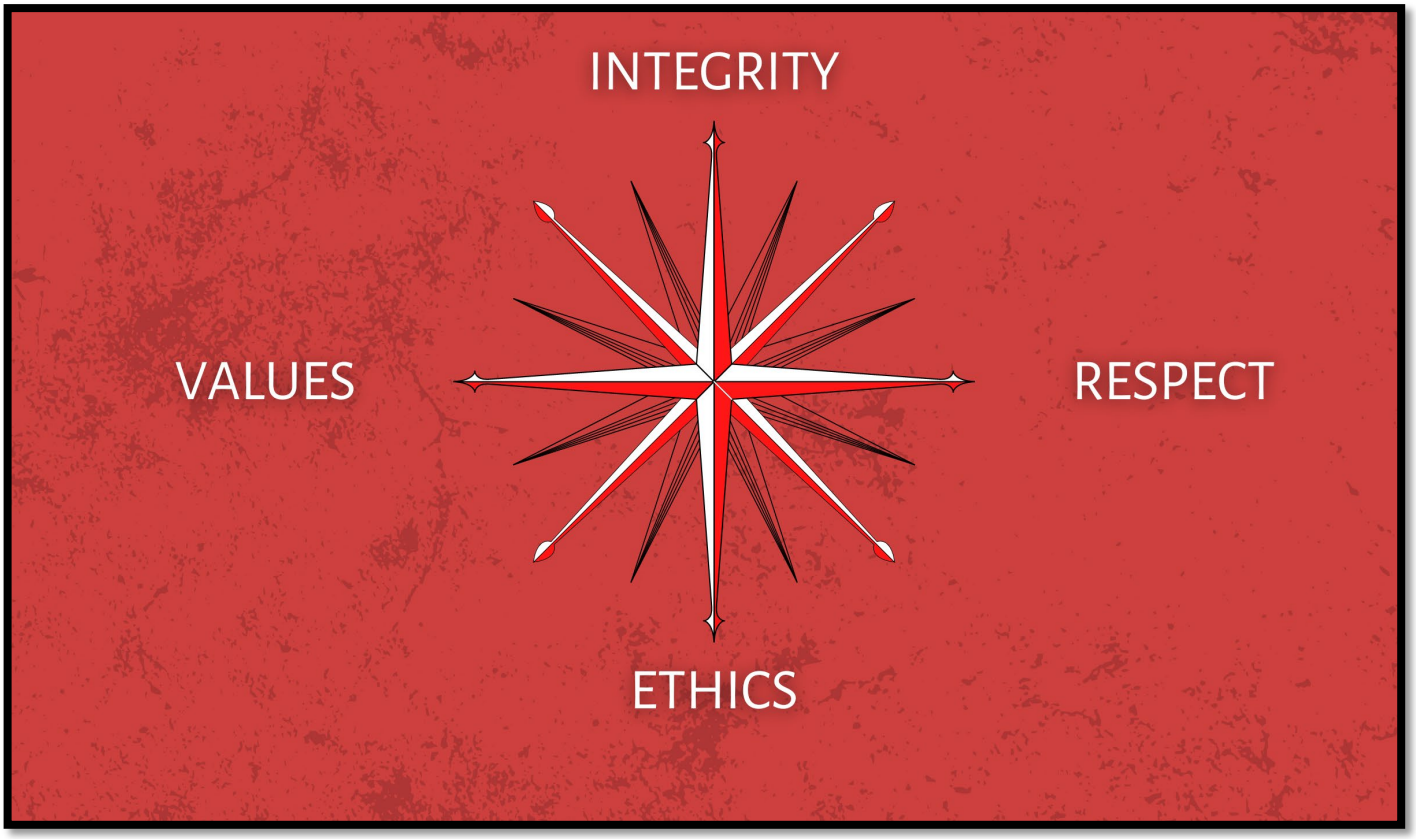
TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER

HUMAN RESEARCH PROTECTION PROGRAM MANUAL

Version September 2026



ACRONYMS USED IN THIS MANUAL

AHRPP Association for the Accreditation of Human Research Protection Program
AVP-RI Assistant Vice President – Research Integrity
CFR Code of Federal Regulations
CITI Collaborative Institutional Training Initiative
COIRC Conflict of Interest in Research Committee
CRI Clinical Research Institute
CRU Clinical Research Unit
CV Curriculum Vitae
DHHS Department of Health and Human Services
DNA Deoxyribonucleic Acid
ESCRO Embryonic Stem Cell Research Oversight Committee
FCOI Financial Conflict of Interest
FDA Food and Drug Administration
FWA Federal Wide Assurance
GINA Genetic Information Nondiscrimination Act
hESC Human Embryonic Stem Cells
HRPP Human Research Protection Program
HIPAA Health Insurance Portability and Accountability Act
IBC Institutional Biosafety Committee
ICH-GCP International Conference on Harmonization – Good Clinical Practice
IDE Investigational Device Exemption
IND Investigational New Drug
IRB Institutional Review Board
IRS Internal Revenue Service
IO Institutional Official
MISC Miscellaneous
NCI National Cancer Institute
NIH National Institutes of Health
NSR Nonsignificant Risk (usually in reference to a device)
OHRP Office of Human Research Protections
OP Operating Policy & Procedure
OSP Office of Sponsored Programs
PHI Protected Health Information
PI Principal Investigator
PRIM&R Public Responsibility in Medicine and Research
QIRB Quality Improvement Review Board
RCC Research Compliance Committee
RSC Radiation Safety Committee
RIO Research Integrity Office
SAE Serious Adverse Event
SR Significant Risk (usually in reference to a device)
EVP Executive Vice President for Research and Innovation
TTU Texas Tech University
TTUHSC Texas Tech University Health Sciences Center

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ORGANIZATION OF THE TEXAS TECH UNIVERSITY HUMAN RESEARCH PROTECTION PROGRAM

1.1 Introduction and Organizational Summary

This manual describes the policies and procedures of the Texas Tech University Health Sciences Center (TTUHSC) Human Research Protection Program (HRPP). This Manual is provided in an effort to communicate comprehensive information about the organization, structure, and function of the human research protection program to the members of the research community at TTUHSC including regional campuses and affiliated institutions. This Manual incorporates TTUHSC's program to protect human subjects (also referred to as research participants), the Institutional Review Boards' (IRBs') operating procedures and references to TTUHSC Institution -Wide Operating Policies and Procedures in one core document. The document is organized around the elements and standards required by the Association for the Accreditation of Human Research Protection Programs . This Manual describes TTUHSC's compliance with applicable regulations such as the Common Rule (45 CFR 46 – pre2018 and 2018) and Food and Drug Administration regulations relating to human subjects (21 CFR 50 and 21 CFR 56) and relies upon following ethical standards as found in the Belmont Report.

All members of the TTUHSC community who engage in research involving human subjects must be knowledgeable about the requirements of the HRPP. All information governing the conduct and review of research involving human subjects under the purview of the TTUHSC HRPP can be found at the TTUHSC Research website.

In order to protect and promote the rights and welfare of those who serve as participants in biomedical or behavioral research projects, Texas Tech University Health Sciences Center has developed and implemented a Human Research Protection Program (HRPP), an integrated system of research administration and oversight functions, including education, compliance, and review by Institutional Review Boards (IRBs).Together, these functions and the individuals who carry them outpromote excellence in all aspects of human research. The goal of the TTUHSC HRPP is to promote ethical treatment of those who volunteer to serve as research subjects through compliance with relevant regulations and ethical standards at all levels. The HR PP also addresses the needs and concerns of investigators, study coordinators and study sponsors and enhances support of their research endeavors.

The HRPP is led by the Executive Vice President for Research and Innovation (EVP) who has been designated as the Institutional Official (IO) for purposes of executive responsibility for research programs at TTUHSC. Delegation of day-to-day responsibility of the TTUHSC Human Research Protection Program is shared by personnel in the Research Integrity Office (RIO), TTUHSC IRB chairs and IRB members. Ultimately, however, success of TTUHSC's HRPP requires commitments from all parties involved in human research, including TTUHSC administrators, faculty, staff, residents, students, sponsors and affiliates.

The Executive Vice President for Research and Innovation/IO and Assistant Vice President - Research Integrity engage in an on-going review of the status of the HRPP via bi -weekly meetings of the TTUHSC Research Directors or through additional ad hoc meetings held as necessary to discuss pertinent issues. Monthly reports and an annual written summary of the IRBs' activities areprepared by the IRB administrators andprovided to the Assistant Vice President- Research Integrity (AVP-RI) and the SVPR. Monthly reports are utilized as part of a semi-annual HRPP review prepared by the Research Compliance Officer. The annual summary is used to assess IRB composition and provides a basis for adjusting membership if needed. The institutional quality assurance process also provides ongoing quality

assessment and quality improvement goals for issues related to the efficiency of the TTUHSC HRPP.

The TTUHSC Research Integrity Office budget covers most full-time personnel, maintenance and operations of the TTUHSC Human Research Protection Program. The RIO budget is part of the overall Office of Research budget. The Office of Research and/or RIO budgets provide financial support to several components of the HRPP including the Office of Sponsored Programs, Conflict of Interest in Research Committee and Quality Improvement Review Board. The budget is reviewed at least annually with the SVPR by Office of Research Administration, including the Assistant VP-Research Integrity.

Adjustments are made as necessary to cover any unexpected expenses or resources required for community outreach activities sponsored by the Office of Research or Research Integrity Office. IRB review fees provide supplemental funding support for the HRPP program. Fees include initial and continuing review of industry-sponsored research and/or for provision of IRB services to local affiliates as outlined in contractual agreements. These fees are used primarily for education, conference registration, and travel expenses incurred by RIO staff and IRB Chairs and members as well as membership fees and certifications for professional organizations.

Non-financial resources required to support the TTUHSC HRPP generally involve requests for personnel to serve on committees or to provide consultation to the HRPP (Office of General Counsel, HIPAA Officers, requests to Deans and Department Chairs, Information Technology, etc.) Evaluation of the need for these non-financial resources is informal and ongoing. Requests for assistance are made by RIO staff, the Assistant Vice President – Research Integrity or the SVPR.

1.2 Statement of Ethical Principles

The TTUHSC IRBs are guided by ethical principles applicable to all research involving humans as subjects as set forth in the report of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (known as the Belmont Report).

The ethical principles set forth in the Belmont Report are:

- Respect for Persons: recognition of the personal dignity and autonomy of individuals and special protection of those persons with diminished autonomy;
- Beneficence: obligation to protect persons from harm by maximizing anticipated benefits and minimizing possible risks of harm; and
- Justice: fairness in the distribution of research benefits and burdens.

International and multi-site clinical trials conducted at TTUHSC will be conducted in accordance with International Conference on Harmonization – Good Clinical Practice Guidelines (ICH-GCP). These guidelines have their origins in the Declaration of Helsinki and were developed with consideration of current good clinical practices in the United States, Canada, the European Union and other countries and organizations. Although compliance with all ICH-GCP guidelines are required for international and multi-site clinical trials as indicated in the clinical trial agreement, some elements of the guidelines have been incorporated into this manual as required procedures for all research involving human subjects. The ICH-GCP guidelines that are implemented for all research at TTUHSC are incorporated into relevant sections of this manual.

1.3 Components of the TTUHSC Human Research Protection Program

In order to function effectively, the TTUHSC Human Research Protection Program (HRPP) requires commitments and assistance from many areas within and outside of the institution. The major components of the TTUHSC Human Research Protection Program include:

- **The Institutional Official.** The Executive Vice President for Research and Innovation (EVP) serves as the Institutional Official with overall responsibility for the TTUHSC Human Research Protection Program. Specific duties and responsibilities of the SVPR with regard to the Human Research Protection Program can be found under Institutional Authority.
- **Research Integrity Office.** The Assistant Vice President - Research Integrity is recognized by the Institutional Official as the point of contact with Department of Health and Human Services' (DHHS) Office of Human Research Protections (OHRP). RIO staff members exercise operational responsibility, on a day-to-day basis, for the HRPP. This includes IRB administration, as well as the compliance, education, and quality improvement components of the TTUHSC HRPP. Review of clinical trial agreements is also addressed through the Research Integrity Office. The Director of Clinical Contracting reviews and manages the confidential disclosure agreements and funding agreements for compliance with Federal and State regulations, TTUHSC and HRPP policies and procedures.
- **Institutional Review Boards (IRBs).** TTUHSC has two IRBs, located on the Lubbock and Amarillo campuses. The Lubbock IRB reviews research involving human subjects conducted under the oversight of Principal Investigators (PIs) at the Lubbock campus. The Amarillo IRB reviews projects under the oversight of Principal Investigators at the Amarillo, Dallas , Permian Basin and Abilene campuses. The IRBs have the authority to approve, require modifications to secure approval, or disapprove all human research overseen and conducted by TTUHSC. The IRB or chairperson, acting on behalf of the IRB, may also 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 subjects. The IRB may observe, or have a third party oversee, the consent process and the conduct of human research.
- **Department Chairpersons/Signatory Authorities.** Each project submitted for IRB review must be electronically signed by a Department Signatory Authority (generally, the Department Chair) attesting to the study's scientific merit, available resources, study feasibility and is described in more detail under Principal Investigator Sign-off.
- **General Counsel.** The Texas Tech University (TTU) System Office of General Counsel is available to provide advice upon request of the SVPR, IRB, and other individuals involved with the HRPP. The Office of General Counsel may provide legal guidance and interpretation of TTUHSC policies, State and Federal laws and regulations as they relate to the conduct of research involving human subjects.
- **Office of Sponsored Programs (OSP).** The TTUHSC Office of Sponsored Programs handles grant administration. Personnel in those offices review sponsored contracts and funding agreements for compliance with Federal and State regulations, TTUHSC and HRPP policies and procedures.
- **Conflict of Interest in Research Committee (COIRC).** Studies in which an investigator has a financial conflict of interest in the research must be reviewed by the COIRC and, if necessary, have an approved Conflict Management Plan in

place prior to approval by a TTUHSC IRB. Further details can be found in TTUHSC OP 73.09.

- **Quality Improvement Review Board (QIRB).** Scholarly projects conducted by TTUHSC faculty, staff or students which are designed to bring about immediate change in a specific department or unit, generally using Plan-Do-Study-Act cycles, do not meet the definition of research with human subjects described elsewhere in this document. The QIRB director reviews, provides feedback to project personnel, and provides institutional approval for these types of projects whose results may be disseminated outside of TTUHSC.
- **Health Insurance Portability and Accountability Act (HIPAA) Privacy Officers.** These individuals (housed at each TTUHSC campus) are responsible for HIPAA Privacy oversight at their campus. Each HIPAA Privacy Officer reports to the Institutional Compliance Office.
- **Investigators and Research Staff.** Investigators and research staff have a responsibility to follow the HRPP requirements described throughout the HRPP Manual and to comply with all determinations of the IRB and the SVPR.
- **Deans/Department Chairs.** These individuals are responsible for "setting the tone" for responsible conduct and oversight of human research in their department or school, for providing opportunities for education regarding ethical and compliant actions as they relate to research, for fostering support of IRB members, and for providing adequate resources to conduct human research at TTUHSC.
- **Clinical Research Institute (CRI)/Clinical Research Unit (CRU).** These groups are established to facilitate the conduct of ethical clinical, epidemiological, and educational research by TTUHSC faculty and students.
- **All TTUHSC Faculty, Staff and Students.** Everyone associated with TTUHSC should have a general idea of human research protections and should consult the IRB when faced with uncertainty about whether an activity involves research with human subjects. Individuals should report allegations of possible research misconduct as outlined in TTUHSC OP 73.14, Research Compliance and TTUHSC OP 73.07, Honesty in Research and Allegations of Scientific Misconduct

1.3.1 Communication Between Components

TTUHSC institutes several mechanisms by which to communicate information relevant to the HRPP. These include a general announcements website which posts all institutional policy changes/updates on a monthly basis. In addition, changes specifically pertinent to human research investigators/staff are communicated via the web-based Cayuse software system (Human Ethics module). Announcement feature. Cayuse announcements, (for example: updates to the HRPP manual, template form changes, relevant policy changes) are sent as needed.

The Assistant Vice President - Research Integrity serves as a central liaison between the HRPP and other research compliance committees, the Institutional Official, various departments and the Office of Research. The Assistant Vice President - Research Integrity also serves as the facilitator of the institutional Research Compliance Committee (RCC). The RCC serves as a conduit for sharing information across the various research compliance committees.

The IRB application form serves as a primary tool for assessment of the various institutional components which may be required to ensure protection of subjects involved in a human research project. The IRB and IRB staff review each submission to verify that these institutional components are adequately described. Examples

include the presence of signatory authorization, consent template language reflecting terminology required in the clinical study contract, training and financial disclosures of all study personnel, and presence of approved conflict management plans when necessary. If the IRB or IRB staff determines that any institutional requirements necessary to protect participants are lacking, the principal investigator will be notified in writing to address the issue(s) and to provide additional necessary documents or information needed to comply with institutional policies/ procedures.

1.4 Scope

Only research that involves the use of human subjects requires review by the TTUHSC IRBs Further, TTUHSC, or an affiliated entity with which TTUHSC has a written agreement to serve as an IRB of record, must be engaged in the research project in order to require review by a TTUHSC IRB. To determine whether an activity meets the definition of research involving human subjects, the following definitions should be considered.

1.4.1 2018 Common Rule Requirements

TTUHSC adopted the 2018 Common Rule Requirements on January 21, 2019. The implementation of the 2018 Requirements includes the following:

a. All studies approved prior to January 21, 2019, operate under the pre-2018 Requirements.
b. All studies approved after January 21, 2019, operate under the 2018 Requirements.
c. With few exceptions, the TTUHSC IRBs are not going to transition any studies operating under the pre-2018 Requirements to the 2018 Requirements. These studies remain under the pre-2018 Requirements throughout the life of the study.
d. References within this document have been updated to include pre-2018 Requirements, 2018 Requirements, and FDA references when appropriate. If references are not identified as pre-2018 Requirements and 2018 Requirements, the reference did not change between versions.
e. Continuing reviews will continue to be conducted for all studies that are required to comply with FDA regulations.

1.4.2 Definitions

1.4.2.1 Research

A systematic investigation, including research development, testing and evaluation, designed to contribute to generalizable knowledge (45 CFR 46.102[l]).

Clinical investigations required to follow FDA-specific regulations are defined as any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) or 520 (g) of the Federal Food, Drug and Cosmetic Act, or need not meet the requirements for prior submission to the Food and Drug Administration under these sections of the Federal Food, Drug and Cosmetic Act, but the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application of a research or marketing permit. (21 CFR 50.3[c]; 21 CFR 56.102[c]). Further, when medical device research involves in vitro diagnostics and unidentified tissue specimens, the FDA defines the unidentified tissue specimens as human subjects.

For purposes of determining whether a project requires IRB review and approval, a “systematic investigation” can usually be recognized by a hypothesis-driven

project, with a specific question or questions to be answered and an a priori written plan for obtaining data which will test the hypothesis. "Generalizable knowledge" refers to the results of the project having predictive value which can be applied in settings other than the specific one(s) where the data were collected.

