coded, any circumstances under which recipient investigators will access to or be provided with the key or other means to re-identify; and
- Agreements with recipient investigators specifying the terms of use.

25.2.3 IRB Oversight

IRB approval is required for the establishment and operation of a research repository when the data/specimens that are accessed, received, stored, or distributed are identifiable. In general, private information or specimens are considered individually identifiable when the identities of the subjects are known to investigators/repository operators or when the data/specimens can be linked to specific individuals either directly or indirectly through coding systems.

Separate IRB approval is required for the use of data/specimens from a repository when the recipient investigator(s) know or may readily ascertain the identity of individual subjects, and, regardless of identifiability, when specimens will be used to evaluate the safety or effectiveness of a medical device. Research under the auspices of KCU that includes the use of coded private

information or specimens, must either be submitted for IRB review or for a "Human Subjects Research Determination" (See Section 8). The only exception to this policy is when the coded private information or specimens are to be obtained from an IRB-approved repository and the rules of that repository forbid the release of identifiable information, the release of the key to the code or other means that would allow re-identification, or the release of sufficient information that investigators could readily ascertain the identity of subjects.

25.3 Transnational Research

The KCU IRB reviews transnational research involving human subjects to ensure that adequate provisions are in place to protect the rights and welfare of the subjects. All policies and procedures that are applied to research conducted domestically are applied to research in international settings, as appropriate. Approval of research is permitted if *"the procedures prescribed by the foreign institution afford protections that are at least equivalent to those provided in 45 CFR 46."*

For federally conducted or supported research, approval of research for foreign institutions or sites "engaged" in research is only permitted if the foreign institution or site holds a FWA with OHRP and local IRB review and approval is obtained.

Approval of research for foreign institutions or sites "not engaged" in research is only permitted if one or more of the following circumstances exist:

- When the foreign institution or site has an established IRB/EC, the investigator must obtain approval to conduct the research at the "not engaged" site from the site's IRB/IEC or provide documentation that the site's IRB/EC has determined that approval is not necessary for the investigator to conduct the proposed research at the site.
- When the foreign institution or site does not have an established IRB/IEC, a letter of cooperation must be obtained demonstrating that the appropriate institutional or oversight officials permit the research to be conducted at the performance site.
- IRB approval to conduct research at the foreign institution or site is contingent upon receiving documentation of the performance site's IRB/EC determination, or letter of cooperation, as applicable.

The KCU IRB seeks sufficient knowledge of the local research context by requesting approval for the project from local IRBs or ethics committees (which may or may not be OHRP-registered) and/or local letters of support. The source of this information will depend on the nature of the study, on the country, and on the resources available to the investigator. Where there is a local IRB/EC, KCU IRB must receive and review the foreign institution or site's IRB/EC review and approval of each study prior to beginning the research at the foreign institution or site.

In settings where there are no IRBs/ECs, KCU IRB may require additional verification and information from people outside the particular research project who are familiar with the customs, practices, or standards of care where the research will be taking place, including other IRBs or committees with experience reviewing research in the region, other KCU investigators with knowledge of the region, or a consultant who is an expert on the region, prior to approval.

These individuals may either provide a written review of the research protocol or attend an IRB meeting to provide the KCU IRB with recommendations based on his or her expertise. Additionally, if the proposed international site does not have a IRB/EC, the KCU researcher may submit the project for review to the KCU IRB which will hold the review to the same standards as if was being conducted in the United States.

25.3.1 IRB Responsibilities

In addition to the IRB review considerations discussed elsewhere in this manual, the IRB will consider the following when reviewing transnational research:

1. The qualifications of the investigator and research staff to conduct research in that country including knowledge of relevant laws, regulations, guidance and custom;
2. Whether the consent process and consent documents are appropriate for the language(s) of the subjects and the subject population, and that arrangements are made to be able to communicate with subjects throughout the study (e.g., to ask and answer questions);
3. How modifications to the research will be handled;
4. How complaints, noncompliance, protocol deviations and unanticipated problems involving risks to subjects or others are handled;
5. How post-approval monitoring will be managed;
6. Whether the investigator has obtained the appropriate host country permissions to conduct research (e.g., institutional, governmental or ministerial, IRB, local, or tribal). When appropriate, the IRB communicates and coordinates with the local institutions or ethics committees; and
7. Mechanisms for communicating with the investigators and research staff when they are conducting the research in other countries.

25.3.2 Investigator Responsibilities

The investigator conducting transnational research is responsible for:

1. Ensuring that the resources and facilities are appropriate for the nature of the research;
2. Verifying the qualifications of the investigators and research staff for conducting research in the country(ies);
3. Obtaining all appropriate host country permissions to conduct research (e.g., institutional, governmental or ministerial, IRB, local, or tribal);
4. Complying with the requirements of country law; including, when applicable, requirements for research involving investigational articles;
5. Ensuring that the consent process and consent document are appropriate for the language(s) of the subjects and the subject population, and that arrangements are made

to be able to communicate with subjects throughout the study (e.g., to ask and answer questions);

6. Ensuring that the following activities will occur:
7. Initial review, continuing review, and review of modifications;
8. Post-approval monitoring of the conduct of the research in accordance with the plan approved by the IRB; and
9. Handling of complaints, noncompliance and unanticipated problems involving risk to subjects or others;
10. Not relying upon an IRB or EC that does not have policies and procedures for the activities listed above;
11. Ensuring that reportable information such as complaints, noncompliance, protocol deviations and unanticipated problems involving risks to participants or other are communicated to the IRB;
12. Notifying the IRB promptly if a change in research activities alters the performance site's engagement in the research (e.g., performance site "not engaged" begins to obtain consent of research participants, etc.); and
13. Ensuring that there are mechanisms for communicating with the IRB when they are conducting the research in other countries.

25.3.3 Consent Documents

The informed consent documents must be appropriate for and in a language understandable to the proposed subjects. The IRB will review the proposed document and a back translation of the exact content contained in the foreign language informed consent document, with the credentials of the translator detailed in the IRB application or Modification Request form. All documents, including verification of the back translation, are maintained in the IRB file.

25.3.4 Monitoring of Approved Transnational Research

The IRB is responsible for the ongoing review of international research conducted under its jurisdiction through the continuing review process or progress report in accordance with all applicable federal regulations. When the IRB and a local ethics committee are both involved in the review of research, there is a plan for coordination and communication with the local IRB/ECs.

The IRB requires documentation of regular correspondence between the KCU investigator and the foreign institution or site and may require verification from sources other than the KCU investigator that there have been no changes made to the research since its last review.

25.4 FDA-Regulated Research [RESERVED; KCU does not currently conduct FDA regulated research]

25.4.1 When do FDA regulations apply?

FDA's research regulations may apply when a protocol is studying or evaluating one or more FDA-regulated products, even when the data or specimens may have been generated for other purposes (e.g., clinical care) or are anonymized. FDA research regulations generally do not apply when a marketed FDA-regulated product (such as an MRI) is being used in a manner consistent with its labeling as a tool to gather or generate data in research that is evaluating a hypothesis that is not about the product itself. Because FDA regulates such a broad range of products, from band-aids to medical apps and other software to neurostimulators, and the nuances of the regulations are complex, investigators are encouraged to consult with the IRB office in advance of any application to the IRB that involves the evaluation or off-label use of a medical or health product.

FDA regulations apply to research that involves an FDA-regulated *test article* in a *clinical investigation* involving *human subjects* as defined by the FDA regulations, and per the definitions below. For FDA-regulated research, the IRB must apply the FDA regulations at 21 CFR 50 and 21 CFR 56. If the research is conducted or supported by a Common Rule agency or department, or if compliance with the Common Rule is required by state law or the terms of an award or contract, then the Common Rule must also be applied.

The following procedures describe the review of FDA-regulated research by the KCU IRB.

25.4.2 Definitions

Clinical Investigation. Clinical investigation means any experiment that involves a test article and one or more human subjects, and that either is subject to the requirements for prior submission to the FDA under section 505(i) or 520(g) of the Federal Food, Drug, and Cosmetic Act ("Act"), or is not subject to the requirements for prior submission to the FDA under these sections of the Act, but the results of which are intended to be later submitted to, or held for inspection by, the FDA as part of an application for a research or marketing permit. The terms research, clinical research, clinical study, study, and clinical investigation are synonymous for purposes of FDA regulations. [21 CFR 50.3(c), 21 CFR 56.102(c)]

Experiment. Experiment means any use of a drug other than the use of an approved drug in the course of medical practice [21 CFR 312.3(b)] or any activity that evaluates the safety or effectiveness of a medical device. [21 CFR 812.2(a)]

Human Subject. For research covered by FDA regulations (21 CFR 50 and 56), human subject means an individual who is or becomes a participant in a clinical investigation (as defined above), either as a recipient of the test article or as a control. A subject may be in normal health or may have a medical condition or disease. In the case of a medical device, a human subject/participant also includes any individual on whose tissue specimen an investigational device is used or tested. Importantly, the FDA regulations do not exclude unidentified specimens.

Investigational Drug. Investigational *or* experimental drugs are new drugs that have not yet been approved by the FDA or approved drugs that are being studied in a clinical investigation.

Investigational Device. Investigational device means a device (including a transitional device) that is the object of an investigation. Investigation, as it pertains to devices, means a clinical investigation or research involving one or more subjects to determine the safety or effectiveness of a device.

Test Article. *Test article* means any drug for human use, biological product for human use, medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the Federal Food, Drug, and Cosmetic Act, as amended (secs. 201-902, 52 Stat. 1040 *et seq.,* as amended (21 U.S.C. 321-392)) or under sections 351 and 354-360F of the Public Health Service Act [42 U.S.C. 262 and 263b-263n]. [21 CFR 50.3(j)]

Test articles covered under the FDA regulations include, but are not limited to:

1. **Human drugs** – A drug is defined as a substance recognized by an official pharmacopoeia or formulary; a substance intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease; a substance (other than food) intended to affect the structure or any function of the body; a substance intended for use as a component of a medicine but not a device or a component, part or accessory of a device. Biological products are included within this definition and are generally covered by the same laws and regulations, but differences exist regarding their manufacturing processes (chemical process versus biological process). The primary intended use of a drug product is achieved through chemical action or by being metabolized by the body.
2. **Medical Devices** - A device is "an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is: recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them; intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals; or intended to affect the structure or any function of the body of man or other animals, and which does not achieve any of its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes."
3. **Biological Products** - include a wide range of products such as vaccines, blood and blood components, allergenics, somatic cells, gene therapy, tissues, and recombinant therapeutic proteins. Biologics can be composed of sugars, proteins, or nucleic acids or complex combinations of these substances, or may be living entities such as cells and tissues. Biologics are isolated from a variety of natural sources — human, animal, or microorganism — and may be produced by biotechnology methods and other cutting-edge technologies. Gene-based and cellular biologics, for example, often are at the forefront of biomedical research, and may be used to treat a variety of medical conditions for which no other treatments are available.

4. **Dietary Supplements** – A dietary supplement is a product taken by mouth that is intended to supplement the diet and that contains one or more "dietary ingredients." The "dietary ingredients" in these products may include vitamins, minerals, herbs or other botanicals, amino acids, and other substances found in the human diet, such as enzymes. When a dietary supplement meets the definition of drug, it is regulated as such.
5. **Medical Foods** – A medical food, as defined in section 5(b) of the Orphan Drug Act (21 U.S.C. 360ee (b) (3)), is a food which is formulated to be consumed or administered enter ally under the supervision of a physician and which is intended for the specific dietary management of a disease or condition for which distinctive nutritional requirements, based on recognized scientific principles, are established by medical evaluation.
6. **Mobile Medical Apps** - Mobile apps are software programs that run on smartphones and other mobile communication devices. They can also be accessories that attach to a smartphone or other mobile communication devices, or a combination of accessories and software. Mobile Medical Apps are medical devices that are (a) mobile apps, (b) meet the definition of a medical device and (c) are either an accessory to a regulated medical device or transform a mobile platform into a regulated medical device.
7. **Radioactive Drugs** – The term radioactive drug means any substance defined as a drug which exhibits spontaneous disintegration of unstable nuclei with the emission of nuclear particles or photons and includes any nonradioactive reagent kit or nuclide generator which is intended to be used in the preparation of any such substance but does not include drugs such as carbon-containing compounds or potassium-containing salts which contain trace quantities of naturally occurring radionuclides. The term "radioactive drug" includes "radioactive biological product".
8. **Radiation-Emitting Electronic Products** - a radiation-emitting electronic product as any electrically-powered product that can emit any form of radiation on the electromagnetic spectrum. These include a variety of medical and non-medical products such as mammography devices, magnetic resonance imaging (MRI) devices, laser toys, laser pointers, liquid crystal displays (LCDs), and light emitting diodes (LEDs).