The following activities are deemed not to be research:

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 individual about whom the information is collected [i.e., single case report, case series (n=3)].

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).

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.

Quality improvement projects, which are systematic, data-driven activities designed to address a specific problem in a specific setting (usually a clinical or educational setting) using evidence-based interventions. While clinical research projects are designed to discover new information and to create generalizable knowledge, the scope of a quality improvement project is narrower; QI projects are designed to implement and measure improvement on a specific performance gap in a single setting, with a goal of providing an immediate benefit to the patients, students, or employees in that setting. TTUHSC has implemented a separate process for review of quality improvement projects. Please see Quality Improvement Review for more information.

Decisions regarding whether a particular project meets the definition of research and whether a research project is exempt from formal IRB review are made by the IRB Administrator or IRB member. If a project submitted for IRB review is determined not to meet the definition of research, the study team will be notified in writing that the project is "not research" and that IRB review is not required. Similarly, if an investigator requests an exemption determination for a submitted project which does not meet the criteria for exemption, the study team will be notified in writing that a non-exempt IRB application and other supporting documents must be submitted for formal IRB review. Additional information about research which is exempt from formal IRB review can be found in Section 2.9 Determination of Exempt Human Research

Investigators who are not sure whether a project will meet the definition of research are encouraged to consult their IRB Administrator. A written summary of the consultation discussion and decision will be provided to the investigator upon request.

1.4.2.2 Human Subjects/Participants

Human subject means a living individual about whom an investigator (whether professional or student) 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.

The Food and Drug Administration (FDA) defines a human subject as an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient (21 CFR 50.3[g]).

Research using unidentifiable publicly or commercially available databases, human cell lines, or material from human cadavers is not considered to meet the definition of a human subject, and, as such, does not require IRB review or approval. Data that had been previously collected for an IRB-approved research project may be re-analyzed to answer a new research question ONLY if the data have been completely de-identified prior to the new analysis. Any other research involving these data requires a new submission to the IRB prior to the analysis.

The federal regulations make no explicit distinction between human research conducted on oneself versus others. Therefore, TTUHSC investigators who intend to conduct research using themselves as a research subject (or intend to use their own tissues or specimens) are required to submit the project for review and approval by a TTUHSC IRB prior to engaging in the research activity.

1.4.2.3 Engagement

TTUHSC is considered to be “engaged” in a human research project if any one or more of the following criteria is met:

- The research is conducted by or under the direction of any employee, student or agent of TTUHSC in connection with responsibilities to TTUHSC.
- The research is conducted by or under the direction of any employee, student or agent of an entity with which TTUHSC has a written agreement to serve as the IRB of record, if the project falls under the auspices of the agreement.
- The research involves TTUHSC patient’s identifiable nonpublic information maintained by TTUHSC or an affiliated entity.
- The research is conducted in accordance with an assurance filed with the DHHS Office of Human Research Protection in which a TTUHSC IRB is designated as the IRB of record.
- TTUHSC may also be engaged in the research, and require IRB approval, if either of the following applies:
- The research takes place at any property or facility of TTUHSC
  OR
- The research is sponsored by TTUHSC.

Investigators and study personnel who are unsure whether a proposed project meets the criteria for research, whether the project utilizes human subjects, or whether TTUHSC is engaged in the project should contact their local IRB Office or

the Research Integrity Office for assistance with making the determination. A valuable resource for assisting in making these decisions can be found using the **OHRP Decision Charts** or the **OHRP Guidance on Engagement of Institutions in Human Subjects Research** references.

1.5 Authority

Unless otherwise explicitly stated in this document, all research involving human subjects conducted at or in affiliation with TTUHSC, regardless of funding source, shall be conducted in accordance with federal regulations and TTUHSC OP 73.06, Research Involving Human Subjects. Applicable federal regulations as specified in the Code of Federal Regulations (CFR), include, but are not limited to:

- 45 CFR 46 (pre2018 and 2018), generally known as the Common Rule, and subparts B, C, & D;
- 21 CFR 50, Human Subject Protection (Informed Consent);
- 21 CFR 56, Institutional Review Boards;
- 21 CFR 312, Investigational New Drug Application;
- 21 CFR 812, Investigational Device Exemptions

Any changes made to these regulations will be immediately adopted by all TTUHSC IRBs, supplanting anything written in the TTUHSC Policies and Procedures.

1.5.1 Federalwide Assurance

TTUHSC has an approved, signed Federalwide Assurance (FWA00006767) filed with the Department of Health and Human Services (DHHS). The FWA is TTUHSC's assurance of compliance that all research involving human subjects will be conducted in accordance with the ethical principles of the Belmont Report and DHHS regulations at 45 CFR 46. Although the assurance applies only to federally funded research, the regulations under 45 CFR 46, including all Subparts, provide the practical basis for the review and approval of all human research at TTUHSC, regardless of funding source.

1.5.2 Institutional Authority

The Executive Vice President for Research and Innovation (EVP) is the TTUHSC Institutional Official with overall responsibility for the TTUHSC Human Research Protection Program. Components of the Human Research Protection Program have been described previously in this document. Additional references include TTUHSC Operating Policy (OP) 73.06, Research Involving Human Subjects, Federalwide Assurance 00006767, the Research Integrity Office (RIO) and the TTUHSC Research Compliance Program.

The SVPR/Institutional Official responsibilities include, but are not limited to, the following areas:

- Appointing IRB members.
- Suspending or terminating the IRB membership of any individual for whom it has been determined that membership obligations or responsibilities are not being fulfilled.
- Appointing IRB chairs and Co-Chairs.
- Suspending or terminating the appointment of any Chair or Co-Chair for whom it has been determined that leadership obligations or responsibilities are not being fulfilled.
- Managing and administering funds.

- Ensuring that adequate personnel, space, and other resources are allocated to the HRPP.
- Conducting periodic review of HRPP funds and staffing levels.
- Reviewing and signing Memoranda of Understanding and cooperative agreements between TTUHSC and other organizations, including those that establish reliance on TTUHSC IRBs of record for collaborative research.
- Serving as the point of contact for correspondence to OHRP, the FDA and other agencies as applicable, including reports to federal agencies.
- Serving as signatory authority for the Federalwide Assurance.
- Ensuring that the IRBs function independently and that the Chairs and Members have direct access to the Institutional Official if they experience undue influence or if they have concerns about the function of the IRB.

The SVPR/Institutional Official has access to the web-based Cayuse software system (Human Ethics module), which contains all documents, correspondence, and deliberations regarding each pro ject reviewed by one of the TTUHSC IRBs. This access permits review of all activities of the TTUHSC IRBs as well as all documents submitted. H owever, the SVPR is not permitted to be involved in the day-to-day operations of the IRBs.

Day-to-day operation of the TTUHSC IRBs is delegated to staff members in the TTUHSC Research Integrity Office who are assigned to oversee the various components of the TTUHSC Human Research Protection Program.

1.5.2.1 Limitation on Institutional Authority

All human research conducted by TTUHSC must be approved by an Institutional Review Board (IRB) or acknowledged as exempt from formal IRB review before it can begin. Specifics regarding obtaining IRB approval or acknowledgement of exemption can be found in this TTUHSC Human Research Protection Program Manual. Research that has been reviewed and approved by a TTUHSC IRB may be subject to further review and disapproval by other review bodies or officials (including the Executive Vice President for Researchand Innovation); however, no person or group may override the IRB's disapproval determination and approve research that had been previously disapproved by the IRB.

1.5.3 IRB Authority

The TTUHSC IRBs are autonomous administrative bodies that have the authority to approve, disapprove, or require modifications to research activities involving human subjects. The IRBs also have the authority to require continuing reviews of previously approved research, and to observe or appoint a designee to observe the consent process or any aspect of the research, inspect research facilities, obtain records and other relevant information relating to the use of human subjects in research, and take such actions that are in its judgment necessary to ensure compliance with the federal guidelines and regulations, other applicable federal and state law, TTUHSC policies, and IRB procedures established hereunder. This includes authority to suspend or terminate approval of the research if the IRB determines that there has been serious or continuing noncompliance with any federal regulation or with the requirements or determinations of the IRB.

The Chair or authorized designee of each TTUHSC IRB shall have signatory power for review and actions taken by each local IRB. Electronic documents found in—Cayuse - including all finalized IRB minutes, stamped documents, documents referenced in

electronic letters, and official correspondence -have the full approval of the IRB chair/designee and have the authority of signed documents. Handwritten signatures of the IRB chair/designee are not required under this policy.

1.5.4 State Authority

Compliance with these procedures will not render inapplicable pertinent laws of the State of Texas, any local law which may bear upon the proposed activity, the **TTUHSC policies** or **TTU System Regents' Rules**. In the case of conflicting federal law, state law and institutional policies, federal law will override state laws or institutional policies, and state laws will override institutional policies. The **TTU System Office of General Counsel** provides the IRB and other components of the Human Research Protections Program (HRPP) with counsel on an as needed basis, primarily on matters related to state laws, cooperative agreements, conflicts of interest, and contractual issues on research involving human subjects.

1.6 Separation of Leadership and Review Functions

Persons in positions of TTUHSC leadership (ex: President, Vice -Presidents, Provosts, Deans, Development Office, Office of Sponsored Programs officials) are prohibited from serving as members, alternate members or ex-officio members of the TTUHSC IRBs. These persons are also prohibited from carrying out day-to-day operations of the IRB review process.

1.7 Protection from Undue Influence

IRB chairs, IRB members, and Research Integrity Office (RIO) staff who are involved in the Human Research Protection Program have numerous interactions with investigators and others in the performance of their assigned roles. TTUHSC will investigate and resolve any reported attempt to inappropriately pressure an IRB chair, IRB member or other representative of the TTUHSC HRPP through undue influence. Undue influence includes interference with the normal functioning or decision-making of a representative of a TTUHSC HRPP representative outside of established processes in order to obtain a favorable outcome.

Any attempt to exercise undue influence over an IRB chair, member or RIO staff member should be reported and investigated as follows:

- An IRB chair, IRB member, or RIO staff member who experiences undue influence should report the occurrence to the Assistant Vice President - Research Integrity who will attempt to mediate or resolve the concern in consultation with the Executive Vice President for Research and Innovation, Associate Vice President for Research, and/or Research Compliance Officer.
- Alternatively, the person(s) experiencing undue influence may report directly to the Executive Vice President for Research and Innovation acting as the Institutional Official.
- Any individual who believes that undue influence is being exerted by an official in the above reporting chain, or who believes that the undue influence has not been appropriately or timely resolved, should report to the next higher level in the reporting chain, and ultimately to the Institutional Compliance Office, Human Resources, or the Office of General Counsel.

1.7.1 Institutional Conflicts of Interest

As it relates to research with human subjects, institutional conflict of interest (ICOI) refers to a situation in which licensing, technology transfer, patents, or investments of—

or gifts to—Texas Tech University Health Sciences Center OR the financial interests of TTUHSC senior administrators (Deans, Vice Presidents or President) might affect or reasonably appear to affect institutional processes for the design, conduct, reporting, review or oversight of human subjects research.

Financial and other interests of senior administrators will be disclosed and reviewed according to processes outlined in TTUHSC OP 10.05 Conflict of Interest and Commitment Policy and TTU System Regents' Rules. Other potential sources of ICOIs (gifts, institutional licensing agreements, etc.) which are not related to a particular individual will be reported to the institution's Conflict of Interest/Commitment Committee (COICC) for review. Representatives from the Office of Research, Office of General Counsel, Purchasing, Development Office, or Office of Research Commercialization are most likely to have knowledge of these institutional level conflicts.

The TTUS Chief Financial Officer will have primary responsibility for reviewing the financial disclosures of TTUHSC senior administrators. Any potential conflicts of interest will be referred to the Office of General Counsel as indicated in TTUHSC OP 10.05. The COICC will have primary responsibility for reviewing disclosures involving gifts to the institution. Potential ICOIs that involve research, including research with human subjects, will be forwarded by the Office of General Counsel, the TTUS Institutional Conflict of Interest Committee, or the COICC for review by the Conflict of Interest in Research Committee (COIRC) as described in TTUHSC OP 73.09 Financial Conflicts of Interest in Research. If the COIRC determines that there is little potential risk to the institution or to research participants, this information will be documented and shared with the IRB Chair(s) and Administrator(s) for notification to the IRB members. If the COICC determines that there is potential for reputational or other risk to the institution or to research participants, a plan to manage, reduce, or eliminate the conflict will be developed as described in HSC OP 73.09.

1.8 Confidential Medical Committee

The IRBs are committees of TTUHSC established for the purpose of carrying out requirements governing research involving human subjects under federal law and TTUHSC policies and procedures. The IRBs are "medical committees" as defined under Texas Health & Safety Code Chapter 161 Subchapter D and/or other applicable state and federal statutes. All documents generated by, submitted to, or for the purposes of fulfilling IRB committee duties are confidential and privileged as "medical committee documents."

1.9 IRB Relation to Other Entities

1.9.1 Other TTUHSC Compliance Committees

The TTUHSC IRB functions independently of, but in coordination with other TTUHSC research committees, including but not limited to:

- **Conflict of Interest Research Committee** (COIRC)
- **Institutional Biosafety Committee** (IBC)
- **Radiation Safety Committee** (RSC)
- **Quality Improvement Review Board** (QIRB)
- **Embryonic Stem Cell Research Oversight Committee** (ESCRO)

The IRB may request that approval be obtained from any of these committees or additional committees prior to TTUHSC IRB approval. For more detailed information refer to **TTUHSC OP 73.14, Research Compliance**.

1.9.2 Affiliated Entities

The TTUHSC IRBs may work cooperatively with the IRBs of other institutions in projects involving multiple sites and/or investigators. The Board may also agree to function as the IRB of record for another institution. Such agreements will require written contracts and amendments to the Office for Human Research Protections (OHRP) assurances as appropriate. Templates for contractual agreements between TTUHSC and other institutions can be obtained through the Assistant Vice President - Research Integrity.

Institutions for which the TTUHSC IRB is the IRB of record may reserve the regulatory right (FDA 21 CFR 56.112, DHHS 45 CFR 46.112) to exercise institutional disapproval of research the Board has approved but may not approve research that has been disapproved by a TTUHSC IRB serving as the IRB of record.

1.9.3 Cooperative Research Activities Involving Other Entities

When TTUHSC researchers conduct research at other institutions or are involved in multi-site research, IRB review may be conducted in one of three ways: single (TTUHSC) IRB review, separate review by each institution's designated IRB, or delegation to an external IRB.

1.9.3.1 Single IRB Review

When single (TTUHSC) IRB review or delegation to an external IRB is involved, TTUHSC must enter into a formal written agreement to define the responsibilities of each entity. No research may begin until an agreement has been formally executed and the designated IRB has approved the project.

In determining the need for establishing these formal agreements, the TTUHSC Office of Research will take into consideration the source of funding for the research activity(ies), federal and state regulations, specific sponsor regulations governing human research protections and institutional policies.

Institutions which routinely permit collaborations with TTUHSC researchers may establish agreements with TTUHSC that allow a single IRB to review and provide continuing oversight of human research covered by a single institution's Federalwide Assurance. These agreements define the parameters for single IRB review, including the conditions under which the review will be considered, each institution's responsibilities and financial commitments. Generally, TTUHSC will serve as the reviewing IRB if the other institution's IRB is not an accredited IRB. Exceptions will be made for collaborative research between Texas Tech University and TTUHSC faculty. Other exceptions to deferring IRB review to a non-accredited IRB will be considered individually by the Assistant Vice President for Research Integrity.

An up-to-date list of entities with which TTUHSC has formal affiliation agreements can be found on the research integrity website.

Federally sponsored clinical trials (National Cancer Institute [NCI] cooperative group studies; multi-site National Institutes of Health [NIH] sponsored clinical trials) require review by a single IRB. TTUHSC will enter into agreements with accredited designated reviewing IRBs as necessary in order to comply with regulatory requirements.

1.9.3.2 Separate Review by Each Institution's IRB

Collaborative research for which no formal agreement has been executed requires review and approval by each institutions' IRB before the research may begin.

At present, TTUHSC will not permit the delegation of IRB review to an external IRB for multi-site industry-sponsored clinical trials for which TTUHSC faculty are serving as local site investigators. Individual exceptions will be reviewed on a case-by-case basis by the Associate Vice President for Research Integrity.

At present, the TTUHSC IRB does not have the resources necessary to serve as the single/primary IRB of record when a TTUHSC investigator is the lead researcher of a multi-site study. If single IRB review is required for this type of trial where a TTUHSC faculty member is the lead researcher, the TTUHSC Office of Research and Office of General Counsel will provide assistance as requested to develop a formal, written agreement with an external IRB to serve in this role.

1.9.3.3 Delegation of Review to an External IRB

Investigators who wish to utilize external or single IRB review should contact their local IRB Administrator for details on specific requirements associated with each executed IRB reliance agreement and/or for questions related to establishment of a new IRB reliance agreement. An abbreviated IRB application to a TTUHSC IRB is required and the research may not begin until TTUHSC IRB local IRB review approval is received.

1.10 Developing and Maintaining Human Research Protection Program Policies and Procedures

Research Integrity Office staff, with input from the Institutional Official, IRB chairs, IRB members and research staff have developed written policies and procedures governing the conduct and review of human research in compliance with federal regulations , Texas law, TTUHSC Operating Policies, and standards of regulatory, accreditation, and funding agencies that apply to research conducted under the auspices of the TTUHSC human research protection program.

This **TTUHSC HRPP Manual** presents the most current information for reference by IRB chairs, IRB members, IRB administrators, principal investigators (PIs) and research staff. It is not meant to be a static document. The Assistant Vice President - Research Integrity or designee will keep the research community apprised of new information that may affect the TTUHSC human research protection program including laws, regulations, guidance documents, policies, procedures and emerging ethical and scientific issues. The updated information will be included on the TTUHSC Research website and incorporated, as needed into the **TTUHSC HRPP Manual** . Changes that directly or immediately affect the investigators will be posted as an announcement in Cayuse and may also be sent as an email to those involved with research involving human subjects at TTUHSC.

The Assistant Vice President - Research Integrity will maintain the **TTUHSC HRPP Manual**. When portions of the manual are revised, the Assistant Vice President - Research Integrity will maintain a historical archive of all previous versions. The entire manual will be reviewed at least once every odd-numbered year by the Assistant Vice President - Research Integrity and the IRB administrators. If no changes are required, the Assistant Vice President - Research Integrity will make and file a note to that effect.

2 INSTITUTIONAL REVIEW BOARD STRUCTURE AND FUNCTION

2.1 Organization of the Institutional Review Boards (IRBs)

2.1.1 TTUHSC IRBs

There are two registered IRBs.

- IRB #1 Lubbock (ID #IRB00000096) (Reviews projects submitted by investigators from Lubbock)
- IRB #2 Amarillo (ID #IRB00000097) (Reviews projects submitted by investigators from Amarillo, Dallas, Permian Basin and Abilene).

Each IRB may also be referred to as the "local IRB".

2.2 IRB Scope

The TTUHSC IRBs are responsible for reviewing research that involves human subjects when TTUHSC is engaged in the research. Generally, research conducted by TTUHSC faculty, using TTUHSC facilities or private records (such as medical records) overseen by TTUHSC, or research where TTUHSC receives funds to conduct the research must be reviewed and approved by a TTUHSC IRB prior to beginning any research activities.

TTUHSC also has written affiliation agreements with several other institutions. Each of those written agreements spells out the conditions under which TTUHSC IRB review and approval is required prior to commencement of the research. Throughout this document, the TTHUSC IRB policies and processes apply to those affiliated entities when TTUHSC serves as the IRB of record.

2.2.1 Research Conducted at More Than One TTUHSC Campus by a Single PI

If a research project takes place under the jurisdiction of both TTUHSC IRBs (example: Lubbock and Abilene, Amarillo and Permian Basin, etc.) the PI will submit the project to the IRB of her/his home campus. The local IRB administrator will notify the other IRB administrator of the research project and request review for local context issues to ensure understanding of the jurisdictional differences.

Occasionally, a researcher will wish to open a currently approved research protocol on another campus/site. If the research will continue to be conducted under the supervision of the original PI, but on another campus or site, an amendment must be submitted adding the second campus or other site as an additional site. NOTE: The amendment must include additional investigators/study personnel required to conduct the research at the second campus/site and study documents must be revised to reflect the inclusion of the new site.

2.2.2 Research Conducted at More Than One TTUHSC Campus by Different PIs

If either an external sponsor or the investigator wishes to open a second, independent site for a study that is already open on a campus of TTUHSC with a different PI and a different research team than the original study, the second protocol must be submitted to the local IRB as a new, independent application.

For example, Dr Smith is the TTUHSC PI for the IRB approved, commercially sponsored *XYZ Study* on the Amarillo campus. The commercial sponsor of the *XYZ Study* approaches Dr Jones on the Lubbock campus and requests he also participate in the *XYZ study*. Dr Jones has his own study team, is an experienced investigator, is based in Lubbock and would like to participate in this study. In this instance Dr Jones will be considered a PI, prepare an IRB submission and submit the *XYZ study* to the Lubbock IRB for review. Although the *XYZ* study on both campuses is identical, the conduct of Dr Smith's *XYZ study* in Amarillo is overseen by the Amarillo IRB and the conduct of Dr Jones' *XYZ study* in Lubbock is overseen by the Lubbock IRB.

OHRP rules do not allow for research protocols, even if they are identical, that are being run by independent research teams to be considered as the same proposal. Each of these open studies must have all amendments, continuing reviews, and other documents submitted separately. Note that the IRB administrators will not routinely communicate with one another regarding these studies.

2.2.3 Research Conducted by Students/Residents with IRB Approval from Another Institution

In certain cases, TTUHSC students or residents who are engaging in research projects which have been reviewed and approved by another institution's IRB may not require separate review by a TTUHSC IRB.

TTUHSC will not generally require a separate review of a study protocol in which a TTUHSC student or resident is involved IF ALL of the following conditions are met.

- The research is being conducted at an institution with an OHRP Federal-Wide Assurance.
- All research activity will occur at the other site.
- No research activity will be taking place at TTUHSC or at an institution affiliated with a TTUHSC IRB.
- A principal investigator from the other institution will be responsible for oversight of the project.
- The student/resident is listed as research personnel on the IRB-approved protocol at the research site.
- TTUHSC is not the recipient of funding for the research project.

If any of the conditions above are not met, the project will require review and approval by a TTUHSC IRB as well as the other institution's IRB prior to the student/resident's involvement in the project.

If all of the conditions are met, the student/resident involved in the project will be responsible for providing a copy of the IRB approval letter (and approved informed consent document, if applicable) to his or her TTUHSC IRB Office **prior to participation** in the project. TTUHSC reserves the right to limit, suspend or terminate the involvement of TTUHSC students or residents in studies approved by another institution's IRB.

2.2.4 Local Research Context

TTUHSC's responsibilities under its FWA apply whenever TTUHSC or its employees are engaged in human subjects research which is not otherwise exempt from applicable federal regulations, regardless of the geographic location of the research. This is particularly critical when the research involves greater than minimal risk to subjects or vulnerable categories of subjects.

When the location of the research is removed from the TTUHSC service region, the IRB must demonstrate that it has obtained necessary information about the local research setting through compliance with one of the standards below.

- When possible, the TTUHSC will request a local IRB to review the project in order to address local context issues.
- Copies of the non-TTUHSC IRB must be submitted to and acknowledged by the TTUHSC IRB prior to initiating the research.
- If a geographically local IRB is not available, the IRB shall document in writing that it has obtained necessary information about the local research setting(s) through written materials or discussions with appropriate consultants.

2.2.5 Community Based Participatory Research

In some studies, the design and implementation of research can be enhanced when individuals from the community in which the research will occur are involved in the design, conduct and analysis of data from the research. Investigators.

2.2.5.1 Additional Considerations

Use of a community advisory board or forming partnerships with community-based organizations is strongly encouraged.

Additional information about the inclusion of community members in the design and implementation of the research may include but is not limited to:

- Specific education for IRB members relevant to the project which may be required and may be met through the use of a consultant.
- A description of the training to be provided to community members to perform research functions.
- A description of the communication plan between research staff and community members.
- A description of how and by whom participants will be approached and recruited.
- A description of how participants will be include d in the design of the research.
- A description of how community members will be included in the dissemination of results.
- Community members who serve as study personnel will be expected to abide by the TTUHSC OP 10.28 on Volunteers. Community members serving in this dual role should be given contact information for the IRB Office or the EthicsPoint hotline number found on informed consent documents if they have questions about their rights as a study team member and/or as a subject.

2.2.5.2 Community Outreach Activities

TTUHSC and the Office of Research engage in activities designed to educate the local community about benefits of research activities. Examples include Community Medical School and the Office of Research Science Camp. Evaluations of the efficacy of these activities are periodically conducted.

2.2.6 International Research

The IRB reviews all research involving human subjects conducted under the auspices of TTUHSC, regardless of the research location, including research conducted in foreign countries. For research conducted in foreign countries, the standard initial

review, continuing review and review of modifications are required throughout the duration of the conduct of the research.

The IRB must also consider the following when reviewing international research: Qualifications of researcher and research staff for conducting research in the non-US setting. This will typically be accomplished through review of statements of qualifications provided by the PI in the IRB submission.

Local research context - Whenever possible, local IRB or Ethics Committee review of the project should take place, and approval should be obtained prior to submission of the project to the local TTUHSC IRB for review. When a formal IRB/Ethics Committee review at the non -US setting is not possible, it is the responsibility of the Principal Investigator to obtain information regarding local ethical customs and to partner with an academic entity in the area where the research will take place in order to permit some type of local ethics review of the project. If the non-US research setting has additional ethical requirements, then the additional requirements must also be met.

Reporting of any complaints, non -compliance, and unanticipated problems involving risk to participants or others as described elsewhere (2.19 Compliance) in this document.

The IRB reviews all relevant research documents (including informed consent, recruitment materials, and questionnaires, etc.). If translations into another language are required, copies of these translated documents must also be submitted and approved prior to their use in the study as described elsewhere (2.11 Informed Consent) in this document.

Protections afforded to subjects participating in research in a foreign country must approximate the protections provided to subjects in the United States.

Requests to review and modify standard elements of domestic approvals may be considered by the IRB.

On a case-by-case basis the IRB may require:
Local Consultant - not otherwise associated with the research to provide knowledge of the local research context and perceived level of risk (using the cultural standard of that country). NOTE: Consultant costs are the responsibility of the submittingprincipal investigator and should be factored into the cost of conducting the research
Ongoing Cultural/Legal Expertise– depending upon the interaction with the research subjects, it may be necessary for a person to collaborate with the research staff on an ongoing basis to ensure that the research activities are in the best interest of the community and its members and meet other applicable laws of the foreign country.

2.3 IRB Membership

2.3.1 Composition of IRB Committee

The membership requirements of each IRB will be consistent with the requirements indicated in **45 CFR 46** and **21 CFR 56**. Each IRB shall be comprised of at least five members. Each IRB must include at least one member whose primary interests are in a scientific area, one member whose primary interests are in a non-scientific area, one member who serves as a participant ad vocate, and at least one member who is unaffiliated with TTUHSC (i.e. not a family member or spouse of an employee , or a

former employee who is receiving financial benefits from TTUHSC). A single member may fulfill more than one of these characteristics.

2.3.2 Diversity

Consideration must be given to the inclusion of members with diverse backgrounds including experience, gender, professions and ethnic backgrounds. A TTUHSC IRB that serves as the IRB of record for non-TTUHSC entities may appoint at least one member from each affiliate.

2.3.3 Unaffiliated Member

Consistent with OHRP IRB member registration guidelines, unaffiliated members may not be employees of TTUHSC or immediate family members of TTUHSC employees because TTUHSC is the organization operating the IRB. Unaffiliated members may have primary interests in a scientific area or non-scientific area. Unaffiliated members may be employees of TTUHSC affiliate entities.

2.3.4 Non-Scientific Member

This member is a person whose primary interests are in non-scientific areas. At least one non-scientific member must be present and able to vote on all submissions at all convened meetings.

2.3.5 Prisoner Advocate

Federal Regulations require that the IRB membership be modified if the IRB is to review research involving prisoners. At this time TTUHSC IRBs do not have this representation, therefore no research specifically targeting prisoners may be reviewed by a TTUHSC IRB.

2.3.6 Participant Advocate

At least one member of each TTUHSC IRB will be designated as a Participant Advocate to work with the Research Compliance Officer to provide assurance to the IRBs and other interested parties that appropriate efforts are being made to protect research participants. At the request of the IRB, a principal investigator or others, the member designated as a participant advocate may provide education to research participants, observe informed consent processes, or assist potential research participants in their understanding of research participation.

2.3.7 Child or Minor Representative

An IRB considering a study involving children as subjects shall assess its needs for pediatric medical experience among the IRB voting membership to assure that it possesses the professional competence necessary to review the specific research activities and consider inclusion of one or more individuals who are knowledgeable about and have professional medical experience with children. To fulfill this requirement, the IRB may invite non-voting individuals to assist in the review of issues which require expertise beyond, or in addition to, that available among voting IRB members.

2.3.8 Consultants

If an IRB is reviewing a protocol that is outside the level of expertise of IRB members, an expert consultant may be requested to assess the protocol and present findings, written and/or orally to the IRB. Generally, the need for a consultant to assist with a review of a protocol will be triggered by the IRB member originally assigned to review

the protocol. Any member who does not believe him/herself to have adequate knowledge or expertise to conduct an adequate review of an assigned protocol should contact the IRB Director/Manager and ask to have the review re-assigned to another (or additional) IRB member or to an outside consultant. The decision to enlist a consultant for a given protocol will be discussed with the IRB Chair to determine who could best serve in this capacity for a given protocol.

The consultant is not counted toward quorum and must leave the meeting during the final discussion and vote on the protocol. Consultants must sign a confidentiality agreement and disclose known or potential conflicts of interest prior to review. If a conflict of interest is disclosed, this will be presented to the IRB members and documented in the minutes.

2.4 IRB Management

2.4.1 Liability Coverage

IRB members are covered by the Texas Torts Claims Act for actions conducted in the course and scope of their role and responsibility (ies) as an IRB member and in good faith.

2.4.2 IRB Staff Education

2.4.2.1 Initial Education

Listed below are the web-based courses that are currently REQUIRED to be successfully completed within the first week of employment

- CITI Biomedical Investigator Course (or any version of this training from the Human Subjects Research series -Biomedical in CITI, completed at any institution) - this is the institutionally approved basic course in the Protection of Human Research Subjects offered through the Collaborative Institutional Training Initiative (CITI).

FOR CRAs and PIs: In special circumstances, Clinical Research Coordinators and Principal Investigators may be permitted to substitute pre-approved CITI courses and/or recognized certifications in place of the CITI Biomedical Investigator Training course. The IRB Staff may be contacted for more information.

- TTUHSC Conflict of Interest and Commitment (COIC) – this is the institutionally approved conflict of interest and training and includes the financial disclosure form.

Any additional education is conducted by the supervisor or designee during the first month of employment and continues as needed throughout the employee's tenure.

The information presented during the first month includes and is designed to provide education on the following topics:

- Use of the web-based Cayuse software system (Human Ethics module) for processing IRB submissions.
- TTUHSC Human Research and Protection Policies and Procedures;
- Interaction between the IRB Office and the Board;
- Terms and regulations (FDA, OHRP, NIH, TTUHSC, etc.);
- Meeting basics (quorum, voting procedures, acceptable templates, etc.);
- Vulnerable populations.

Information provided to new staff members during the first month of employment includes:

- The Belmont Report;
- 45 CFR 46;
- FDA 21 CFR 50, 21 CFR 56;
- Local IRB Member Roster and IRB Office Roster;
- TTUHSC Human Research Protection Program Manual

2.4.2.2 Continuing Education

IRB staff are encouraged to participate in ongoing continuing education on the protection of human research subjects. Engaging in any of the following is considered evidence of continuing education.

- Attending educational presentations as part of regularly scheduled IRB meetings, including changes in Federal Regulations, IRB processes, or forms;
- Reviewing relevant books, periodicals, or handouts furnished to IRB members;
- Attending TTUHSC training seminars focusing on relevant topics;
- Attending webinars hosted by outside organizations such as Association of Human Research Protection Program (AAHRPP) or Public Responsibility in Medicine and Research (PRIM&R).
- Attending regional or national seminars or conferences which involve discussion of research ethics. A stipend is available to IRB members to help defray costs of attending regional/national meeting;
- Certification specific to their position (example: Certified IRB Professional, Certified Healthcare Compliance, etc.) is strongly encouraged.

Required Education: Listed below are the web-based courses that are currently REQUIRED to be successfully completed

- CITI Biomedical Investigator Course - completed at least once every 3 years (or the approved certificate or CITI course).
- TTUHSC Conflict of Interest and Commitment (COIC) – completed annually

All required education is monitored by the IRB Staff on an on-going basis.

Evaluation of staff performance is an ongoing activity involving each staff member and their supervisor. Completion of training, educational activities and performance improvement is formally evaluated at least annually as part of the TTUHSC performance management program. The formal evaluation process includes a self-evaluation and further evaluation by both the direct supervisor and next-level supervisor. Feedback is provided individually by the direct supervisor. Growth plans for the upcoming year will generally be agreed upon by the employee and direct supervisor.

2.4.3 IRB Member Conflicts of Interest

Neither the sponsor, the investigator, nor any individual involved in the design, conduct or reporting of the research activity under review will participate in the IRB review or conclusions except to provide information. No IRB member may participate in the IRB's initial or continuing review of any project in which the member has conflicting interest, either financial or non-financial, except to provide information requested by the Board.

2.4.3.1 Definition

IRB member conflict of interest exists when the member or immediate family (spouse, unmarried domestic partner or dependent children) have a significant interest that could directly and significantly affect or appear to affect the design, conduct or reporting of a project. Significant interests may be financial or non-financial. "Financial interests related to the research" mean financial interest in the sponsor, product, or service being tested. Examples of significant financial interests include a value of over $5,000 associated with the sponsor or ownership interest in the company sponsoring the research. Examples of non-financial interest include a personal belief system that precludes objective review of a particular project or being a member of the research team.

2.4.3.2 Process

All IRB members, alternate members, and consultants are required to complete TTUHSC conflict of interest training and a financial disclosure form prior to the initial appointment and annually thereafter in accordance with institutional policy and OHRPP Policy. A financial conflict of interest (FCOI) is defined in TTUHSC Operating Policy **73.09, Financial Conflicts of Interest in Research** TTUHSC's policy regarding non-financial conflicts of interest can be found here: **HSC OP 10.05, Conflict of Interest and Commitment Policy**.

Financial and non-financial disclosures are reviewed by a representative from the conflict of interest committee and any conflicts are forwarded to the IRB staff. The IRB staff maintain a record of any financial and non-financial disclosures made by IRB members to preclude assignments for review of conflicted research. Should an IRB member receive an assignment and upon review, discover they have an undisclosed conflict or personal belief system that precludes them from providing an objective review of the submission, he/she must notify the IRB staff regarding the conflict and disqualify themselves from conducting the review or participating in discussion of the submission except to provide information on request. This applies to all assignments and types of review (convened IRB, expedited procedure, review of unanticipated problems, review of non-compliance, etc.).

Further, the web-based Cayuse software programused by the TTUHSC IRBs does not permit any IRB member who is listed on a study to access the IRB review comments or meeting discussions for that project.

Conflicted IRB members, alternate members, or consultants shall leave a convened meeting during the discussion and may not vote on the research in question. These members are not considered as contributing to the quorum for the discussion and vote on the conflicted research.

2.4.4 IRB Member Education

2.4.4.1 Initial Education

New Member Orientation: New IRB members are required to attend an orientation session prior to participating as a voting member on the IRB. This training is conducted by the IRB administrator or designee. Additionally, new members are encouraged to attend and observe a Board meeting prior to beginning their appointment.

The orientation session is designed to provide education on the following topics:

- Responsibilities and obligations of IRB members;

- Interaction between the IRB Office and the Board;
- Effective meeting skills;
- Terms and regulations (FDA, OHRP, NIH, TTUHSC, etc.);
- Meeting basics (quorum, voting procedures, acceptable templates, etc.);
- Vulnerable populations;
- Liability issues; and
- The use of the web-based Cayuse software system (Human Ethics module) for reviewing IRB submissions.

Information provided to new IRB members includes:

- The **Belmont Report**;
- **45 CFR 46**;
- FDA **21 CFR 50**, **21 CFR 56**;
- Local IRB Member Roster and IRB Office Roster;
- TTUHSC Human Research Protection Program Manual.

Required Education: Listed below are the web -based courses that are currently REQUIRED to be successfully completed by all new IRB members prior to participating as a voting member of the IRB.

- CITI Biomedical Investigator Course , or previously approved alternative - this is the institutionally approved basic course in the Protection of Human Research Subjects offered through the Collaborative Institutional Training Initiative (CITI)
- TTUHSC Conflict of Interest and Commitment (COIC) – this is the institutionally approved conflict of interest and training and includes the financial disclosure form.

All required education is monitored by the IRB Staff on an on-going basis.

2.4.4.2 Continuing Education

IRB members are encouraged to participate in at least six (6) hours of continuing education annually on the protection of human research subjects. The SVPR will be kept aware of the continuing education opportunities made available to IRB members via monthly reports provided by the IRB Administrators . Engaging in any of the following is considered evidence of continuing education.