25.4.3 FDA Exemptions

The following categories of clinical investigations are exempt from the requirements of FDA regulations for IRB review:

1. Emergency use of a test article, provided that such emergency use is reported to the IRB within 5 working days. Any subsequent use of the test article at the institution is subject to IRB review. [21 CFR §56.104(c)]
2. Taste and food quality evaluations and consumer acceptance studies, if wholesome foods without additives are consumed or if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural, chemical, or environmental contaminant at or below the level found to be safe, by the FDA or

approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture. [21 CFR §56.104(d)]

25.4.4 Procedures

1. At initial submission, the PI must indicate whether the research involves the administration or evaluation of an FDA-regulated product on the application form.
2. During the pre-review process, the IRB Staff will confirm whether FDA regulations are applicable. If FDA regulations apply, the IRB Staff will obtain any additional information needed from the investigator (e.g., justification for why an IND is not required) and indicate on the agenda or in pre-review comments that the protocol is an FDA-regulated study.
3. The IRB, or designated reviewer, will review the research in accordance with the following requirements and the same criteria it would use in considering approval of any research involving an FDA-regulated product. [21 CFR 50 and 21 CFR 56]

25.4.5 Clinical Investigations of Articles Regulated as Drugs or Devices

25.4.5.1 IND Exemptions

For drugs, an IND is not necessary if the research falls in one of the following seven (7) categories:

1. The drug being used in the research is lawfully marketed in the United States and all of the following requirements are met:
    a. The research is not intended to be reported to FDA as a well-controlled study in support of a new indication and there is no intent to use it to support any other significant change in the labeling of the drug;
    b. In the case of a prescription drug, the research is not intended to support a significant change in the advertising for the product;
    c. The research does not involve a route of administration, dose, subject population, or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product;
    d. The research is conducted in compliance with the requirements for IRB review and informed consent [21 CFR parts 56 and 50, respectively];
    e. The research is conducted in compliance with the requirements of 21 CFR 312.7 (i.e., the research is not intended to promote or commercialize the drug product); and
    f. The research does not intend to invoke FDA regulations for planned emergency research [21 CFR 50.24].
2. The research only involves one or more of the following: (a) Blood grouping serum, (b) Reagent red blood cells or (c) Anti-human globulin;

3. For clinical investigations involving an in vitro diagnostic biological product, an IND is not necessary if a) it is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established, diagnostic product or procedure; and b) it is shipped in compliance with 312.160
4. A clinical investigation involving use of a placebo is exempt from the requirements of part 312 if the investigation does not otherwise require submission of an IND.
5. Bioavailability or Bioequivalence (BA/BE) studies if all of the following conditions are met:
    a. The drug product does not contain a new chemical entity [21 CFR 314.108], is not radioactively labeled, and is not cytotoxic;
    b. The dose (single dose or total daily dose) does not exceed the dose specified in the labeling of the approved version of the drug product;
    c. The investigation is conducted in compliance with the requirements for IRB review and informed consent [21 CFR parts 56 and 50, respectively]; and
    d. The sponsor meets the requirements for retention of test article samples [21 CFR 320.31(d)(1)] and safety reporting [21 CFR 320.31(d)(3)].
6. Research using a radioactive drug or biological product if all of the following conditions are met:
    a. It involves basic research not intended for immediate therapeutic, diagnostic, or similar purposes, or otherwise to determine the safety and efficacy of the product;
    b. The use in humans is approved by a Radioactive Drug Research Committee (RDRC) that is composed and approved by FDA;
    c. The dose to be administered is known not to cause any clinically detectable pharmacological effect in humans, and
    d. The total amount of radiation to be administered as part of the study is the smallest radiation dose practical to perform the study without jeopardizing the benefits of the study and is within specified limits.
7. FDA practices enforcement discretion for research using cold isotopes of unapproved drugs if all of the following conditions are met:
    a. The research is intended to obtain basic information regarding the metabolism (including kinetics, distribution, and localization) of a drug labeled with a cold isotope or regarding human physiology, pathophysiology, or biochemistry;
    b. The research is not intended for immediate therapeutic, diagnostic, or preventive benefit to the study subject;
    c. The dose to be administered is known not to cause any clinically detectable pharmacologic effect in humans based on clinical data from published literature or other valid human studies;
    d. The quality of the cold isotope meets relevant quality standards; and

e. The investigation is conducted in compliance with the requirements for IRB review and informed consent. [21 CFR parts 56 and 50, respectively]

If the FDA has already determined whether an IND is required, documentation evidencing such should be provided to the IRB. The FDA's determination is final and the IRB does not have to make the determination.

When the FDA has not made a determination, the sponsor or investigator is responsible for providing the IRB with justification explaining why, in their opinion, an IND is not required and any other information that may help the IRB in evaluating the IND status of the study.

The IRB will review the information provided by the sponsor and investigator including, but not limited to: the sponsor or investigator's IND assessment, the drug labeling (for marketed drugs), reports of prior investigations of the drug (if applicable), the proposed investigational plan, subject selection criteria, and the drug accountability plan. If the study entails greater than minimal risk, a plan for Data and Safety Monitoring must be included. When the IRB determines that an IND is required, or is uncertain if an IND is needed, the IRB will require evaluation by the FDA prior to approving the study. When an IND is required or when otherwise appropriate (e.g., the IRB lacks the needed expertise), KCU may require review by an external IRB.