- Attending educational presentations as part of regularly scheduled IRB meetings, including changes in Federal Regulations, IRB processes, or forms;
- Reviewing relevant books, periodicals, or handouts furnished to IRB members;
- Attending TTUHSC training seminars focusing on relevant topics;
- Attending webinars hosted by outside organizat ions such as Association of Human Research Protection Program (AAHRPP) or Public Responsibility in Medicine and Research (PRIM&R).
- Attending regional or national seminars or conferences which involve discussion of research ethics. A stipend is available to IRB members to help defray costs of attending regional/national meetings.

Required Education : Listed below are the web -based courses that are currently REQUIRED to be successfully completed by all IRB membersand may be included in the 6 hours of required IRB continuing education.

- CITI Biomedical Investigator Course, or previously approved alternative- completed at least once every 3 years
- TTUHSC Conflict of Interest and Commitment (COIC) – completed annually

All required education is monitored by the IRB Staff on an on-going basis.

2.4.5 IRB Chairperson and Vice-Chairperson

2.4.5.1 Appointment

The SVPR in collaboration with the Assistant Vice President - Research Integrity appoints the IRB chairperson and vice -chairperson for a two -year term that will automatically renew at each new term, unless notice is provided to end the appointment. Generally, terms will begin on September 1 of each even-numbered year. Board needs will be assessed prior to the appointment, at which time a new chairperson will be appointed, or the incumbent will be reappointed. T he IRB chairperson may be removed or reappointed at any time upon written notice by the EVP or designee.

At the time of appointment/reappointment the IRB chairperson and vice - chairperson will sign an agreement to serve and a confidentiality agreement and shall have an up-to-date disclosure of potential conflicts of interest on file with the TTUHSC Institutional Compliance Office.

2.4.5.2 Duties

The chairperson will conduct the IRB's meetings In the chairperson's absence the vice-chairperson will conduct the meeting. Another IRB member may also be designated to run the meeting in the event that neither the chairperson nor vice - chairperson can be present. The chairperson and vice-chairperson are considered voting members of the IRB committee for purposes of establishing the quorum.

The IRB chair or designee shall assign each submission requiring full board review to at least one IRB member and/or make a determination that a consultant is required for additional expertise. If more than one IRB member is assigned, one will be designated the primary reviewer and one the secondary reviewer. Efforts will be made to make assignments primarily on the basis of reviewer expertise and knowledge of the study population. Non -scientist members will not be assigned as primary reviewers on an initial review.

The chairperson and vice -chairperson have the responsibility to ensure the compliance of their IRB with all applicable regulations. The chairperson/vice - chairperson manage the matters brought before their IRB according to applicable procedures, regulations, and guidance.

The chair of the meeting monitors quorum during the meeting.

Chairpersons and vice -chairpersons will be designated in each TTUHSC IRB roster.

The chairperson will ensure that the SVPR and Assistant Vice President - Research Integrity are notified of pertinent information to facilitate compliance with federal regulations and TTUHSC policy.

Pertinent information requiring prompt reporting to the SVPR/AVP-RI includes but is not limited to:

- Injuries, unexpected serious harm to subjects or others, or any other unanticipated problem involving risks to human subjects or others arising from research;
- Any serious or continuing non-compliance with regulations or IRB policies, procedures, and determinations;
- Any suspension/ termination of IRB approval of research.

2.4.6 IRB Members

2.4.6.1 Appointment

Any interested party may recommend new members, including self-referrals. The SVPR in collaboration with the Assistant Vice President - Research Integrity appoints the IRB members for a two-year term that will automatically renew at each new term, unless notice is provided to end the appointment. Generally, terms will begin on September 1 of each even-numbered year. Board needs will be assessed prior to the appointment, at which time new members will be appointed. However, any member may be removed, appointed or reappointed at any time upon written notice by the EVP or designee.

At the time of appointment/reappointment the IRB members will sign an agreement to serve, and a confidentiality agreement and shall have an up-to-date disclosure of potential conflicts of interest on file with the TTUHSC Institutional Compliance Office.

2.4.6.2 Duties

The agenda, protocols, proposed informed consent forms and other appropriate documents will be available for review for all members prior to regular meetings at which the member is scheduled to attend. Members should review th e materials before each meeting in order to participate fully in the review of each proposed project. Brief additional information may also be provided to attendees during the meeting. Board members will hold protocols and supporting data in confidence.

The IRB chair or designee shall assign each submission requiring full board review to at least one IRB member. If more than one IRB member is assigned, one will be designated the primary reviewer and one the secondary reviewer. Efforts will be made to make ass ignments primarily on the basis of reviewer expertise and knowledge of the study population. Non-scientist members will not be assigned as primary reviewers on an initial review. The primary and secondary reviewers conduct an in-depth review of all materials and enter their comments into Cayuse. The primary reviewer is required to utilize the Reviewer Checklist to guide and help to ensure a comprehensive evaluation of the initial review of each project. An oral summary of the study and recommendations regarding the disposition of the study shall be presented by the primary and secondary reviewers.

Primary and/or secondary reviewers are encouraged to contact PIs prior to the IRB meeting with any questions they have so that these issues may be addressed in advance of the full board meeting.

Any member may be asked by the chairperson, vice -chairperson or designee to preside over a particular IRB meeting.

Any experienced IRB member (has served as an IRB member for more than 1 year) may be asked to serve as an expedited reviewer. Specific duties of expedited

reviewers can be found under **Duties of the IRB Member Conducting Expedited Review**.

2.4.6.3 Attendance

The importance of voting IRB member (affiliated, non-affiliated, participant advocate, scientist, non-scientist, etc.) attendance cannot be overstressed. Member absences may affect the quorum and therefore the ability to conduct business. Notification of an expected absence is required. Members absent more than 3 times in a fiscal year may be contacted by the IRB administrator or IRB chairperson to confirm their commitment/ ability to continue as an IRB member.

2.4.7 IRB Alternate Members

2.4.7.1 Appointment

Any IRB member may recommend an alternate member who fulfills the same role(s) and has similar qualifications. Alternate member attendance satisfies the attendance requirement for the regularly appointed IRB member. Self-referrals for alternate positions and other person's recommendations for alternates will also be considered.

The SVPR in collaboration with the Assistant Vice President - Research Integrity appoints the IRB alternate members, generally for a two-year term beginning September 1 of each even-numbered year. Any alternate member may be removed or reappointed at any time upon written notice by the SVPR.

At the time of appointment/reappointment the alternate IRB members will sign an agreement to serve and a confidentiality agreement and shall have an up-to-date disclosure of potential conflicts of interest on file with the TTUHSC Institutional Compliance Office.

2.4.7.2 Duties

Alternates may vote in place of an absent or excused regular member. Any experienced alternate IRB member (has served as an IRB member for more than 1 year or in an alternate position with prior IRB experience) may be asked to serve as an expedited reviewer.

2.4.7.3 Attendance

Alternates may attend all meetings; however, their votes are counted only in the absence of the regular member. Meeting minutes must indicate when an alternate member replaces the appointed member.

2.4.8 IRB Member Evaluation

At the time of each reappointment to the IRB each IRB chairperson, Vice Chairperson, and member will be asked to complete a self-evaluation tool regarding their IRB membership and knowledge. Assessment of current training is also included. The IRB administrators and Assistant Vice President - Research Integrity will review the self-evaluations and offer individual or group feedback sessions in identified areas of weakness or concern, including any delinquent training. The feedback sessions may be conducted in a group (i.e. at a convened meeting of the IRB) and may be provided as a written document to all IRB members or individually, in person or in writing, and may include additional training, mentoring or other methods of strengthening the knowledge of current IRB members. Group feedback sessions that take place during a

convened meeting of the IRB will be noted in the meeting minutes. Written feedback provided to all members will also be available as part of the meeting minutes.

2.5 IRB Meeting Minutes

The minutes of all IRB meetings must be in sufficient detail to demonstrate the following:

- attendance at the meetings and presence of quorum;
- actions taken by the IRB;
- for each agenda item, the following are documented:
  - The basis for requiring changes in or disapproving research;
  - Determinations regarding inclusion of vulnerable subjects, including those with diminished capacity;
  - Summary of the discussion, including consultant input, controverted issues and their resolution, and any discussion with external participants;
  - Dissenting reports and opinions;
  - Determinations required by the regulations and study specific findings justifying those determinations for:
  - Waiver or alteration of the consent process;
  - Research involving pregnant women, fetuses and neonates;
  - Research involving children;
  - Risk determination (for initial reviews only);
  - The rationale for significant risk/non-significant risk device determinations.
- For initial and continuing review, the length of the approval period;
- Documentation for the rationale for conducting continuing review of research that would otherwise not require continuing review [per 45 CFR 46.109(f) (applicable under 2018 Requirements only)];
- the vote on each of these actions including: (a) members present for the vote (located in the IRB Voting section in Cayuse for each submission), (b) the number of members voting for, (c) against, and (d) abstaining (include member name);
- the basis for requiring changes in or disapproving initial and continuing research; and
- summary discussion of controverted issues and their resolution.

The IRB meeting minutes must also reflect the following as applicable:

- names of IRB members recused from a discussion/vote due to a conflict of interest.

TTUHSC IRB meeting minutes are created through the Cayuse system based on the information provided in written reviews of all IRB submissions since the last convened meeting, as well as from documented discussion that takes place during a convened meeting of the IRB. Meeting minutes will be distributed for review by the IRB administrator/designee prior to the next convened IRB meeting. At each convened meeting, members will vote to approve the minutes from the previous review period. Documentation of approval of meeting minutes will be noted on the agenda and in the next review period's meeting minutes.

2.6 IRB Record Keeping

2.6.1 File Composition

The IRB Office files shall be maintained, either electronically or on paper, in a manner that reflects a complete history of all IRB actions related to review and approval of a

research study, including continuing reviews, amendments, and serious adverse event reports. IRB office files include all submissions to the IRB, including all attachments to each submission. The submissions and attachments may include, but are not limited to:

- all submitted versions of the IRB application;
- all submitted versions of the protocol;
- any scientific evaluations provided to the IRB;
- all submitted consent documents;
- progress reports/DSMB report summaries;
- continuing review form describing research activities (as necessary);
- requests to modify or amend the approved research project;
- reports of unexpected events, including protocol deviations, unanticipated problems involving risks to injuries to subjects or others, serious adverse events, or adverse device events;
- all official study correspondence;
- statements of significant new findings provided to participants;
- reports of audit findings, including non-compliance;
- requests to close a study (final report);
- notices or approval letters from other TTUHSC Compliance Committees (e.g., Radiation Safety Committee);
- drug or device information (including Investigator's Brochures, as applicable);
- recruitment materials.

2.6.2 Record Retention

The IRB Office shall retain IRB paper files for three (3) years after the final closure date of the research study.

Electronic files are maintained in Cayuse for a minimum of three (3) years after final closure date of the research study.

Both paper and electronic records will be maintained for three years after the final closure date of the research study even if the project is cancelled without participant enrollment.

2.6.3 Access to Records

The IRB secures all paper and electronic IRB records and limits access to the IRB members, staff, compliance officer(s), institutional official and other authorized affiliated institution and TTU System representatives, and officials of federal and state regulatory agencies including representatives from the Office for Human Research Protections (OHRP), the Food and Drug Administration (FDA), and accrediting bodies. IRB records are accessible for inspection and copying by these representatives at reasonable times and in a reasonable manner.

IRB staff may grant other TTUHSC/TTUS personnel access to necessary records on an as-needed basis for official business. Investigators or their authorized study personnel have reasonable access to files related to their research activities. Access to IRB files is limited to those who have legitimate need for them, as determined by the IRB staff, Assistant Vice President – Research Integrity or Institutional Official.

2.7 IRB Submission Process

2.7.1 Submission Mechanism

All information relative to human research projects must be submitted using the web-based Cayuse software program (Human Ethics module). Assigned privileges within Cayuse provide all IRB members access to all study documents for all studies submitted for review at the local IRB unless a particular IRB member is included as study personnel on the project. In those cases, the conflicted IRB member may not access the IRB review or deliberation on the study.

Materials for convened meeting of the IRB must be received by the established deadline (see **Institutional Review Boards Submission Deadlines**).

Information is communicated between the IRB and investigators via Cayuse. All correspondence generated by Cayuse and sent to research personnel is considered official and does not require the handwritten signature of an IRB chairperson or designee.

2.7.2 Documents

The following documents, as applicable to the study and type of submission, must be submitted through Cayuse for IRB review:

- completed electronic IRB study application form;
- completed Cayuse submission form relevant to the type of submission (i.e. Initial Review form; Continuing Review form; Amendment form; Unanticipated Event form, etc.)
- Full protocol - the full protocol should contain a review of prior work in the area, specific objectives, hypotheses, study design, study procedures, statistical analyses and references;
- Investigational New Drug (IND) or Investigational Device Exemption (IDE) number;
- Investigator's Brochure;
- Data Safety Monitoring Reports;
- proposed informed consent document using TTUHSC IRB-approved template which may include an Authorization to Use and Disclose Protected Health Information (PHI) for Research (HIPAA authorization form);
- any proposed data collection forms;
- letters of approval or support from non-TTUHSC research sites;
- recruitment materials;
- surveys, questionnaires, or videotapes;
- non-English versions of any materials to be seen by subjects (as needed and only after English versions are approved);
- certificate of confidentiality as needed (**http://grants.nih.gov/grants/policy/coc/**);
- documentation of review/approval by required TTUHSC compliance committees (example: Institutional Biosafety Committee, Conflict of Interest in Research Committee, etc.);
- curriculum Vitae (CV) of Principal Investigators and/or others as requested;
- other materials necessary to allow the IRB to effectively review the proposal.

2.7.3 Scientific Review of Proposed Research

In order to approve research, the IRB must determine that risks to subjects are minimized by using procedures that are consistent with sound scientific design (45 CFR 46.111 (a)1; 21 CFR 56.111.(a)1). The IRB may utilize any of several alternatives for ensuring that sound scientific design. All initial reviews (for exempt, expedited, and studies reviewed at a convened meeting) must be reviewed and approved by a Department Signatory Authority prior to submission for IRB review as noted here. The Department Signatory Authority must review the proposal and attest that it is consistent with TTUHSC's research mission, is based on sound scientific principles and that the study design is adequate to address the proposed research question. For studies that are classified as Exempt from formal IRB review or those which receive Expedited review, the Signatory Authority's attestation may be sufficient, though assigned reviewers may request changes or clarification of the research design prior to approval/acknowledgement of the research.

For projects to be reviewed at a convened meeting of the IRB, scientific review beyond the attestation of the signatory authority will be required. The following types of protocols will generally be considered to have received a scientific review prior to IRB submission and will not require a scientific review by the IRB, though the IRB retains the discretion to request clarification or changes to the research design prior to approving the research:

- Grant-funded projects which have received full peer review (e.g., review by a study section or grant committee);
- Industry-sponsored, multi-site clinical trials;
- Internally sponsored (investigator-initiated) research which is submitted through a School/ Department which provides documentation of a formal scientific review process.

Studies which are to be reviewed at a convened meeting of the IRB for which no scientific review outside of the Signatory Authority's signature has taken place will receive a scientific review by the primary reviewer and/or IRB chairperson or designee as part of the initial review process. The scientific review will address the following issues:

- Has a literature search supporting study rationale been conducted?
- Will testing the hypothesis provide important knowledge for the field?
- Are the hypothesis/specific goals and aims clearly stated?
- Are the outcomes clearly stated and defined?
- Is the study design appropriate?
- Will the proposed tests/measurements address the hypotheses?
- Are all of the proposed tests/measures required/related to at least one proposed outcome?
- Are the validity/reliability of measures established?
- Are the proposed statistical methods clearly stated/correlate with study design?
- Is the proposed sample size adequately justified?
- Is the Principal Investigator appropriately qualified, knowledgeable and experienced to perform the procedures?

If the IRB does not feel that they have adequate knowledge to conduct a scientific review, a consultant with the appropriate knowledge may be asked to perform the scientific review, or an *ad hoc* committee may be formed to conduct the scientific

review. Further IRB review of the project will be **Tabled/Deferred** until the scientific review has been conducted.

If necessary, the IRB administrator and IRB chairperson will determine an appropriate consultant or committee member(s) to conduct the scientific review.

2.7.4 Principal Investigator Sign-off

Initial and continuing review submissions must be electronically signed by the Principal Investigator (PI) in Cayuse prior to the IRB receiving the submission. In signing the submissions, the Principal Investigator is indicating that s/he has reviewed the information in the submission. Prior to submitting an initial review, the signature of the principal investigator also indicates understanding/agreement with the following:

- The research will be conducted by the PI or under his/her close supervision;
- Changes or modifications in the research will not be initiated without prior IRB approval;
- Unanticipated events will be reported promptly to the IRB;
- Investigational drugs used on an in-patient basis will be stored in an appropriate pharmacy;
- Legally effective informed consent will be sought and documented for each participant unless a waiver or alteration of the consent process is approved by the IRB;
- Continuing reviews will be submitted as often as requested by the IRB;
- The IRB will be notified of completion of the study and a final report will be submitted;
- The IRB has authority to monitor the project for compliance
- The IRB has the authority to suspend/terminate any research project for non-compliance;
- Significant financial interests have been reported and financial conflicts have been managed as required by regulations and internal policies.

Before approval or during the course of conduct of any project, the IRB may ask for verification from the Principal Investigator that any of these requirements is, in fact, being met. Routine audits of ongoing research will be conducted in order to assess compliance with these and other requirements. See the Research Compliance section of this manual for more information.

2.7.5 Department Signatory Sign-off

In addition to the Principal Investigator, a Departmental designated authority is required to electronically sign all initial reviews prior to the IRB receiving the submission. In providing an electronic signature, the designated authority is attesting that:

- The project is based on sound scientific principles and the study design is adequate to address the proposed research question(s);
- The project's goals are consistent with TTUHSC's research mission.
- The principal investigator is qualified to conduct the research project.
- There is adequate time for the researchers to conduct and complete the research;
- An adequate number of qualified staff are available;
- Adequate facilities to conduct the research will be provided;
- Access to a population that will allow recruitment of the necessary number of participants is available; and

- Resources that participants may need as a part of the research (includes medical or psychosocial resources) are available.

The IRB may request documentation from the Department Signatory Authority regarding review and approval of any of these requirements.

2.7.6 Submission Screening

All IRB submissions will be prescreened by the local IRB Office Staff. If the submission is incomplete or otherwise not fully prepared for review, it will be returned to the PI with a request for completion. When the submission is adequately prepared, it will be acknowledged or assigned to an IRB member or members for review.

2.7.7 Agenda

The IRB agenda consists of all IRB submissions which have been prescreened by local IRB staff and acknowledged or assigned. IRB Staff, in consultation with the IRB Chair as necessary, make assignments based on their initial assessment of whether the submission requires expedited or full board review. Because reviews of submissions that are to be acknowledged or receive expedited review take place on a continual basis, the agenda is an evolving document until finalized at the time of the convened meeting.

The agenda serves as the working document to inform IRB members of all submissions which have been acknowledged or have received expedited review since the last convened meeting of the IRB. The agenda provides an up-to-date reference for the review status of each submission.

2.7.8 Notifications to Investigators

All IRB decisions are communicated to the principal investigator and designated research team members via the Cayuse system. This includes but is not limited to approval, disapproval, clarifications or modifications to secure approval. Generally, IRB decisions will be communicated within 3 business days of the IRBs determination.

2.8 IRB Actions

2.8.1 Approval

In conducting the review of proposed research, each IRB must obtain information in sufficient detail to make the determinations required under federal and state regulations and institutional policies. This review may be conducted administratively for projects that meet the criteria for exemption from formal IRB review, through expedited procedures for projects that meet regulatory criteria or at a convened meeting of the IRB.

2.8.1.1 Approval Requirements

Each IRB must determine that the following requirements are satisfied before it approves a proposed research project. These requirements are delineated by federal regulations found at **45 CFR 46**.111 and, if applicable, subparts B, C, or D, **21 CFR 50** and **21 CFR 56**.

1. Risks to subjects are minimized:
   a. by using procedures consistent with sound research design;
   b. by using procedures which do not unnecessarily expose subjects to risk; and

c. whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes (FDA 21 CFR 56.111(a)(1); DHHS 45 CFR 46.111(a)(1)).

2. Risks to subjects are reasonable:
   a. in relationship to anticipated benefits, if any, to subjects; and
   b. in relationship to the importance of the knowledge that may be expected to result.
   Note: In evaluating risks and benefits, the Board should consider only those risks and benefits that may result from the research, as distinguished from risks and benefits of therapies that 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 as among those research risks that fall within the purview of its responsibility (ICH E6 2.2; 21 CFR 56 .111(a)(2); DHHS 45 CFR 46.111(a)(2)).
3. Selection of subjects is equitable.
   This will be done in accordance with FDA 21 CFR 56 .111(a) (3) and (b); DHHS 45 CFR 46.111(a) (3) and (b)).
4. Informed consent will be sought from each prospective subject or the subject's legally authorized representative.
   This is to be done in accordance with FDA 21 CFR 50, DHHS 45 CFR 46.116, ICH E6 2.9; FDA 21 CFR 56.111(a)(4); DHHS 45 CFR 46.111(a)(4).
5. Informed consent will be appropriately documented.
   This will be done in accordance with and to the extent required by FDA 21 CFR 50.27 and DHHS 45 CFR 46.117.
6. When appropriate, there are adequate provisions in the research plan for monitoring the data collected to ensure the safety of subjects.
   This will be done in accordance with (FDA 21 CFR 56.111(a) (6); DHHS 45 CFR 46.111(a) (6)).
   a. When research is minimal risk, the IRB may determine that no formal data safety monitoring is required.
   b. For research greater than minimal risk, the IRB will assess the research's provisions for data safety monitoring. The IRB will not approve research with inadequate provisions for data safety monitoring.
   c. Provisions which may be required by the IRB for the effective monitoring of data may include, but are not limited to, requiring the collection of safety information including both a description of what safety information will be collected, and how frequent ly it will be collected; data review by an independent reviewer at specified frequencies (e.g., every six months or after every 3rd participant is enrolled) the establishment of an independent data safety monitoring committee to be responsible for data and safety review; or the pre-establishment of conditions for which the investigator or the IRB will immediately suspend or terminate the research.
7. When appropriate, there are adequate provisions to protect privacy of subjects and to maintain the confidentiality of the data. This will be done in accordance with (ICH E6 2.11; FDA 21 CFR 56.111(a) (7); DHHS 45 CFR 46.111(a) (7)).
8. There are appropriate additional safeguards for vulnerable subjects.
   Subjects who are likely to be vulnerable to coercion or undue influence may include children, prisoners, pregnant women, handicapped, individuals with

impaired decision -making capacity , or economically or educationally disadvantaged persons. (DHHS **45 CFR 46**.111(b); FDA **21 CFR 56**.111(b)).

9. In addition, the IRB shall review proposed research for the following:
   a. The research does not violate existing local laws, regulations, or other applicable institutional policies or accepted practices
   b. The research has been described in a clear and detailed protocol document
   c. plans for subject recruitment that involve advertising or other direct contact with potential subjects are consistent with the protocol, the consent form, and FDA guidelines

2.8.1.2 Determination of Risk

IRB member(s) will make a determination of the risk level of a study based on assessments including but not limited to: 1) the vulnerability and health of the research participants, 2) the level of innovation involved in the drugs, devices and/or procedures involved in the project, 3) the likelihood of participants experiencing physical or psychological effects from the ad ministration of study drugs/procedures, etc. Non -exempt projects will be assigned minimal risk or greater than minimal risk.

A minimal risk determination is required for projects that are initially reviewed and approved through an expedited procedure. If the reviewer does not believe a minimal risk determination is acceptable, full board review is required.

If a determination of greater than minimal risk is assigned , the IRB may consider requiring additional data and safety monitoring provisions such as:

- a plan that includes more frequent collection of safety information and submission of such reports to the IRB;
- regularly scheduled audits by TTUHSC research compliance officer;
- establishment of an independent data safety monitoring committee;
- establishment of specific stopping rules.

2.8.1.3 Determination of Review Cycle

For those projects that require continuing review, IRB member(s) will make a determination of the interval between continuing reviews based on assessments including but not limited to:

- the vulnerability and health of the research participants;
- the level of innovation involved in the drugs, devices and/or procedures involved in the project;
- the likelihood of participants experiencing physical or psychological effects from the administration of study drugs/procedures;
- anticipated accrual rate in the local population;
- local experience of the investigator and or research team, etc.

IRB review cycles are generally 3, 6, 9 and 12 months.

2.8.1.4 IRB Approval and Expiration Dates

Approval Date - If IRB approval is required, t he approval date is the date all approval requirements have been met and the principal investigator is formally notified in writing that the project has received IRB approval. No research may be conducted prior to the approval date(s) or after the expiration date(s) for ongoing research.

Expiration Date – Only research that has been reviewed and approved at a convened meeting will be assigned an expiration date. The expiration date is determined by the date of the convened meeting, not necessarily the date of approval. For example, a research project may require minor modification prior to formal approval. The date of approval will be assigned when the minor modification has been adequately addressed.

The expiration date is assigned at the time of recommendation to approve the research at a convened meeting. The research always expires one day less than the assigned review interval. For example, research project approved for annual review on 11/4/2013 will expire on 11/3/2014. Research activities are allowed to take place on 11/3/2014 (the day of expiration).

Typically NO Expiration Date -If the project meets expedited review criteria no expiration date will be assigned unless the reviewer explicitly justifies why continuing review would enhance protection of research subjects. If such a determination is justified, the expiration date for research reviewed and approved via the expedited procedure is determined by the actual approval date.

No Expiration Date - No expiration dates are assigned for projects determined to meet the criteria for exemption from formal IRB review.

2.8.2 Additional Information Required (Request for modifications)

The Board (for research reviewed at a convened meeting) or experienced IRB member (for research reviewed by expedited procedure) may request additional information prior to approval of a submission in order to make all of the determinations required for approval under the HHS regulations at **45 CFR 46**.111 and, if applicable, subparts B, C, or D, **21 CFR 50** and **21 CFR 56**.

The Board/experienced IRB member may request clarifications, protocol modifications, revisions to the informed consent document, or other supporting documentation. In Cayuse, these requests are entitled “Stipulations”. Stipulations must be satisfactorily addressed before approval is effective.

Modifications for submissions requiring review at a convened meeting will be classified by the Board as minor (a change that would not materially affect an assessment of the risks and benefits of the study or does not substantially change the specific aims or design of the study) or greater -than-minor. Investigator response(s) to minor modifications may be reviewed using expedited or administrative procedures. Greater-than-minor modifications are considered substantive and must be reviewed at a subsequent convened IRB meeting.

Responses to stipulations in Cayuse are due within 60 days of the date of the request for additional information unless otherwise specified. If no response has been received after 60 days, the study will be administratively closed by the IRB and further review of the study will require a new application to be submitted to the IRB.

2.8.3 Disapproval

When the IRB disapproves new research, it is rejecting oversight of the project as submitted, and the research is not allowed to go forward.

When the IRB disapproves a change in research, the change cannot be implemented, and it is expected the research will continue as previously approved by the Board. Disapproval may occur for a variety of reasons, most of which involve subject safety and/or scientific validity.

The IRB cannot disapprove a submission that has previously been approved. Disapproval is only valid when the Board is considering an item that is not yet approved.

The IRB shall provide the PI with written notification of the reasons for its decision to disapprove. The PI may request reconsideration of the IRB's decision in writing within ten (10) days of the date of notice. The PI shall provide a rationale for the request to reconsider and any other relevant supporting documentation. The PI may also address the IRB in person. The IRB shall notify the PI in writing of its final decision after reconsideration and the reason(s) for its decision. No further request for reconsideration by the PI is permitted following the final decision by the IRB. Pursuant to the regulations in **45 CFR 46**.112 and **21 CFR 56**.112, TTUHSC officials can not approve research if it is disapproved by the IRB.

2.8.4 Table/Defer

To table or defer means to remove an item from board consideration at a convened meeting. The IRB may decide to table a submission for the following reason(s):

- Numerous changes are required;
- Incomplete submission;
- IRB member/consultants not available for review;
- Loss of quorum;
- Necessary documentation from other pertinent TTUHSC committees (e.g., Conflict of Interest Committee) has not been provided.

NOTE: All studies that are tabled at a full board meeting will require subsequent full board review unless substantial changes indicate that the study will now be able to be reviewed by **45 CFR 46**.110 (expedited review) requirements.

IRB staff will send a written notice to the investigator to describe the reason(s) for table/deferral. If additional information is required, stipulations will be stated. Responses to stipulations in Cayuse are generally due within 60 days of the date of the request for additional information unless otherwise specified. If no response has been received after 60 days, the study may be administratively closed by the IRB and further review of the study will require a new application to be submitted to the IRB.

2.8.5 Suspend Enrollment

When the IRB suspends enrollment, the investigator may not enroll new subjects in the study, but may continue subject participation for those already enrolled. For example, this action may be used when new research activity must cease, but the Board requires the investigator to continue following subjects for safety reasons (such as, when subjects have an implanted research device, or study drug must be tapered off). This action may also be used to maintain oversight of a study, while subjects are being transferred to another investigator.

When the Board requires follow-up of participants for safety reasons, the Board considers whether participants should be informed.

This action may be used as a response to alleged or known non-compliance. The Assistant Vice President - Research Integrity will be notified of this action and will evaluate the need for reporting to other TTUHSC officials or outside entities.

Board oversight continues, so the research is considered active. Investigators must continue to follow the Board's requirements for reporting unanticipated problems, changes in research, and so forth.

Enrollment remains suspended until the investigator is notified by the IRB in writing. If an investigator (rather than the IRB) decides to temporarily or permanently suspend enrollment for any reason, the study status in Cayuse will be changed to "closed to accrual".

2.8.6 Suspend Research Activity

When the IRB suspends activity, the investigator is required to cease all research activities. Research activity can only be suspended by the full board at a convened meeting. This is true for studies which qualified for expedited initial/continuing review as well as those which were originally approved by the full board at a convened meeting. A majority vote of the voting members present is required to formalize a decision to suspend research activity.

This action is used when research-related activity must cease, but the Board has requirements the investigator is expected to fulfill in order to resume research activity. This includes ceasing research visits for subjects enrolled in the study, unless the principal investigator provides information in writing to the IRB indicating that failure to perform study-related procedures on previously enrolled subjects would be detrimental to the subjects' health or welfare. Any data analysis must also halt at the time of suspension.

Suspension may occur as a result of the need:

- for a response to serious or recurring non-compliance with the regulations or TTUHSC IRB requirements;
- to protect the safety, welfare, and rights of subjects; or
- other situations, as the Board deems appropriate.

2.8.6.1 IRB Considerations

IRB deliberations will include consideration of:

- the actions to protect the rights and welfare of currently enrolled participants;
- whether procedures for withdrawal of enrolled subject(s) took into account their rights and welfare (for example were arrangements for medical care provided or was the possibility of continuing in the research allowable under another researcher);
- whether current participants should be informed of the suspension;
- any serious adverse event or outcome reported to the IRB.

The IRB will notify the PI in writing of suspension of IRB approval along with the reasons for the suspension.
The IRB will notify the Assistant Vice President - Research Integrity and the SVPR of decision to suspend within 2 business days of the decision.

The SVPR, serving as the institutional official, will promptly (within 30 days) notify other TTUHSC officials or outside entities (HHS, FDA, NIH, affiliated institutions, etc.) as required to comply with the FWA.

Board oversight continues, so the research is considered active . Investigators must continue to follow the Board's requirements for reporting unanticipated problems, changes in research, and so forth.

The PI will be required to submit a written corrective action plan for review and approval by the IRB before any research activities can resume. More details can be found regarding corrective action plans in the **Research Compliance Section** of this manual.

2.8.6.2 Suspension by Institutional Official or IRB Chairperson

In urgent situations, the SVPR acting in the role as institutional official or the IRB Chairperson acting on behalf of the IRB, may determine that research activity must be suspended immediately. If this action occurs, the SVPR/IRB Chairperson must provide a written report of this action to the IRB for review at the next convened meeting. The report shall include any actions taken to protect rights, welfare and safety of currently enrolled participants and whether they have been notified of the suspension.

2.8.6.3 Appeal of Suspension

The PI may appeal the decision of the IRB or SVPR by submitting a written request to the IRB and providing a rationale for the appeal and any other supporting documentation. The PI must submit an appeal within five business days of the date of notification of suspension.

Within 14 days of the appeal of suspension, the PI's request for reconsideration shall be reviewed by a subcommittee consisting of the IRB chair and two IRB members jointly selected by the IRB chair and IRB administrator. The subcommittee may also invite individuals with expertise in that area ofresearch to assist the subcommittee in its review of the issues. The local IRB administrator and research compliance office r will provide assistance to the subcommittee as needed, though they will not be considered members of the subcommittee. Individuals assisting the subcommittee shall maintain confidentiality of the IRB proceedings.

This subcommittee shall review the PI's documentation, the research, the suspension documentation, and may speak with the PI. The subcommittee shall submit findings and recommendations to the full b oard at its next regularly scheduled meeting, if possible.

At the discretion and invitation of the subcommittee, the PI may address the IRB in person at its next regularly scheduled meeting.

The full board shall consider the subcommittee's recommendation(s) and make a ruling to accept or revise the s ubcommittee's recommendation(s). If the subcommittee recommends that suspension be upheld and the IRB accepts this recommendation, then a formal plan of correction must be submitted to and approved at a convened meeting of the IRB in order for the research to resume.

The post-appeal decision by the full IRB to suspend a research projectis final and may not be reversed by the SVPR or any other officer/agency of TTUHSC or affiliated entities.

2.8.7 Terminate Research Activity

When the IRB terminates approval, the investigator is required to permanently cease all research activities, including data analysis, for the terminated study(ies). A research study can only be terminated by the full board at a convened meeting. This is true for studies which qualified for expedited initial/continuing review as well as those which were originally approved by the full board at a convened meeting. A majority vote of the voting members present is required to formalize a decision to terminate a research study. Termination will occur as a result of 1) the need to protect the safety, welfare, and rights of subjects, 2) serious or continued non-compliance and/or 3) other situations, as the Board deems appropriate.

2.8.7.1 IRB Considerations

IRB deliberations will include consideration of:

- the actions to protect the rights and welfare of currently enrolled participants;
- whether procedures for withdrawal of enrolled subject(s) took into account their rights and welfare;
- whether current participants should be informed of the termination;
- any serious adverse event or outcome reported to the IRB.

The IRB will notify the PI in writing of termination of IRB approval along with the reasons for the termination.

The IRB will notify the Assistant Vice President - Research Integrity and the SVPR of decision to terminate approval within 2 business days of the decision. The SVPR, serving as the institutional official, will promptly (within 30 days) notify other TTUHSC officials or outside entities (HHS, FDA, NIH, affiliated institutions, etc.) as required to comply with our FWA.

2.8.7.2 Termination by Institutional Official or IRB Chairperson

In urgent situations the SVPR acting in the role of institutional official or the IRB Chairperson acting on behalf of the IRB may determine that research activity must be terminated immediately. If this action occurs, the SVPR/IRB Chairperson must provide a written report of this action to the IRB for review at the next convened meeting. The report shall include any actions taken to protect rights, welfare and safety of currently enrolled participants and whether they have been notified of the suspension.

2.8.7.3 Appeal of Termination

The PI may appeal the decision of the IRB or SVPR by submitting a written request to the IRB and providing a rationale for the appeal and any other supporting documentation. The PI must submit an appeal within five business days of the date of notification of termination.

Within 14 days of the appeal of termination, the PI's request for reconsideration shall be reviewed by a subcommittee consisting of, the IRB chair and two IRB members jointly selected by the IRB chair, IRB administrator and Assistant Vice President - Research Integrity. The subcommittee may also invite individuals with expertise in that area of research to assist the subcommittee in its review of the issues. The local IRB administrator, research compliance officer, and Assistant Vice President - Research Integrity will provide assistance to the subcommittee as needed, though they will not be considered members of the subcommittee. Individuals assisting the subcommittee shall maintain confidentiality of the IRB proceedings.

This subcommittee shall review the PI's documentation, the research, the termination documentation, and may speak with the PI. The subcommittee shall submit findings and recommendations to the full b oard at the next regularly scheduled IRB meeting, if possible. At the discretion and invitation of the subcommittee, the PI may address the IRB in person at the next regularly scheduled meeting.

The full board shall consider the subcommittee's recommendation(s) and make a ruling to accept or revise the subcommittee's recommendation(s).

If the subcommittee recommends that termination be upheld and the IRB accepts this recommendation and votes accordingly, there is no further appeal within TTUHSC. (**45 CFR 46**.112 and **21 CFR 56**.112).

The post-appeal decision by the full IRB to terminate a research project is final and may not be reversed by the SVPR or any other officer/agency of TTUHSC or affiliated entities.

2.9 IRB Types of Review

2.9.1 Determination of Exempt Human Research

Federal regulations 2018 45 CFR 46 .104 provides for eight specific categories of activities that may qualify as exempt from 45 CFR 46 subpart A requirements IF specified requirements listed below are met. TTUHSC currently allows for six of these eight categories.

2.9.1.1 Use of the exemption categories for research subject to the requirements of subparts B, C, and D:

Application of the exemption categories to research subject to the requirements of 45 CFR part 46, subparts B, C, and D, is as follows:
(1) *Subpart B.* Each of the exemptions at this section may be applied to research subject to subpart B if the conditions of the exemption are met.
(2) *Subpart C.* The exemptions at this section do not apply to research subject to subpart C, except for research aimed at involving a broader subject population that only incidentally includes prisoners.(3)
(3) *Subpart D.* The exemptions of categories 1, 4, 5, and 6 cited in section 2.9.1.2 (below) may be applied to research subject to subpart D(children) if the conditions of the exemption are met.
Research described in category 2 paragraphs (i) and (ii) that involves children may only apply to research involving educational tests or the observation of public behavior when the investigator(s) do not participate in the activities being observed. Research described in category (2)(iii) may not be applied to research involving children.