25.4.5.2 Dietary Supplements

Research involving dietary supplements may or may not fall under FDA regulations. Under the Dietary Supplement Health and Education Act (DSHEA) of 1994, a dietary supplement is not considered a drug and is not subject to the premarket approval requirements for drugs if the intended use for which it is marketed is only to affect the structure or any function of the body (i.e., not intended to be used for a therapeutic purpose). Whether a study falls under FDA oversight is determined by the intent of the clinical investigation. If the clinical investigation is intended only to evaluate the dietary supplement's effect on the structure or function of the body, FDA research regulations do not apply. However, if the study is intended to evaluate the dietary supplement's ability to diagnose, cure, mitigate, treat, or prevent a disease, then FDA regulations do apply. Studies involving the ingestion of dietary supplements that are not subject to FDA oversight are still research, and therefore must be reviewed by the IRB.

Similarly, whether an IND is needed for a study evaluating a dietary supplement is determined by the intent of the study. If the study is intended only to evaluate the dietary supplement's effect on the structure or function of the body, an IND is not required. However, if the study is intended to evaluate the dietary supplement's ability to diagnose, cure, mitigate, treat, or prevent a disease, an IND is required under part 312.

As with any research involving a test article, the investigator must supply the IRB with sufficient information to determine that the criteria for approval are satisfied and to determine or verify whether the research requires an IND. Applications should provide detail consistent with that expected on a drug protocol and consistent with the level of risk associated or anticipated with the research. At a minimum, the research plan should provide the following information regarding the supplement: Name, Manufacturer, Formulation, Dosage, Method/Route of Administration, Mechanism of Action, Known Drug Interactions, Risk Profile, IND number (or

justification for why an IND is unnecessary), documentation of approval for use in humans, documentation or certification of Quality or Purity. As with drugs and devices there should be an accountability plan for the product describing where the product will be stored and how it will be dispensed, usage tracked, and disposal or return. If the study entails greater than minimal risk, a plan for Data and Safety Monitoring must be included.

25.4.5.3 IDE Exemptions

For clinical investigations of medical devices, an IDE is not necessary if:

1. The research involves a device, other than a transitional device, in commercial distribution immediately before May 28, 1976, when used or investigated in accordance with the indications in labeling in effect at that time;
2. The research involves a device other than a transitional device, introduced into commercial distribution on or after May 28, 1976, that FDA has determined to be substantially equivalent to a device in commercial distribution immediately before May 28, 1976, and that is used or investigated in accordance with the indications in the labeling FDA reviewed under subpart E of 21 CFR 807 in determining substantial equivalence (a "501k" device);
3. The research involves a diagnostic device, if the sponsor complies with applicable requirements in 21 CFR 809.10(c) and if the testing:
    a. Is noninvasive,
    b. Does not require an invasive sampling procedure that presents significant risk,
    c. Does not by design or intention introduce energy into a subject, and
    d. Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure;
4. The research involves a device undergoing consumer preference testing, testing of a modification, or testing of a combination of two or more devices in commercial distribution, if the testing is not for the purpose of determining safety or effectiveness and does not put subjects at risk;
5. The research involves a device intended solely for veterinary use;
6. The research involves a device shipped solely for research on or with laboratory animals and labeled in accordance with 21 CFR 812.5(c);
7. The research involves a custom device as defined in 21 CFR 812.3(b), unless the device is being used to determine safety or effectiveness for commercial distribution.

If the FDA has already determined a study to be IDE exempt, documentation evidencing such should be provided to the IRB. The FDA's determination is final and the IRB does not have to make the device determination.

Unless the FDA has already issued a determination, the IRB will review studies that the sponsor or investigator have put forth as IDE-exempt to determine if the study is IDE-exempt.

The sponsor or sponsor-investigator is responsible for providing the IRB with an explanation describing the basis for their initial determination of IDE-exempt and any other information that may help the IRB in evaluating the IDE status of the study.

The IRB will review the information provided by the sponsor and investigator including, but not limited to: the sponsor or investigator's IDE-exempt assessment, the description of the device, reports of prior investigations of the device (if applicable), the proposed investigational plan, subject selection criteria, and the device accountability plan. If the study entails greater than minimal risk, a plan for Data and Safety Monitoring must be included. When the IRB determines that a study is not IDE-exempt, it will inform the investigator and may require submission of additional information to support its evaluation of whether the study is Significant or Non-Significant Risk or may require evaluation by the FDA. The IRB will not finalize approval of a medical device study until the device determination is made.

25.4.5.4 Significant and Non-Significant Risk Device Studies

A device study is a Non-Significant Risk (NSR) Device study if it is not IDE-exempt and does not meet the definition of a Significant Risk (SR) Device study.

Under 21 CFR 812.3(m), an SR device means an investigational device that:

1. Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject;
2. Is purported or represented to be for use supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject;
3. Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or
4. Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

If the FDA has already determined a study to be SR or NSR, documentation evidencing such should be provided to the IRB. The FDA's determination is final and the IRB does not have to make the device determination.

Unless the FDA has already made a device determination for the study, the IRB will review studies that the sponsor or investigator have put forth as NSR at a convened meeting to determine if the device represents SR or NSR.

The sponsor or sponsor-investigator is responsible for providing the IRB with an explanation describing the basis for their initial determination of NSR and any other information that may help the IRB in evaluating the risk of the study (e.g., reports of prior investigations of the device).

The IRB will review the information provided by the sponsor and investigator including, but not limited to: the sponsor or investigator's NSR assessment, the description of the device, reports of prior investigations of the device (if applicable), the proposed investigational plan, subject

selection criteria, and the device accountability plan. If the study entails greater than minimal risk, a plan for Data and Safety Monitoring must be included.

The NSR/SR determination made by the IRB will be based on the proposed use of the device in the investigation, not on the device alone. The IRB will consider the nature of any harms that may result from use of the device, including potential harms from additional procedures subjects would need to undergo as part of the investigation (e.g., procedures for inserting, implanting, or deploying the device). The IRB may consult with the FDA or require the sponsor or investigator to obtain a determination from the FDA. The IRB will document the SR or NSR determination and the basis for it in the meeting minutes and provide the investigator, and sponsor when applicable, with the determination in writing. When a study is determined to be SR or when otherwise appropriate (e.g., the IRB lacks the needed expertise), KCU may require review by an external IRB. SR device studies cannot begin until an IDE is obtained from the FDA and IRB approval is finalized.