2.9.1.2 Exempt Research Categories as Outlined in 2018 45 CFR 46

Category 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 ed ucators 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.

Category 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 ***NOTE:*** *This type of research may involve children ONLY IF the investigators do not participate in the activities being involved*;

(ii) Any disclosure of the humansubjects' 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 . ***NOTE:*** *This type of research may involve children ONLY IF the investigators do not participate in the activities being involved*; 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 §46.111(a)(7) ***. NOTE:*** *This type of research may not involve children.*

Category 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 §46.111(a)(7).

(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.

Category 4 Secondary research for which consent is not required: Secondary research uses of identifiable private information or identifiable biospecimens, if at least one of the following criteria is met:

(i) The identifiable private information or identifiable biospecimens are publicly available; **OR**

(ii) Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects; **OR**

(iii) The research involves only information collection and analysis involving the investigator's use of identifiable health information when that use is regulated under 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 non-research 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.*

Category 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 Web site 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.

Category 6 Taste and food quality evaluation and consumer acceptance studies:
(i) If wholesome foods without additives are consumed, or
(ii) If a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by th e Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

2.9.1.3 Exempt Research Categories as Outlined in Pre 2018 45 CFR 46

Category 1 Research conducted in established or commonly accepted educational settings involving normal educational practices;

Category 2 Research involving the use of educational tests, surveys, or questionnaires, provided that human subjects cannot be identified and that responses by the subjects will not place them at risk of liability or be damaging to financial standing or reputation. **Note:** Surveys or questionnaires involving children may not be considered exempt.

Category 3 Research involving the use of educational tests or observation of public behavior that is not exempt under the previous category if, 1) the human subjects are elected or appointed public officials or candidates for public office, or 2) the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter;

Category 4 Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the PI in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects. An example of this category is a retrospective chart review where no identifying information is recorded by the investigator. The exemptionmust be granted by the IRB office prior to the research taking place. In addition, this category requires that all data are already in existence at the time the application for exemption is made to the IRB;

Category 5 Research and demonstration projects which are conducted by or subject to the approval of Federal Department or Agency heads in order toreview public service programs; procedures for obtaining benefits under those programs; possible changes to those programs or possible changes in methods or levels of payment for benefits under those programs;

Category 6 Taste and food quality evaluation and consumer acceptance studies. NOTE: This is the only exempt category also permitted by the FDA under21 CFR 56.104

2.9.1.4 Exempt Review Process

The determination of whether a TTUHSC study qualifies forexempt status may be made by any experienced IRB member (one who has served as a voting member of an IRB for at least one year), by IRB staff, or by the Assistant Vice President—Research Integrity. TTUHSC researchers or departmental representative may not make these judgments themselves. The designation must be granted prior to the

research commencing. IRB acknowledgement of exempt human research may never be granted for research already in progress or completed.

If an investigator has a question regarding the applicability of the federal exemption categories s/he may contact the IRB office . For a study meeting the criteria for exempt status, the following documents need to be submitted:

- IRB Application indicating the nature of the requested exemption;
- the full research protocol, (if applicable);
- any other available documentation to help support the application (example: data collection forms, surveys, recruitment letters, etc.).

The review of the required documents includes an assessment of risk level, equitable selection of subjects, provisions to maintain confidentiality of data and privacy interests of the participants. If there are interactions with participants, the reviewer will consider disclosure to participants that the activity involves research, the participation is voluntary, name and contact information of the researcher. The reviewer may request additional information and/or refer for additional IRB member(s) review.

If the research application does not meet the criteria for exemption or if there are questions regarding the protection of participants in the research , the IRB Office will provide written notice to the investigator specifying the additional information needed. The IRB chair/designee retains the right to refer any application for expedited or full board review, even if it appears to meet the qualifications for exemption.

If the research does meet the exemption criteria, the IRB office will provide written notice to the investigator acknowledging this screening and status. This notice will document the regulatory code(s) justifying the exempt determination or an indication that the project meets the criteria for exemption and may be initiated as described in the approved protocol.

2.9.2 Review by Expedited Procedure

Federal regulations limit the use of expedited review procedures to specific research categories published in the Federal Register and that present no more than minimal risk to human subjects.

The acceptable categories of research that may receive expedited review are summarized below and the full text can be found on the HHS.gov website.

2.9.2.1 Expedited Review Categories

1. Clinical studies of drugs and medical devices only when:
   a. Research on drugs for which an investigational new drug application (**21 CFR 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.), **OR**
   b. Research on medical devices for which (i) an investigational device exemption application (**21 CFR 812**) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.
2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:

a. from healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8-week period and collection may not occur more frequently than 2 times per week; or
b. from other adults and children considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8-week period and collection may not occur more frequently than 2 times per week.

3. Prospective collection of biological specimens for research purposes by non-invasive means.
4. Collection of data through non-invasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.)
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).
6. Collection of data from voice, video, digital, or image recordings made for research purposes.
7. Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. **45 CFR 46.104**. This listing refers only to research that is not exempt.)
8. Continuing review of research previously approved by the convened IRB as follows:
    a. where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or
    b. where no subjects have been enrolled and no additional risks have been identified; or
    c. where the remaining research activities are limited to data analysis.
9. Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

2.9.2.2 Deadlines

Submissions which appear to meet the criteria for expedited review are reviewed in the order in which they are received. As such, there are no specific deadlines

for these types of submissions. In general, these submissions are reviewed by an experienced IRB member within one week of the assignment.

2.9.2.3 Documents

The information required for review using the expedited procedure is identical to those required for review at a convened IRB meeting **(see Documents list)**.

2.9.2.4 Duties of the IRB Member Conducting Expedited Reviews

At least one experienced IRB member will receive and review the same materials that the convened IRB would have received if the submission would have required full board review.

The reviewer must ensure that the submission meets all criteria for approvability and is represented by one or more categories of research eligible for expedited review. Reviewer actions include approval, request for more information and/or referral to the full board. The reviewer may not disapprove any submission.

If the project meets all criteria for expedited review and approval, all documents and reviewer's comments will be included in the agenda provided to the full board for reference at the next convened meeting. This documentation should cite the specific permissible category or categories justifying the expedited review.

If the project DOES NOT meet all criteria for expedited review and/or at the discretion of the IRB member it will be placed on the agenda for consideration at the next convened meeting.

2.9.3 Review at Convened Meetings of the IRB

2.9.3.1 Deadlines

Materials for convened board meetings will be submitted to the IRB Office by pre-established deadlines. Submission deadline dates and IRB meeting dates and times are found in Cayuse and on the TTUHSC Institutional Review Boards **webpage**. Deadlines for submissions of materials for convened board meetings are generally 10 days prior to the meeting date.

When a submission is placed on the IRB agenda, the submission and all attached documents are immediately available for review by all IRB members. The only exception to such availability is for IRB members who are listed as study personnel on a project—those members are blocked by the Cayuse system from viewing the submission. Reviewer assignments for submissions to be reviewed at a convened meeting are made within 48 hours of the published deadline as described in the next section.

The IRB reserves the right to limit the number of submissions at a convened meeting in spite of the deadline. If, in the opinion of the IRB chair or Administrator, more items have been submitted than can be effectively reviewed during the meeting, items w ill be prioritized. Submissions related to previously approved research will take priority over new projects. (Example: continuing reviews, amendments, etc.). Extra submissions will be assigned for review at the next convened meeting.

2.9.3.2 Conduct of the Meeting

TTUHSC IRB meetings are conducted using the Cayuse software program. Generally, each member will have an institutionally provided laptop to allow access to the agenda and all information included with each submission. TTUHSC technology exists to allow non-local members and guests to participate in the meetings via auditory and/or visual access to the meeting materials and each other.

Votes are taken for each full board agenda item and recorded in Cayuse documenting each members' vote including recusals, abstentions, or not present as stated elsewhere in this document.

2.9.3.3 Duties of IRB Member Reviewer

Each submission to be reviewed at a convened meeting will be assigned to a primary and/or secondary reviewer. Efforts will be made to make assignments primarily on the basis of reviewer expertise or knowledge of the subject population. Non-scientist members will not be assigned as primary reviewers. All study materials are routinely available to all IRB members for review through the Cayuse system. Reviews are to be written in the "member comments" section of each submission prior to the meeting. The primary reviewer is responsible for review and presentation of the research protocol, consent document and any supporting information (such as the investigator brochure for a drug). A secondary reviewer is also asked to review all submitted materials with a primary focus on the consent document(s). Both reviewers are responsible for reviewing the project for approvability according to the criteria set out in **45 CFR 46**.111 and/or **21 CFR 56**.111. A reviewer checklist is required to be completed by the primary reviewer to make sure all applicable issues are addressed in the written and oral presentation.

A consultant or the investigator may be asked to assist by presenting the Board with written or verbal information about the protocol and/or the test article. Clarification and discussion by the full board then takes place.

The primary and/or secondary reviewer is responsible for making the formal recommendation for IRB action (approval with risk level and review cycle, disapproval, request for more information, etc.) as appropriate to the submission. A majority consensus of the voting members present is required to formalize IRB decisions.

2.9.3.4 Quorum

A quorum is present when a simple majority of the appointed voting members (or their alternates) of the IRB are present including at least one member whose primary concerns are in non-scientific areas. This is calculated by using the "half-plus-one" technique. When the IRB membership is an odd number, the half is rounded up to the next whole number. For example, if the membership is 15, then majority is 8. Please see OHRP guidance here for more detail. Quorum for convened meetings may include video or teleconferencing, provided that the members participating from remote sites have access to all necessary materials required for review.

The IRB may only review proposed research at convened meetings at which a quorum is present. A quorum is not present when a sitting member who is required (example: a sole nonscientific member in attendance at the meeting) must recuse

him/herself for any reason. No official action may be taken at a meeting where a quorum is not present. Despite the presence of a quorum, no action should be taken at an IRB where the assembled members do not have the expertise to review the proposed research. IRB or TTUHSC administrative staff members who are not appointed to the IRB but attend IRB meetings by virtue of their position may not be counted toward quorum and do not have voting privileges.

2.9.3.5 Investigator Presence during Meetings

Principal Investigators may be in attendance at an IRB meeting during the summary and general discussion of their protocols in order to provide information and clarification. Principal Investigators who wish to attend the meeting must contact the IRB administrator to make arrangements. The IRB may specifically request that the principal investigator be present during discussion at a meeting to address the IRB and/or provide answers to IRB inquiries. The principal investigator will always be dismissed prior to the final discussion and vote.

2.10 IRB Submission Categories

2.10.1 Initial Reviews

In conducting initial reviews the IRB will consider the federal regulations applicable to the research and that must be met found in **45 CFR 46**.111, including Subparts B, C, and D as applicable, 21 CFR 50 and 21 CFR 56 must be met prior to initial IRB approval of a research project. No research involving human subjects that falls under the scope or authority of the TTUHSC IRB may commence prior to IRB approval of the project. In no case will a TTUHSC IRB grant "retroactive" approval to a research project where data have already been collected without IRB approval.

2.10.2 Continuing reviews

Continuing review of all research approved by the IRB will be consistent with these policies.

2.10.2.1 IRB Determination

2.10.2.1.1 Continuing Review Required

Studies that were originally approved by the full board at a convened meeting prior to January 21, 2019, will require continuing reviews in accordance with the pre-2018 federal regulations and the IRB assigned review cycle. This includes studies overseen by external IRBs.

Studies that were originally approved by the full board at a convened meeting January 21, 2019, or after will require continuing reviews in accordance with the 2018 federal regulations and the IRB review cycle. This includes studies overseen by external IRBs.

2.10.2.1.2 No Continuing Review Required

Unless the IRB determines otherwise, the following research projects approved after January 21, 2019, will generally not require continuing review:

- projects that received initial review through the expedited process
  or
- studies that were initially reviewed by the full board and conditions have changed during the current review period to make the research eligible for expedited review under the applicability criteria 46.110 (a).
  or

- projects that have progressed to the point that it involves only one or both of the following, which are part of the IRB-approved study:
  a) activities limited to data analysis, including analysis of identifiable private information or identifiable biospecimens;
  or
  b) projects whose only activity requires accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care

NOTE: Regardless of continuing review status, all projects approved by the IRB require ongoing reporting of changes to the project (amendments), any unanticipated events and study closures as stated elsewhere in this manual (see sections 2.10.3, 2.10.4 and 2.10.5).

2.10.2.2 Frequency

The frequency of the continuing review will primarily be based upon the degree of risk involved as determined by the IRB at the time of initial review. Factors to be considered by the IRB in determining the appropriate interval for review may include, but are not limited to:

- involvement of vulnerable populations;
- location of research site;
- the involvement of recombinant DNA or other types of gene transfer studies;
- the use of waiver or alteration of informed consent procedures,
- classified research;
- research for which subjects would be exposed to additional risks, (e.g., breach of confidentiality, Phase 1 studies, disproportionate number or severity of serious adverse events);
- previous suspension of the research due to compliance, record -keeping or other concerns;
- recommendations from other institutional committees;
- expected or actual rate of subject accrual
- funding sources
- type of initial review (full board vs expedited).

At the time of continuing review , the IRB will reassess the review cycle and may alter it based on the above factors . Projects determined to be of minimal risk , which require continuing review, will usually be assigned a 12-month review cycle.

2.10.2.3 Deadlines

In order to provide timely review and approval of each study, the PI shall submit required documentation no less than 10 days prior to the full b oard meeting preceding the study expiration date. For projects that are assigned to receive expedited continuing review documentation should be submitted no less than 10 days prior to study expiration date. Studies classified as exempt do not require a continuing review report. Although reminders will be sent, the PI is responsible for being aware of upcoming expiration dates in order to submit continuing review materials in a timely manner.

2.10.2.4 Required Information

Information included on the “Continuing Review Form” in Cayuse and which is required for continuing review includes:

- number of subjects enrolled, screened, and withdrawn (with reasons for withdrawal);
- Note that any participant who signs an informed consent document is considered to have been "enrolled" in the project, even if they are later withdrawn from the project (for not meeting all eligibility requirements, for example). Separate "screening" consent forms might be considered if an investigator anticipates a large number of "screen failures" for a particular project.
- a status report on the progress of the research and interim findings;
- any information, including that from recent literature relevant to the study which might affect the possible benefits or risks/benefits to the subjects;
- a summary of any incidents of the following: serious adverse events, unanticipated problems involving the research, and/or complaints about the research since the last IRB review;
- verification that informed consent was obtained from all subjects, that all subjects received a signed copy of the informed consent document and that all signed consent forms are on file (unless requirements were waived by the IRB);
- summary of any previously reported amendments or modifications to the research since the last review;
- an updated complete protocol;
- any relevant multi -center trial or Data Safety Monitoring Board (DSMB) reports, unless already submitted;
- any other information which may be relevant to making a determination regarding the potential risks, benefits, or scientific merit of the study.

2.10.2.5 Submission Screening

Each continuing review submission will be screened by IRB staff to ensure all necessary information is provided. After prescreening, the submission will be processed or assigned to a primary and/or secondary reviewer for expedited review or review at a convened meeting.

2.10.2.6 Duties of IRB Members

All study materials are routinely available to all IRB members for review through the Cayuse system. Based on its review, the IRB may require that the research be modified, restricted, suspended/terminated or administratively closed. Alternatively, previously imposed restrictions by the IRB may be lifted.

In order to approve a continuing review submission, the assigned IRB member(s) will review all the materials and/or information (see **Documents**) including any protocol modifications , unanticipated problems and researchers' current risk/benefit assessment . All this information is available on the electronic continuing review form and all study materials and past submissions are accessible through the Cayuse program to the reviewer(s). This review will be based on the same criteria as was used at the time of initial review (see**Approval Requirements**). In addition, the member(s) will make a determination that the current consent document is still accurate and complete and that any new significant findings that may relate to participants willingness to continue participation is included and will be provided to participants.

2.10.2.7 Verification from Sources Other Than the Investigator

The IRB has authority to determine which research activities need verification from sources other than the investigator (FDA 21 CFR 56 .108(a) & DHHS 45 CFR 46.103

Such sources include, but are not limited to, FDA inspection reports, subject complaints, research staff whistleblowers, data monitoring committee reports, site visit reports, Internet (FDA warning letters, OHRP and FDA debarment lists), and Federal Register notices for review.

If any of the following are true, the IRB can request a directed audit by the research compliance officer with findings to be reported back to the IRB.(See TTUHSC OP 73.14, Research Compliance and Research Compliance.)

- If information provided by the investigator is internally inconsistent or inconsistent with other information known to the IRB, and the inconsistency cannot be satisfactorily resolved by communications with the investigator;
- If the Board has reasons to doubt the veracity of the information provided by the investigator;
- If the investigator has a history of serious or continuing non-compliance with continuing review requirements in the past two years; **or**
- If the Board has other reasons to believe that verification from sources other than the investigator is required in order to determine that no material changes have occurred since prior IRB review.

2.10.2.8 Expiration of IRB Approval

The expiration date is assigned at the time of recommendation to approve the research at a convened meeting. The research expires one day less than the assigned review interval. For example, research project approved for annual review on 11/4/2013 will expire on 11/3/2014. Research activities are allowed to take place on 11/3/2014 (the day of expiration). As stated previously, although reminders will be sent, the PI is responsible for being aware of upcoming expiration dates in order to submit continuing review materials in a timely manner.

2.10.2.9 Failure to Provide Continuing Review Information

If a PI has failed to provide continuing review information to the IRB or the IRB has not reviewed and approved the research study by the expiration date specified by the IRB, all research activity, including enrollment, data collection and analysis, shall stop unless the IRB finds that it is in the best interest of individual subjects to continue participating in the research interventions or interactions. Enrollment of new subjects cannot occur after the expiration of IRB approval until such time as the IRB has re-approved the research.

2.10.2.10 Submission of Continuing Review Materials after Expiration Date

Once IRB approval expires, all research activity, including enrollment and accrual, data collection and analysis must stop . However, the IRB will not immediately inactivate the study, pending continuing review, if the PI submits the continuing review materials to the IRB within 30 calendar days after the expiration date. Extensions to the 30-day deadline will be made on a case-by-case basis. Research activity shall resume only after IRB approval of continuing review. If the PI fails to submit the continuing review materials within thirty days after the expiration date and has not communicated with the IRB regarding extenuating circumstances, the

study will be closed administratively by the IRB. Studies that are administratively closed by the IRB are no longer approved for any research activity. An investigator who wishes to reinitiate a research protocol that has been inactivated must submit the project as an initial application.

2.10.3 Amendments (proposed modifications) to previously approved studies

For previously approved projects (including exempt studies) all planned changes in the conduct of a study and/or changes to the consent document must be approved by the IRB prior to initiation of these changes, unless the change is required immediately in order to eliminate apparent immediate hazards to a subject/subjects.

In addition, any data safety monitoring reports, sponsor updates, etc. must be submitted for IRB review in a timely manner using the Amendment Form found in Cayuse.

IRB approval of amendments only apply to data collected after the IRB has approved the amendment (unless the change was made to eliminate immediate hazards as described above). IRB approval of an amendment does not apply retroactively to data collected prior to the approval of the amendment

2.10.3.1 Minor amendments

A minor amendment is defined as a change that would not materially affect an assessment of the risks and benefits of the study or does not substantially change the specific aims or design of the study. In general, this includes all modifications to studies which were initially approved by the expedited proced ure or those acknowledged as exempt from formal IRB review. Examples may include editorial changes or corrections to study documents, submission of missing documents, letters of support, changes to advertisements, etc.

Minor modifications will be reviewed by the IRB chairperson, member designee, and/or administrative staff. No reviewer may disapprove a requested modification via an expedited review procedure.

Amendments that involve o nly c hanges in study status based on the approved protocol study design may be considered a minor modification. For example , a project status changing from “open” to “permanently closed to accrual due to completion of required enrollment numbers ” or notification that all study subjects have completed the trial interventions and the study is now open only for long term “follow-up”. In such instances, the administrative staff may revise the study status to the appropriate category (closed to accrual/ follow-up) and risk status to minimal and may allow for expedited review of future submissions if 45 CFR 46.110 category requirements are then met.

Other minor changes to a study that may be acknowledged by the administrative staff include personnel changes (other than changes to the principal investigator) correction of typos in study documents, data safety or monitoring committee reports with recomm endation to continue study without changes, or updated contact information.

Modifications of any study document (IRB Application, protocol, consent document, recruitment materials, etc.) require submission of an updated copy of the proposed revised document with changes clearly identified. All minor modifications which have been a pproved or acknowledged will be immediately available on the IRB agenda for review by all IRB members at any time.

2.10.3.2 Greater than minor Amendment

A greater-than-minor amendment is defined as any change that could materially increase the potential risks, limit benefits of the study, substantially change the specific aims or design of the study or affect the subject's willingness to continue participation.

Examples of greater -than-minor changes include but are not limited to: newly discovered risks of the study drugs or study procedures, previously omitted or changed items that may increase the level of risk; an increase in the number of study subjects; a change in procedure that increases the level of risk for the study, or changes in the inclusion/ exclusion criteria.

Modifications of any study document (IRB Application, protocol, consent document, recruitment materials, etc.) require submission of an updated copy of the proposed revised document with changes clearly identified.

All greater than minor modifications will be reviewed at a convened meeting and assigned to a primary and/or secondary reviewer. All members (including alternate members) have immediate access to all modification requests and associated documents via Cayuse.

The IRB will use the same criteria used to initially approve the research (**45 CFR 46**.111 and/or **21 CFR 56**.111) as the basis for review/approval of the amendment. If the IRB determines the amendment includes information that might relate to participants' willingness to continue participation the investigators may be instructed to notify participants.
In rare instances changes in approved research must be initiated without IRB approval in order to eliminate apparent immediate hazards to the participant. When this is required, changes must:

- be promptly (within 30 days) reported to the IRB, and
- be reviewed by the IRB to determine whether each change was consistent with ensuring participant's continued welfare.

When stipulations are sent r esponses to major amendments may be reviewed by expedited procedure (if requirements **45 CFR 46**.110 are met) or full board review. If no response has been received from the investigator within 60 days of the request for additional information, the amendment request will be inactivated and will no longer be under consideration by the IRB.

2.10.3.3 Notification to the Investigator

The decisions by the IRB will be promptly conveyed to investigator s in writing by the IRB Office.

2.10.4 Unanticipated Events

Unanticipated events include protocol deviations, unanticipated problems involving risk to subjects or others (UPIRSOs), and serious local adverse events. The form used for reporting these events to the IRB is the Internal Unanticipated Event Form found in Cayuse. Questions about whether or not to report any particular event may be directed to the respective IRB administrator or Chair. If uncertainty remains, the event should be reported to the IRB.

2.10.4.1 Protocol Deviations

2.10.4.1.1 Definition

Protocol deviations are unplanned or unforeseen changes in the implementation of an IRB -approved protocol. They generally refer to a modification of procedures that has already occurred for a single subject; they are not intended to modify the protocol.
Protocol deviations:

- may involve a single exception to the protocol for an individual subject in order to provide a safeguard, eliminate or prevent an immediate harm;
- do not increase the risk to the subjects;
- do not affect the scientific validity of the study;
- do not result from deliberate misconduct of the investigator;
- do not necessitate any change to the approved protocol.

Examples of protocol deviations include delayed follow -up visits (if no medication, treatment, or supervision is missed) short delays in the delivery of medication, or extra compensation inadvertently given to a study subject.

If the investigator determines the deviation is not an exception and change should occur for all future subjects, this becomes the basis for a protocol modification and an amendment request should be submitted to the IRB for approval prior to incorporation into the study procedures.

2.10.4.1.2 Reporting to IRB

Any report of a protocol deviation that is submitted to the IRB must contain the following information:

- a detailed description of what happened;
- an explanation of the basis for determining that the incident represents a protocol deviation;
- a description of any changes to the conduct of the study or other corrective actions that have been taken or are proposed.
- Protocol deviations should be reported to the IRB promptly, generally within 30 days of the PI becoming aware of the event.

2.10.4.1.3 Assessment/ Review

The purpose of reporting these occurrences is to help in the IRB assessment of overall study conduct.

IRB staff prescreen protocol deviation submissions for completeness. If adequate, the submission is assigned to the research compliance officer or designee for initial review.

The compliance officer's /designee's review may include acknowledgement, request for additional information, or a determination to initiate a compliance audit. The compliance officer may maintain a separate record of protocol deviations per study in order to track trends or newly occurring problems.[See **Compliance**].

2.10.4.2 Unanticipated Problems Involving Risks to Subjects or Others (UPIRSOs)

2.10.4.2.1 Definition

Unanticipated problems involving risk to subjects or others are events that meet all of the following criteria:

- unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol -related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied (note: the unfounded classification of a serious adverse event as "anticipated" constitutes non-compliance);
- definitely related or probably related to participation in the research; and
- suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

2.10.4.2.2 Reporting to IRB

Any report of an UPIRSO will be submitted for IRB review using the Unanticipated Events Form found in Cayuse. The completed form must contain the following information:

- a detailed description of what happened;
- an explanation of the basis for determining that the incident represents a UPIRSO;
- a description of any changes to the conduct of the study or other corrective actions that have been taken or are proposed.

The following are examples of UPIRSO which require reporting to the IRB:

- Safety monitoring indicates that a particular side effect is more severe, or more frequent than initially expected.
- A paper is published from another study that shows that an arm of your research study is of no therapeutic value.
- Breach of confidentiality.
- Change in FDA labeling or withdrawal from marketing of a drug, device, or biologic used in a research protocol.
- Change to the protocol taken without prior IRB review to eliminate apparent immediate hazard to a research participant.
- Incarceration of a participant when the research was not previously approved under Subpart C and the investigator believes it is in the best interest of the subject to remain on the study.
- Complaint of a participant when the complaint indicates unexpected risks or the complaint cannot be resolved by the research team.
- Protocol deviation (accidental or unintentional) that in the opinion of the PI placed one or more participants at increased risk. **NOTE:** If such an event is submitted as a UPIRSO, it is not required to also be submitted as a Protocol Deviation.
- Sponsor imposed suspension and/or internal event(s) thatare required to be promptly reported to the sponsor by the PI.
- UPIRSOs should be reported to the IRBas soon as possible, but in any event, no later than ten (10) business days after the PI becomes aware of the event.

Questions about whether or not to report any particular occurrence may be directed to the respective IRB administrator or Chair. However, study team members are urged to err on the side of caution if there is a question about whether or not to report a particular occurrence to the IRB.

2.10.4.2.3 Assessment / Review

IRB staff prescreen UPIRSO submissions for completeness which includes an initial assessment of whether the information meets the criteria of a UPIRSO. If adequate, the submission is assigned for IRB chair or designee(s) review.

The research compliance officer/designee will also receive notification of the UPIRSO to allow input and/or recommendations for the IRB.

The IRB reviewer may acknowledge the information, request additional information and/or refer to the full board for review. In all cases, if the reviewer determines that the UPIRSO involves more than minimal risks to participants or others, the submission will be referred to the convened meeting for review.

2.10.4.2.4 Convened IRB Actions for UPIRSO

The following are examples of actions that are authorized by the IRB for UPIRSOs involving more than minimal risk:

- no additional action;
- a letter requiring explanation or clarification;
- suspension of enrollment in one or all related studies;
- termination of approval of one or all related studies;
- modification of the research protocol;
- modification of the information disclosed during the consent process;
- additional information be provided to past and/or current participants;
- notification of current participants (required when such information may relate to participants' willingness to continue to take part in the research);
- modification of the continuing review schedule;
- directed audit of the research;
- observation of the consent process;
- suspension of activities for the research;
- referral to other organizational entities (such as legal counsel, privacy officer);
- referral to other organizations' entities, if applicable (such as an affiliated institution's legal counsel, risk management, institutional official, auditing department).

The IRB may assign a deadline for complete response to any of the requested action(s).

2.10.4.2.5 Reporting to Regulatory Agencies

If the IRB determines that the increased risk is significant, the IRB chair or Administrator will notify the Institutional Official's (IO) office. The IO will notify OHRP and/or FDA within 30 days, in compliance with the TTUHSC Federalwide Assurance.

2.10.4.3 Serious Adverse Events (SAEs)

2.10.4.3.1 Definition

SAEs are internal events that include:

- Death
- Life-threatening experience
- Hospitalization (for a person not already hospitalized)
- Prolongation of hospitalization (for a person already hospitalized)

- Persistent of significant disability or incapacity
- Congenital anomaly and/or birth defects
- Any event that jeopardizes the subject and may require medical or surgical treatment to prevent one of the preceding outcomes.

2.10.4.3.2 Reporting to IRB

Any report of an SAE that is submitted to the IRB must contain the following information:

- adverse event category, attribution and grade (if applicable)
- a detailed description of what happened;
- an explanation of the basis for determining that the incident represents a SAE
- a description of any changes to the conduct of the study or other corrective actions that have been taken or are proposed.
- these events should be reported to the IRB as soon as possible, but in any event, no later than ten (10) business days after the PI becomes aware of the event

2.10.4.3.3 Exceptions for Reporting to IRB

For research projects that will have expected SAE's (research with pregnant women where hospitalization for childbirth is expected during the time of the research, for example) investigators may request permission from the IRB at the time of the initial review or via an amendment to not report all these specific SAEs as they occur. These requests will be reviewed on a n individual basis by the IRB.

When study interventions/treatment/ procedures have been completed and follow-up procedures for all locally enrolled subjects are the same as for patients managed off study, the study is generally considered to be in a follow-up status. During this follow-up time, local subjects may be hospitalized for co-morbid conditions definitely not related to the study. These hospitalizations are not considered to be SAEs and are not reportable to the IRB. In addition , subject deaths during this follow-up time are not reportable as SAEs but are to be reported at the time of continuing review.

2.10.4.3.4 Assessment / Review

IRB staff prescreen SAE submissions for completeness which includes an initial assessment of whether the information meets the criteria of a n SAE. If adequate, the submission is assigned for IRB chair or designee(s) review.The IRB reviewer may acknowledge the information, request additional information and/or refer to the full board for review. In all cases, if the reviewer determines that the SAE involves more than minimal risk to participants or others, the submission will be referred to the convened meeting for review.

2.10.4.3.5 Convened IRB Action for SAE

The following are examples of actions that are authorized by the IRB forSAEs more than minimal risk:

- no additional action;
- a letter requiring explanation or clarification;
- suspension of enrollment in one or all related studies;
- termination of approval of one or all related studies;
- modification of the research protocol;
- modification of the information disclosed during the consent process;

- additional information be provided to past and/or current participants;
- notification of current participants (required when such information may relate to participants' willingness to continue to take part in the research);
- modification of the continuing review schedule;
- directed audit of the research;
- observation of the consent process;
- suspension of activities for the research;
- referral to other organizational entities (such as legal counsel, privacy, officer);
- referral to other organizations' entities, if applicable (such as an institution's legal counsel, risk management, institutional official, auditing department).

The IRB may assign a deadline for complete response to any of the requested action(s).

2.10.4.3.6 Reporting to Regulatory Agencies

If the increased risk is significant, the IRB will notify the Institutional Official (IO). The IO will notify OHRP and/or FDA within 30 days, in compliance with the TTUHSC Federalwide Assurance.

2.10.4.4 External Adverse Event

2.10.4.4.1 Definition

External adverse events are defined as adverse events experienced by subjects enrolled by investigators at other sites in a multi -site trial who are participating in the same clinical trial (or using the same investigational drug or device) as investigations under oversight of the TTUHSC IRB. In order to require reporting to the TTUHSC IRB, the adverse event must exhibit all of the following characteristics:

- Non-local event reported in an externally sponsored multisite research project **AND**
- Unexpected **AND**
- Serious **AND**
- have implications for the conduct of the study (e.g. , requires a significant and usually safety-related change in the protocol)

2.10.4.4.2 Reporting to the IRB

Events that meet the definition must be submitted to the IRB using the Amendment Form in Cayuse. Typically, these events will result in changes to the study protocol, consent or other documents and will be reviewed at a convened meeting. In some cases, the IRB or the study sponsor may choose to temporarily suspend enrollment in the research project until an updated protocol and consent form can be reviewed and approved by the IRB.

If an External Adverse Event does not meet all of the above criteria, it does not need to be submitted to the IRB. If, however, a sponsor requires IRB submission, the investigator may submit such events using the External Adverse Event form in Cayuse. The submission will be acknowledged by the IRB Office personnel. These reports will be available for IRB members to review, but will generally not be individually deliberated at a convened meeting of the IRB.

2.10.5 Study Closures

Studies which have been approved by the IRB may be closed by the investigator, the sponsor, the IRB, TTUHSC, or by an affiliated entity. When the decision to permanently, temporarily or prematurely close a study is made by the investigator, an affiliated entity, or the study sponsor, the PI must promptly notify the IRB through Cayuse and include a summary of findings to date

2.10.5.1 Study Status - Completed

Studies that have been completed and are closed at the local research site will be designated as "Completed" in Cayuse. The PI shall submit the Study Closure Report Form to the IRB, which will include the total number of subjects, any major problems, and a summary of the findings. A manuscript may be substituted for the summary of the findings. Prior to the study being designated "Completed"all data from original projects conducted by a single investigator must be de-identified and stored separately from any information that may identify the participants. Additionally, any other identifiable information (videos, tapes, etc.) that the study protocol or IRB application targeted for destruction at the completion of the study must be destroyed. Study materials (paper or electronic records) must be stored for a minimum of 3 years to meet federal and institutional requirements and must be stored as long as additional applicable federal or contractual regulations stipulate.

Once the IRB has sent a written acknowledgment that the study is designated "Completed", no further actions are necessary by the PI. No further research activity is permitted for studies which are completed. Any further activity on such studies will require the submission of a new application to the IRB.

2.10.5.2 Study Status - Cancelled

If, after IRB approval, a study is permanently closed by the Principal Investigator or sponsor for any reason prior to its completion, it will be designated as "Cancelled" in Cayuse. The PI shall submit the "Study Closure Report" to the IRB which will include the total number of subjects (approved and enrolled), any major problems, and a summary of the findings. Prior to the designation of "Cancelled," all data must be de-identified and stored separately from any information that may identify the participants. Additionally, any other identifiable information (videos, tapes, etc.) that the study protocol or IRB application targeted for destruction at the completion of the study must be destroyed. Once the IRB has sent a written acknowledgment that the study is "Cancelled", no further actions are necessary by the PI. No further research activity is permitted for studies which are cancelled. Any further activity on such studies will require the submission of a new application to the IRB.

2.10.5.3 Study Status -Temporarily Closed

Studies that are temporarily closed to accrual of new subjects by the PI or Sponsor will be placed in "Closed to Accrual" status in Cayuse. No new subject enrollment may take place while studies have this designation. Submission of co ntinuing reviews, amendments, unanticipated events thatmay affect those participants who have already been enrolled, etc are required when a study is in this status Unless otherwise determined and communicated in writing to the investigator by the sponsor or IRB, subjects who had previously consented to participate in the research project may continue to complete protocol requirements while the study is closed to enrollment of new subjects.

The PI must notify the IRB upon temporary closure and when reopening is planned. Screening and/or enrollment of new subjects may not resume until the PI receives written approval from the IRB.

2.10.5.4 Study Status - Administratively Closed

Studies may be "Administratively Closed" by written notice to the PI by the IRB for reasons including, but not limited to:

- non-responsiveness to requests for information from the investigator, OR
- no study activity at the local site for a period of three or more years.

No further research activity is permitted for studies which are administratively closed. Any further activity on such studies will require the submission of a new application to the IRB.

2.11 Informed Consent

2.11.1 Documents

2.11.1.1 Template Consent Forms

Consent form templates are available for download inCayuse. Investigators must use these templates as a guide to create study specific consent forms unless the IRB grants exceptions or a waiver. These templates include all of the necessary and additional elements of a consent document outlined in **45 CFR 46.116** and **21 CFR 50.25** and are considered a baseline document. Legal documentation of informed consent requires participants or their legally authorized representative's signature and date on the IRB approved consent document. To be accepted as a valid informed consent the document must also be signed and dated by IRB approved research personnel who conducted the informed consent discussion.

If the clinical trial is required to comply with standards found in ICH-GCP (E6), the informed consent document provided to participants must also include the following: that the monitor, the auditor, the IRB, and the regulatory authority will be granted direct access to the participant's original medical records for verification of clinical trial procedures or data, without violating the confidentiality of the participant, to the extent permitted by the applicable laws and regulations and that, by signing a written consent form, the participant or the participant's legally acceptable representative is authorizing such access. The IRB will review the informed consent to determine whether this information is included.

2.11.1.2 English Document

All research studies requiring documentation of consent shall utilize one of the TTUHSC Informed Consent templates found in Cayuse. The consent form must be written in non-scientific language that is easily understood by all subjects. The IRB may also require additional information beyond the template baseline form to be added to the document.This may occur when the IRB determines the additional information would meaningfully add to the protection of the rights and welfare of subjects. HIPAA language in the consent form is unnecessary and will not replace the requirement for a separate HIPAA form.

2.11.1.3 Non-English Document

Consistent with the Belmont requirement that selection of subjects be equitable, individuals should not routinely be excluded from participation in research simply because they do not understand English. If the investigator or IRB determines that

the research project is likely to involve the participation of subjects whose primary language is not English, a translated consent document is required. The foreign language version of a consent document should be a certified translation of the IRB approved English version. It is, therefore, submitted after the IRB has approved the English version along with a certificate verifying the translation was provided by a certified translation service. Certified translations may be acknowledged and stamped with approval by IRB staff.

In limited cases the IRB may consider non-certified translations of English consent documents if the investigator has provided the qualifications of the translator and ensures the accuracy of the document (by having someone else back-translate the document, for instance). Submission of a non-certified translation is likely to delay the approval of the translated document.