Non-significant risk device studies do not require submission of an IDE application to the FDA but must be conducted in accordance with the abbreviated requirements of IDE regulations (21 CFR 812.2(b)). Under the abbreviated requirements, the following categories of investigations are considered to have approved applications for IDE's, unless FDA has notified a sponsor under 812.20(a) that FDA approval of an application is required:

1. An investigation of a device other than a significant risk device, if the device is not a banned device and the sponsor (or sponsor-investigator):
    a. Labels the device in accordance with 812.5;
    b. Obtains IRB approval of the investigation after presenting the reviewing IRB with an explanation of why the device is not a significant risk device, and maintains such approval;
    c. Ensures that each investigator participating in an investigation of the device obtains from each subject under the investigator's care, informed consent under part 50 and documents it, unless the requirement is waived by the IRB;
    d. Complies with the requirements of 812.46 with respect to monitoring investigations;
    e. Maintains the records required under 812.140(b) (4) and (5) and makes the reports required under 812.150(b) (1) through (3) and (5) through (10);
    f. Ensures that participating investigators maintain the records required by 812.140(a)(3)(i) and make the reports required under 812.150(a) (1), (2), (5), and (7); and
    g. Complies with the prohibitions in 812.7 against promotion and other practices.

25.4.6 Investigator Responsibilities

The investigator holds additional responsibilities when conducting a clinical investigation subject to FDA regulations. These responsibilities include, but are not limited to, the following:

1. The investigator is responsible for indicating on the IRB application that the proposed research is FDA-regulated and for providing relevant information regarding the test article.
2. The investigator is responsible for ensuring that a clinical investigation is conducted according to the signed investigator statement for clinical investigations of drugs (including biological products) or agreement for clinical investigations of medical devices, the investigational plan and other applicable regulations, and any requirements imposed by the FDA or IRB.
3. The investigator is responsible for personally conducting or supervising the investigation. When study-related tasks are delegated by an investigator, the investigator is responsible for providing adequate supervision of those to whom tasks are delegated. The investigator is accountable for regulatory violations resulting from failure to adequately supervise the conduct of the clinical study.
4. The investigator must maintain a list of the appropriately qualified persons to whom significant trial-related duties have been delegated. This list should also describe the delegated tasks, identify the training that individuals have received that qualifies them to perform delegated tasks (e.g., it can refer to an individual's CV on file and/or training conducted by the investigator or sponsor), and identify the dates of involvement in the study. An investigator should maintain separate lists for each study conducted by the investigator.
5. The investigator is responsible for protecting the rights, safety, and welfare of subjects under their care during a clinical trial. This responsibility includes:
    a. Informing subjects that the test articles is being used for investigational purposes and ensuring that the requirements relating to obtaining informed consent are met
    b. Providing or arranging for reasonable medical care for study subjects for medical problems arising during participation in the trial that are, or could be, related to the study intervention
    c. Providing reasonable access to needed medical care, either by the investigator or by another identified, qualified individual (e.g., when the investigator is unavailable, or when specialized care is needed)
    d. Adhering to the protocol so that study subjects are not exposed to unreasonable risks
    e. As appropriate, informing the subject's primary physician about the subject's participation in the trial if the subject has a primary physician and the subject agrees to the primary physician being informed.
6. The investigator is responsible for reading and understanding the information in the investigator brochure or device risk information, including the potential risks and side effects of the drug or device.

7. The investigator is responsible for maintaining adequate and accurate records in accordance with FDA regulations and to making those records available for inspection by the FDA. These records include, but are not limited to: correspondence with other investigators, the IRB, the sponsor, monitors, or the FDA; drug and device accountability records; case histories; consent forms; and documentation that consent was obtained prior to any participation in the study. Records must be obtained for a minimum of 2 years following the date a marketing application is approved for the drug for the indication for which it is being investigated; or, if no application is to be filed or if the application is not approved for such. For clinical investigations of medical devices, required records must be maintained for a period of 2 years after the latter of the following two dates: The date on which the investigation is terminated or completed, or the date that the records are no longer required for purposes of supporting a premarket approval application or a notice of completion of a product development protocol. Other regulations, such as HIPAA, organizational policies, or contractual agreements with sponsors may necessitate retention for a longer period of time.
8. The investigator is responsible for controlling test articles according to FDA regulations and the Controlled Substances Act, if applicable.
9. For research reviewed by the KCU IRB, the investigator proposing the clinical investigation will be required to provide a plan – to be evaluated by the IRB - that includes storage, security, and dispensing of the test article.
    a. The investigator is responsible for investigational drug accountability that includes storage, security, dispensing, administration, return, disposition, and records of accountability. Such details will be provided in the IRB submission and reviewed by the IRB for acceptability.
    b. The investigator may delegate in writing, as part of the IRB submission, the responsibility detailed in 'a' above to the Pharmacy Service.
    c. Investigational drugs and devices must be labeled in accordance with federal and state standards.
    d. All devices received for a study must be stored in a locked environment under secure control with limited access. When applicable, proper instructions on the use of the device must be provided to the subjects. A log must be kept regarding the receipt, use, and/or dispensing of the device, and the disposition of remaining devices at the conclusion of the investigation.
10. The investigator shall furnish all reports required by the sponsor of the research including adverse events, progress reports, safety reports, final reports, and financial disclosure reports.
11. The investigator will permit inspection of research records by the sponsor, sponsor representatives, IRB representatives, the FDA, accrediting bodies, and any other agencies or individuals entitled to inspect such records under regulation, organizational policy, or contractual agreement.

25.5 State-Mandated Reporting

[This section is RESERVED for future development consistent with Missouri law]

25.6 Lead Investigator/Coordinating Center

When KCU IRB is serving as the IRB of record for a PI or site who is serving as the lead investigator or lead/coordinating center of a multi-site or collaborative research project, the PI must describe within the protocol and IRB application how the research will be overseen and how issues relevant to the protection of human subjects (e.g., IRB initial and continuing approvals, study modifications, reports of unanticipated problems, interim results, data-safety monitoring, etc.) will be coordinated and communicated among participating sites and investigators.

The lead PI or lead/coordinating center is responsible for serving as the liaison with other participating sites and investigators and for ensuring that all participating investigators obtain IRB review and approval prior to initiating the research, maintain approval, and obtain IRB approval for modifications to the research. The KCU IRB will evaluate whether the plan for research oversight and management of information that is relevant to the protection of human subjects is adequate.

25.7 Certificates of Confidentiality

Certificates of Confidentiality (CoC) protect research information by prohibiting certain disclosures and conditioning others upon consent from the subject. The protections and requirements of CoCs are outlined in 42 U.S.C. 241(d) and NIH policy (when applicable), and summarized below.

CoC's are obtained as follows:

- CoCs are issued automatically when research is conducted or supported by NIH and falls within the scope of the NIH policy.
- Research that is not funded by NIH (non-NIH research) may still have the protections afforded by CoCs through successful application to the NIH, FDA, or other authorized Federal agencies or departments.

Additional information about CoCs and the application process for non-NIH research is available on the NIH CoC Website.

25.7.1 Definitions

Identifiable, sensitive information means information that is about an individual and that is gathered or used during the course of biomedical, behavioral, clinical, or other research and

1. Through which an individual is identified; or
2. For which there is at least a very small risk, as determined by current scientific practices or statistical methods, that some combination of the information, a request for the information, and other available data sources could be used to deduce the identity of an individual.

25.7.2 Protections and Requirements

When a CoC is issued, whether automatically or under an approved application, the person(s) engaged in the research must not disclose or provide the name of a subject or any information, document, or biospecimen that contains identifiable, sensitive information about the subject and that was compiled for the purposes of the research:

1. In any Federal, State, or local civil, criminal, administrative, legislative, or other proceeding, unless the disclosure is made with the consent of the individual to whom the information, document, or biospecimen pertains; or
2. To any other person not connected with the research, unless:
    a. Required by Federal, State, or local laws (e.g., adverse event reporting to the FDA, transmissible disease reporting required under State law), but excluding proceedings as described in "1" above;
    b. Necessary for the medical treatment of the subject to whom the information, document, or biospecimen pertains and made with the consent of the subject;
    c. Made with the consent of the individual to whom the information, document, or biospecimens pertains; or
    d. Made for the purposes of other scientific research that is in compliance with applicable Federal regulations governing the protection of human subjects in research.

Additional Protections

Identifiable, sensitive information protected under a CoC, and all copies thereof, are immune from the legal process, and shall not, without the consent of the individual to whom the information pertains, be admissible as evidence or used in any action, suit, or other judicial, legislative, or administrative proceeding.

Identifiable, sensitive information that has been collected under a CoC, and all copies thereof, are protected for perpetuity. If identifiable, sensitive information covered by a CoC is shared with other researchers or organizations, the researchers or organizations must be informed that the information is covered by a CoC and of their responsibility to protect the information accordingly.

Nothing in the rule (42 U.S.C. 241(d)) may be construed to limit the access of a subject to information about himself or herself collected during the research.

When consent is obtained, the consent should inform subjects that a CoC is in place and describe the protections and limitations.

25.7.3 NIH Policy

The NIH Policy on CoCs applies to *"all biomedical, behavioral, clinical, or other research funded wholly or in part by the NIH, whether supported through grants, cooperative agreements, contracts, other transaction awards, or conducted by the NIH Intramural Research Program, that collects or uses identifiable, sensitive information"* that was commenced or ongoing on or after December 13, 2016.

CoCs are automatically granted, and the requirements of such must be complied with, whenever a NIH-funded activity falls within the scope of the policy. Investigators and institutions are responsible for determining when a NIH-funded activity falls within the scope of the policy.

NIH policy expands upon 42 U.S.C. 241(d) by explaining that NIH considers research in which identifiable, sensitive information is collected or used, to include:

- Human subjects research as defined in 45 CFR 46, including research determined to be exempt (except for exempt research when the information obtained is recorded in such a manner that human subjects cannot be identified or the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects);
- Research involving the collection or use of biospecimens that are identifiable to an individual or for which there is at least a very small risk that some combination of the biospecimen, a request for the biospecimen, and other available data sources could be used to deduce the identity of an individual;
- Research that involves the generation of individual level, human genomic data from biospecimens, or the use of such data, **regardless of whether the data is recorded in such a manner that human subjects can be identified or the identity of the human subjects can readily be ascertained;** or
- Any other research that involves information about an individual for which there is at least a very small risk, as determined by current scientific practices or statistical methods, that some combination of the information, a request for the information, and other available data sources could be used to deduce the identity of an individual, as defined in subsection 301(d) of the Public Health Service Act.

25.7.4 NIH CoC Policy Determination

At KCU, Grants and Contracts staff will, in consultation with the investigator(s) determine if the NIH policy applies to any NIH-funded activity. The questions outlined in the NIH policy will be used to guide the analysis. When it has been determined that the NIH policy doesn't apply, investigators are responsible for consulting with Grants and Contracts whenever they are proposing changes to the NIH-funded activity that may impact or change the analysis.

The NIH policy includes additional responsibilities and requirements for internal controls and for ensuring that recipients of identifiable, sensitive information protected by a CoC understand that they are also subject to the requirements of subsection 301(d) of the Public Health Service Act.

25.7.5 Application Procedures for non-NIH Research

Any person engaged in human subjects research that collects or uses identifiable, sensitive information may apply for a CoC. For most research, CoCs are obtained from NIH, an investigator may apply for a CoC through the NIH Institute or Center funding research in a scientific area similar to the project.

If the research is conducting a sensitive research project that is covered by the Agency for Healthcare Research and Quality (AHRQ) confidentiality statute (42 U.S.C. section 299c-3(c)) or the Department of Justice (DoJ) confidentiality statute (42 U.S.C. section 3789g), then a CoC may not be needed.

If there is an Investigational New Drug Application (IND) or an Investigational Device Exemption (IDE), the sponsor can request a CoC from the FDA.

CoCs may also be issued by other Federal agencies and departments, such as CDC, SAMSHA, or HRSA.

For more information, see the NIH CoC Website.

25.7.6 IRB Review

Investigators are responsible for clearly representing in the IRB submission that a CoC is in place, or that an application for CoC has been submitted. When the CoC application is in process or pending, the IRB may condition final approval upon its receipt.

For studies that are already underway, investigators must submit a Modification Request to the IRB, along with updated consent language (if applicable), when a CoC is applied for, or when automatically issued under the NIH policy.

When reviewing research under a CoC, the KCU IRB will evaluate whether the research plan is consistent with the obligations to protect information and specimens under a CoC and whether the consent language, if applicable, discloses the CoC and appropriately describes the associated protections and limitations. Sample consent language is available on the NIH CoC Website.

When non-NIH research is not under a CoC, the IRB may require an investigator to apply for a CoC if the research includes identifiable, sensitive information and the IRB determines that a CoC is necessary to minimize risks and adequately protect subjects' privacy and the confidentiality of subjects' information or specimens.

25.8 Case Reports Requiring IRB Review

Federal regulations at 45 CFR 46.102(d) and 45 CFR 164.501 define research as a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. The KCU IRB does not consider the retrospective review and analysis of records for publication of a single case report or a case series involving data from two or three individuals to be research, and therefore such a report of 1-3 cases does not need to be submitted to the IRB. This is because reporting on such a small number of individuals does not involve a systematic investigation, including defining a hypothesis that is then investigated

prospectively and systematically, to develop or contribute to generalizable knowledge. The KCU regards such limited case report preparation as an educational activity, not research, and thus it is permissible when the case report will be used internally, or in other learning environments, for educational purposes. When a larger series of individuals is being evaluated for presentation or publication, the commonalities of those individuals are typically explored and conclusions are drawn (i.e., a systematic investigation). Such a systematic investigation more closely resembles prospectively designed research and as such requires IRB review and approval. While drawing such a "bright line" to distinguish non-research from research may seem arbitrary, it serves as a guide to those who would prepare case reports. If a researcher ever does intend a report of 1-3 cases to develop or contribute to generalizable knowledge, or to otherwise constitute research, the report should be submitted to the IRB with a request for a determination whether the case report constitutes research using the procedures outlined in Section 8. As always, anyone who is unsure whether a project requires IRB review should contact the IRB Office for assistance.

Regardless of the number of cases, providers must comply with all applicable laws and KCU policies related to the use and release of private, identifiable information. Permission from the individuals who will be included in the report should be sought whenever possible, and journals may require such as a condition of publication.

A copy of this policy can be provided to journal editors or others who request confirmation of IRB review or waiver. If needed, the IRB office can provide a letter confirming that submission of single case reports or series of up to 3 cases is not required.

25.9 Research Involving or Generating Genetic Information

25.10 Genomic Data Sharing

25.11 Community Based Research

Community based research (CBR) is research that is based in a community and conducted in collaboration with members of that community. *Community* is often self-defined, but general categories of community include geographic community, a community of individuals with a common problem or issue, or a community of individuals with a common interest or goal.

Where research is being conducted in communities, investigators are encouraged to involve members of the community in the research process, including the design and implementation of research and the dissemination of results when appropriate.

The most significant community involvement is in a subset of CBR called Community Based Participatory Research (CBPR) where there is an equal partnership between the academic investigators and members of a community, with the latter actively participating in all phases of the research process including the design and implementation of research and the dissemination of results when appropriate.

Questions to be considered as CBR studies are developed, and issues that the IRB will consider when reviewing CBR, are as follows:

- How was the community involved or consulted in defining the need for the proposed research (i.e., getting the community's agreement to conduct the research)?
- How was the community involved or consulted in generating the study research plan?
- How will the research procedures, including recruitment strategies and consent processes be assessed to ensure sensitivity and appropriateness to various communities (e.g., literacy issues, language barriers, cultural sensitivities, etc.)?
- How will the community be involved in the conduct of the proposed research?
- How will community members who participate in the implementation of the research be trained and supervised?
- How have "power" relationships between investigators and community members on the research team, and in subject recruitment strategies been considered to minimize coercion and undue influence?
- What are the risks and benefits of the research for the community as a whole?
- How will boundaries between multiple roles (e.g., investigator, counselor, peer) be maintained, i.e., what happens when the investigator/research staff is the friend, peer, service provider, doctor, nurse, social worker, educator, funder, etc.)
- How will the research outcomes be disseminated to the community?
- Is there a partnership agreement or memorandum of understanding to be signed by the investigator and community partners that describes how they will work together?

26 Regulations From Other Federal Agencies

26.1 Department of Defense [KCU does not current have DOD funded human subjects research]

26.1.1 Key DOD Standards and Requirements

26.1.1.1 Minimal Risk

26.1.1.2 Education and Training

26.1.1.3 Appointment of a Research Monitor

26.1.1.4 Additional protections for vulnerable subjects

26.1.1.5 Additional Consent Elements

26.1.1.6 Limitation of Waivers and Exceptions from Informed Consent

26.1.1.7 Limitations on Compensation for Human Subjects in Research

26.1.1.8 Reporting Requirements

26.1.1.9 Recordkeeping Requirements

26.1.1.10 Addressing and Reporting Allegations of Non-Compliance with Human Research Protections

26.1.1.11 Addressing and Reporting Allegations of Research Misconduct

26.1.1.12 Prohibition of Research with Detainees

26.1.1.13 Classified research

26.1.1.14 Additional Requirements for DOD Research

26.2 Department of Education [KCU does not current have DOE funded human subjects research]

26.2.1 Family Educational Rights and Privacy Act (FERPA)

The Family Educational Rights and Privacy Act (FERPA) is a Federal law that protects the privacy of student education records at educational entities that receive funds from the ED. In general, schools must have written permission from the parent or eligible student to release any information from a student's education record. However, FERPA allows schools to disclose personally identifiable information from an education record of a student without consent if the

disclosure is to organizations conducting studies for, or on behalf of, educational agencies or institutions to:

1. Develop, validate, or administer predictive tests;
2. Administer student aid programs; or
3. Improve instruction. [34 CFR 99.31(a)(6)]

A written agreement with the receiving organization is required, including:

1. The purpose, scope, and duration of the study(ies);
2. The information to be disclosed;
3. A requirement that the receiving organization uses the personally identifiable information from the educational records only for the purpose(s) of the study as stated in the agreement;
4. A requirement that the receiving organization conducts the study in a manner that does not permit personal identification of students and parents by anyone other than representatives of the organization with legitimate interests; and
5. A requirement that the receiving organization destroys or returns all personally identifiable information when the information is no longer needed for the purposes for which the study was conducted and that specified the time period in which the information must be returned or destroyed.

Education records may be released without consent under FERPA if all personally identifiable information has been removed including:

1. Students' names and other direct identifiers, such as students' Social Security Numbers or student numbers;
2. Indirect identifiers, such as the name of students' parents or other family members, the students' or families addresses, and personal characteristics or other information that would make the students' identities easily traceable, and dates and places of birth and mothers' maiden names;
3. Biometric records, including measurable biological or behavioral characteristics that can be used for automated recognition of an individual, including fingerprints, retina and iris patterns, voiceprints, DNA sequence, facial characteristics, and handwriting; and
4. Other information that, alone, or in combination, is linked or linkable to a student that would allow a reasonable person in the school community, who does not have personal knowledge of the relevant circumstances, to identify to student with reasonable certainty.

At KCU, when FERPA applies, investigators must provide the IRB with information describing how they will ensure compliance with the rule. A letter of support or other documentation from the school supporting the conduct of the research should be provided. The IRB will review the

information provided to verify compliance, including verification that permission for the use of the records will be obtained or that it is not required under an allowed use or exception.

26.2.2 Protection of Pupil Rights Amendment (PPRA)

The Protection of Pupil Rights Amendment (PPRA) affords parents of elementary and secondary students certain rights regarding the conduct of survey, collection and use of information for marketing purposes, and certain physical exams. PPRA applies to the programs and activities of a state educational agency (SEA), local educational agency (LEA), and any other recipient of ED funds. These rights transfer from parents to students when they reach the age of 18 or are an emancipated minor. This section is not intended to address PPRA as a whole, rather it addresses PPRA requirements as they most commonly relate to research.

26.2.2.1 Definitions:

Instructional Material means instructional content that is provided to a student, regardless of its format, including printed or representational materials, audio-visual materials, and materials in electronic or digital formats (such as materials accessible through the Internet). The term does not include academic tests or academic assessments.

Invasive Physical Examination means any medical examination that involves the exposure of private body parts, or any act during such examination that includes incision, insertion, or injection into the body, but does not include a hearing, vision, or scoliosis screening.

Personal Information means individually identifiable information including: (1) a student's or parent's first and last name; (2) a home or other physical address (including a street name and the name of a city or town); (3) a telephone number; or, (4) a Social Security Number.

Research or Experimentation Program or Project means any program or project in any program that is designed to explore or develop new or unproven teaching methods or techniques.

26.2.2.2 Rights under PPRA

When **research is funded by ED (Education Department),** no student can be required to submit **without prior consent** to a survey that concerns one or more of the following protected areas:

1. Political affiliations or beliefs of the student or the student's parent;
2. Mental and psychological problems of the student or his or her family;
3. Sex behavior and attitudes;
4. Illegal, anti-social, self-incriminating, and demeaning behavior;
5. Critical appraisals of other individuals with whom the student has close family relationships;
6. Legally recognized privileged and analogous relationships, such as those of lawyers, physicians, and ministers;
7. Religious practices, affiliations, or beliefs of the student or student's parent; or

8. Income, other than that required by law to determine eligibility for participation in a program or for receiving financial assistance under a program.

Parents have the right to **receive notice and an opportunity to opt a student out** of:

1. Any other survey that concerns any of the above protected areas, **regardless of funding**;
2. Any non-emergency, invasive physical exam or screening required as a condition of attendance, administered by the school or its agent, that is not necessary to protect the health and safety of a student, except for hearing, vision, or scoliosis screenings, or any physical exam or screening permitted or required under state law; and
3. Activities involving collection, disclosure, or use of personal information collected from students for marketing or to sell or otherwise distribute the information to others. (This does not apply to the collection, disclosure, or use of personal information collected from students for the exclusive purpose of developing, evaluating, or providing educational products or services for, or to, students or educational institutions.)

Parents also have the **right to inspect** upon request and before administration or use:

1. Surveys that concern any of the protected areas and surveys created by third parties;
2. Instruments used to collect personal information from students for any of the above marketing, sales, or other distribution purposes;
3. Any instructional material used as part of the educational curriculum for the student; and
4. Instructional material, including teachers' manuals, films, tapes, or other supplementary instructional material, which will be used in conjunction with any research or experimentation program or project.

26.2.2.3 Procedures

At KCU, when PPRA applies, investigators should review the school's PPRA policies and must provide the IRB with information describing how they will ensure compliance with the rule and the school's policies. A letter of support or other documentation from the school supporting the conduct of the research and its compliance with PPRA should be provided. The IRB will review the information provided to verify compliance.

26.3 Department of Energy [KCU currently does not conduct research funded by the DOE.]

26.3.1 Definitions

26.3.2 Human Subjects Research

26.3.3 Protection of Data

26.3.4 Classified Research

26.3.5 DOE Employees, Contractors, and Students

26.3.6 Reporting Requirements

26.4 Department of Justice [KCU currently does not conduct research funded by the DOJ.]

26.4.1 Principal Investigator Responsibilities

26.4.2 Bureau of Prisons

[KCU does not currently conduct research in federal prisons]

26.5 Environmental Protection Agency [KCU currently does not conduct research funded by the EPA]

26.5.1 EPA Definitions:

26.5.2 EPA Human Subjects Research Review Official (HSRRO) Approval

26.5.3 PI Reporting Requirements

26.5.4 Intentional Exposure

26.5.5 Observational Research

26.5.6 Observational Human Exposure Studies

26.5.7 Other EPA Regulations