Note that appropriate interpreter services should be made available throughout the course of the research in order to provide effective communication throughout the research process, not only in obtaining informed consent.

Circumstances may arise where a potential participant is identified whose native language is not frequently encountered and no certified translation of the informed consent document is available. If there is sufficient time before subject enrollment is to take place, investigators should seek a translation of the informed consent document and IRB approval of the document prior to enrolling the subject. If the time frame for enrollment does not permit translation of the entire consent document, a translated short form of the informed consent document or an oral presentation may be used as described elsewhere in this document.

2.11.1.4 Approval Dates

IRB-approved Informed Consent documents will have the TTUHSC seal and approval date affixed to the document.

Approval Date - The date of approval of the informed consent document will be determined based on the type of submission to the IRB. The approval date will be the date of final approval by the IRB for new studies, or the date of approval of a change to the previously approved informed consent document.

2.11.2 Process

The informed consent process involves three key features:

1. disclosing to potential research subjects' information that a reasonable person would want to have 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. Ways to promote voluntariness include allowing sufficient time for potential subjects to consider whether or not they want to participate, assigning study staff other than the principal investigator to conduct the informed consent discussion in an unhurried manner and to ensure any study personnel obtaining consent are adequately trained to do so.

Informed consent is an ongoing communication process between the investigator and subject, beginning with the initial approach of an investigator to the potential subject (e.g., through a flyer, brochure, or any advertisement regarding the research study) and continuing until the completion of the research study. The consent document is not a substitute for discussion among investigators and research subjects.

A description of the proposed informed consent procedure and written form is submitted as part of the IRB application prior to initiation of research.
The following process related questions are addressed in the IRB Study

Application, review of which is conducted by the IRB:

- qualifications (including names and roles on the study) of the study team members. Only study team members listed on the IRB application form may conduct or be part of the informed consent process.
- description of the setting to ensure that it allows for privacy and confidentiality;
- provisions to assess subject's understanding of the research and their participation;
- procedures for obtaining consent for non-English speakers to assure that the information given to the subject or representative is in a language understandable to them;
- description of any potential waiting period between providing information about the research to obtaining the documented informed consent and assures that subjects are given adequate time to consider participation;
- description of subject withdrawal procedures.

In giving informed consent, subjects may not waive or appear to waive any of their legal rights, or release or appear to release the investigator, the sponsor, the entity or agents thereof from liability for negligence.

2.11.2.1 Remote Consent

The expectation is that a signature will be handwritten using a permanent pen by the participant or the participant's LAR; however, investigators who wish to utilize remote consent, or electronic consent (eConsent), methods should contact the local IRB Administrator and the Compliance Officer for details on specific requirements and review process. Regulation requirements for obtaining informed consent must be met. Investigators should not obtain consent electronically unless this has been included in the approved IRB application. Appropriate justification for remote consent must be provided and these requests will be reviewed on a case-by-case basis.

2.11.2.1.1 Process

The informed consent discussion and subject identification verification (see process below) will be conducted via telephone or Zoom. The informed consent form will be sent via postal mail or email to the participant and/or LAR, if applicable, for signature(s). Adobe Sign and REDCap are the only institutionally approved software programs that can be utilized for electronic signature. Consenting parties will be given a copy of the signed informed consent form via Adobe Sign , when applicable.

Identification will be verified by either having the person hold up to the camera their driver's license or, if they have no camera ability, to state a previously provided 4-digit PIN. If the PIN is used, the person will be instructed to write this PIN next to their signature. If camera is available, have them point the camera at the consent form while they are signing it. The signed copy will be returned to the study team and signed. For NCI CIRB regulated studies, under the signature line, the investigator/designee must document a brief reason for performing the informed consent remotely, the method remote consent was conducted, the date of the

informed consent discussion, and the date the signed consent form was received. A copy of the signed consent form must be sent back to the participant electronically or as a hard copy before any research activity occurs.

2.11.3 Alteration or Waiver of Informed Consent

2.11.3.1 Oral Presentation (alteration)

In cases where the subject is unable to read the informed consent document in the language(s) in which it is available, the approved consent form may be read to the subject in its entirety in a language understood by the subject or the subject's representative. A third-party impartial witness unaffiliated with the research study will be present during the reading and will be required to sign and date the consent form as an impartial witness to the consent procedure. For FDA-regulated research or research that is funded by a federal agency a short form written consent document, described below, must also be used.

2.11.3.2 Short Form (alteration)

A short form written consent document stating the elements of informed consent required by 45 CFR 46.117 and 21 CFR 50.27(b) may be presented orally to the subject or subject's representative. This may be especially useful when the potential subject is unable to understand English and no translated informed consent document is available within the time frame required for enrollment. When this method is used there shall be a third-party impartial witness present. Further, the IRB must approve both the translated short form and a written summary of what is to be said to the subject or subject's representative and the impartial witness.

The procedure for use of a short form is as follows:

1. The investigator obtaining informed consent, with assistance of an interpreter if needed, provides orally to the subject the required elements of informed consent. The oral presentation must be in a language understandable to the subject. The investigator answers any questions from the prospective subject. There must be an impartial witness to the oral presentation who is not the person obtaining informed consent who should be fluent in the language of the oral presentation. (The interpreter may serve as the impartial witness).
2. The potential subject is given the IRB-approved translated short form and a copy of the IRB-approved English version of the long form.
3. The short form is signed and dated by the subject.
4. The impartial witness signs both the short form and the copy of the IRB-approved English version of the long form.
5. The investigator or person obtaining consent signs the IRB-approved English version of the long form.

As soon as possible after enrollment in the study, the subject is to be provided a translated version of the IRB-approved long form informed consent document.

2.11.3.3 Waiver of the Informed Consent Process

The IRB may approve a process which waives the requirement to obtain informed consent or parental permission provided that the IRB finds and documents the following, in accordance with 45 CFR 46.116 (e) and the FDA Guidance:

- The research involves no more than minimal risk to the subjects.
- The waiver will not adversely affect the rights and welfare of the subjects.

- The research could not practicably be carried out without the waiver.
- When appropriate, the subjects will be provided with pertinent information after participation.

An investigator who requests a waiver of informed consent or parental permission for a project will include a justification of the four requirements presented here in his/her initial application for IRB review. The request will be reviewed, and, if approved, will be documented in the IRB meeting minutes and on the IRB approval letter. Expedited review of requests to waive the informed consent process is permitted.

2.11.3.4 Waiver of Documentation of Informed Consent

In accordance with 45 CFR 46.117, the IRB may waive the requirement for the PI to obtain a signed consent form for some or all subjects if it finds that, 1) the only record linking the subject and the research is the consent document AND that the principal risk is the potential harm resulting from a breach of confidentiality; OR 2) that the research presents no more than minimal risk of harm to subjects AND does not involve procedures for which written consent is normally required outside of the research context.

In cases in which the documentation of consent requirement is waived, the IRB may require the PI to provide subjects with a written statement regarding the research. Investigators wishing to waive the documentation of informed consent for a project must include a justification for the request in their initial application for IRB review. The request will be reviewed, and, if approved, will be documented in the IRB meeting minutes and on the IRB approval letter. Expedited review of requests to waive documentation of informed consent process is permitted.

2.11.3.5 Exception from Informed Consent Requirements for Emergency Use of a Test Article (Waiver)

Under certain, limited conditions, test articles (drugs, devices or biologics which do not have FDA approval) may be used in life -threatening or debilitating situations. Details of this type of Emergency Use can be found in Section 2.16.4 of this Manual. Even for an emergency use, however, the investigator is required to obtain written informed consent from the subject or his/her authorized representative unless a physician who is not otherwise participating in the investigation certifies in writing all of the following as required by 21 CFR 50.23:

1. That the subject is confronted by a life -threatening situation necessitating the use of the test article.
2. Informed consent cannot be obtained because of inability to communicate with or obtain legally effective informed consent from the subject.
3. Time is not sufficient to obtain consent from the subject's legal representative.
4. No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the subject's life.

In all planned emergency research projects, whether or not FDA regulated, for which an exception from informed consent requirements is granted, the investigator shall be required to obtain informed consent from the subject or his/her authorized representative at the earliest feasible opportunity.

Nothing in this policy is intended to limit the authority of a physician to provide emergency medical care, to the extent the physician is permitted to do so under applicable federal, state, or local law.

2.11.3.6 Legally Authorized Representative

If a subject is not legally capable of giving informed consent or if the subject is cognitively impaired, the State of Texas requires consent from an authorized representative. Texas Code of Statutes Health & Safety Code, Title 4 Health Facilities, Subtitle B. Licensing of Health Facilities, Chapter 241 Hospitals, Subchapter G Disclosure of Health Care Information Section 241.151 (5) defines "Legally authorized representative" as:

- a parent or legal guardian if the patient is a minor;
- a legal guardian if the patient has been adjudicated incapacitated to manage the patient's personal affairs;
- an agent of the patient authorized under a durable power of attorney for health care;
- an attorney ad litem appointed for the patient;
- a person authorized to consent to medical treatment on behalf of the patient under Chapter 313;
- a guardian ad litem appointed for the patient;
- a personal representative or heir of the patient, as defined by Chapter 22, Estates Code,, if the patient is deceased;
- an attorney retained by the patient or by the patient's legally authorized representative; or
- a person exercising a power granted to the person in the person's capacity as an attorney-in-fact or agent of the patient by a statutory durable power of attorney that has been previously signed by the patient.

2.11.4 Withdrawing Consent

When a participant withdraws from a study, the data collected on the participant to the point of withdrawal remains part of the study database and may not be removed. The consent document cannot give the participant the option of having data removed. A researcher may ask a participant who is withdrawing whether the participant wishes to allow continued follow-up and further data collection subsequent to their withdrawal from the interventional portion of the study. Under this circumstance, the discussion with the participant distinguishes between study -related interventions and continued follow-up of associated clinical outcome information, such as medic al course or laboratory results obtained through non -invasive chart review and address the maintenance of privacy and confidentiality of the participant's information.

The researcher must obtain the participant's consent for this limited participation in the study (assuming such a situation was not described in the original consent document). The IRB must approve the consent document.

If a participant withdraws from the interventional portion of a study and does not consent to continued follow-up of associated clinical outcome information, the researcher must not access for purposes related to the study the participant's medical record or other confidential records requiring the participant's consent. However, a researcher may review study data related to the participant collected prior to the participant's withdrawal from the study, and may consult public records, such as those establis hing survival status.

2.11.5 Assent--General

If a subject is not legally capable of giving informed consent or if the subject is cognitively impaired, the IRB must find that adequate provisions are made for soliciting the assent of the subject when in the judgment of the IRB; the subject is capable of providing assent. Failure to object to participate in a research study is not assent.

In determining whether subjects are capable of providing assent, the IRB shall take into account the age, maturity, cognitive, and psychological state of the subjects involved. This judgment may be required for each subject individually or for all subjects in a particular research study as the IRB deems appropriate. If the IRB determines that the capability of some or all of the subjects 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 subject and is available only in the context of the research, the assent of the subject is not a necessary condition for proceeding with the research.

Documentation of a subject's assent will generally be required unless specifically waived by the IRB. Documentation may be through the use of an IRB approved assent form or a note written in the subject's medical record if an assent document has not been approved by the IRB.

2.11.5.1 Child or Minor

A child's/minor's assent is an affirmative agreement to participate in research. If a child/minor merely does not refuse to participate in research, assent has not been obtained. While the IRB may use its discretion as to whether assent of a child/minor is required, and how this shall be obtained (i.e. orally, in writing, etc.), in general, children age 7 and over should be allowed the opportunity to assent. Opportunities for assent should be made in language and under circumstances that ensure that the child/minor understands and minimizes or alleviates a feeling of pressure to participate by parents or professionals. Assent may be waived under normal circumstances where consent would be waived, or if the research offers a promise of direct benefit not available outside of the research and the parent consents.

Parents or guardians of the child/minor must provide written permission for the child/minor to participate in research unless the IRB determines that, for the protection of the child/minor (e.g., research on neglected or abused children), permission of the parent/guardian is not required. In such a case, the IRB must go to extraordinary lengths to ensure that the rights of the child/minor are protected. The process of obtaining parental permission is identical to that of obtaining informed consent, including the possibility for waiving parental permission if the criteria for waivers or alterations are met as described elsewhere in this document.

2.11.5.2 Persons with Impaired Decision-Making Capacity

Individuals likely to have diminished decision-making capacity include those legally determined to be incompetent or incapacitated as well as mentally handicapped or cognitively impaired. Cognitive impairment may be permanent (late-stage dementia) or temporary (ex: in emergency situations).

If the subject lacks the decision-making capacity to offer their informed consent, adequate plans describing the assent process must be submitted and reviewed by the IRB. Such plans must clearly describe the subject population as either permanently impaired or possibly temporarily impaired. If subjects with temporary impairment are included (for example: trauma studies), when the subject does

resume the mental capacity to offer informed consent, they must be offered the choice of continuing with the research project or withdrawing at that time.

2.11.6 Certificate of Confidentiality

Data collection about sensitive issues (such as illegal behavior, alcohol or drug use, or sexual practices or preferences) requires the protection of confidentiality beyond preventing accidental disclosures. Under federal law, an advance grant of confidentiality, known as a Certificate of Confidentiality is available. General information may be found at NIH Grants and Funding.

A Certificate of Confidentiality provides protection for the researcher and the subjects against compelled disclosure of identifying information about subjects of biomedical, behavioral, clinical, and other research (Public Health Service Act 301(d), 42 U. S.C. 241(d)). Under this Act, the Secretary of HHS may authorize persons engaged in research to protect the privacy of subjects by withholding the names or other identifying characteristics of the subjects from all persons not connected with the conduct of the research. This means that researchers may not be compelled in any Federal, State or local civil, criminal, administrative, legislative, or other proceedings to identify their subjects.

The Confidentiality Certificate does not govern the voluntary disclosure of identifying characteristics of research subjects but only protects subjects from compelled disclosure of identifying characteristics by the researcher. Researchers, therefore, are not prevented from the voluntary disclosure of matters such as child abuse or a subject's threatened violence to self or others. If an investigator intends to make such voluntary disclosures, however, the consent form shall clearly indicate this possibili ty to subjects.

In order to seek a Certificate of Confidentiality, a PI shall identify the potential for compelled disclosure in the application. The consent document shall also include and describe possible disclosure situations. The IRB shall determine whether the risks to subjects are minimized, informed consent is appropriate, and privacy and confidentiality protections are adequate. Detailed instructions for obtaining the Certificate of Confidentiality can be found at Certificates of Confidentiality (CoC)– Human Subjects.

2.12 Vulnerable Populations

2.12.1 Pregnant Women and Fetuses

Special DHHS regulations applying to pregnant women and fetuses may be found in 45 CFR 46 Subpart B. No federally funded or FDA regulated research may be conducted with pregnant women or fetuses unless the conditions specified in 45 CFR 46 Subpart B are met.

When the IRB considers research with pregnant women, the following conditions must be met:

1. If scientifically appropriate, preclinical studies, animal studies and studies on non-pregnant women should have already been completed.
2. Any risk to the fetus must be caused only by procedures that hold out the prospect of direct benefit for the woman or the fetus. If there is no prospect of benefit, the risk to the fetus must be minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means.

3. There must be the least possible risk possible to achieve the objective.
4. If there is potential benefit to the mother, potential benefit to the mother and fetus, or no potential benefit to either the mother or fetus AND the risk to the fetus is minimal AND the research can lead to important biomedical knowledge that cannot be obtained by other means, then the mother alone may provide consent for the study.
5. If the research holds out the prospect of direct benefit only to the fetus, then the consent of BOTH the mother and father is necessary unless the father is unavailable, incompetent, temporarily incapacitated, or the pregnancy is the result of rape or incest.
6. Each person giving consent is fully aware of the impact of the research on the fetus or neonate.
7. If the pregnant woman is a child, assent and permission must be obtained in accordance with 45 CFR 46 Subpart D.
8. No inducement may be offered to terminate a pregnancy.
9. Individuals involved in the research may have no involvement in any decisions regarding the termination of the pregnancy or the viability of a neonate.

2.12.2 Research Involving Neonates

Regardless of neonate viability, all research involving neonates must meet the following conditions:

- Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.
- Individuals providing consent are informed regarding the reasonably foreseeable impact of the research on the neonate.
- Individuals involved in the research will have no part in determining the viability of the neonate.

2.12.2.1 Neonates of Uncertain Viability

No research may take place until the following conditions have been met. After presentation of the primary reviewer, the convened IRB must vote to determine that:

- The research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective; or
- The purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research.
- The legally effective informed consent of either parent of the neonate is obtained, **or**
- If neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent designated representative is obtained as stated in the section above.
- The consent of the father or his representative does not need to be obtained if the pregnancy resulted from rape or incest.

2.12.2.2 Nonviable Neonates

After delivery, nonviable neonates may not be involved in research covered by this policy unless all of the following conditions are met:

1. vital functions are not artificially maintained;
2. the research will not terminate the heartbeat or respiration of the neonate;

3. there will be no added risk to the neonate resulting from the research;
4. the purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and the legally effective informed consent of both parents of the neonate must be obtained in accordance with 45 CFR 46 subpart A.
5. However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable neonate will suffice, except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest.

The consent of a legally authorized representative of either or both of the parents of a nonviable neonate will not suffice to meet the requirements.

2.12.2.3 Viable Neonates

Research may be done after delivery of a viable neonate if all rules following informed consent (45 CFR 46.116) and research with children (45 CFR 46 Subpart D) are followed.

2.12.2.4 Research Involving the Placenta, the Dead Fetus or Fetal Material

Research involving, after delivery, the placenta; the dead fetus; macerated fetal material; or cells, tissue, or organs excised from a dead fetus, shall be conducted only in accord with any applicable federal, state, or local laws and regulations regarding such activities.

If information associated with material described in previous paragraph of this section is recorded for research purposes in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research subjects and all pertinent subparts of this part are applicable.

2.12.2.5 Research Not Otherwise Approvable Which Presents an Opportunity to Understand, Prevent, or Alleviate a Serious Problem Affecting the Health or Welfare of Pregnant Women, Fetuses, or Neonates

This type of research can be conducted (or receive federal funding) only if:

1. The IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates; and
2. The Secretary of DHHS, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, ethics, law) and following opportunity for public review and comment, including a public meeting announced in the FEDERAL REGISTER, has determined either:
   a. That the research in fact satisfies the conditions of regulations, as applicable; or the following:
   b. The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates;
   c. The research will be conducted in accord with sound ethical principles; and Informed consent will be obtained in accord with the informed consent provisions.

2.12.3 Prisoners

Special DHHS regulations applying to prisoners may be found in 45 CFR 46, Subpart C. Research reviewed at a convened meeting involving prisoners as subjects must include an individual or individuals knowledgeable and experienced in working with this population. At the present time TTUHSC IRBs do not have this representation. As such, research targeting prisoners cannot be reviewed by a TTUHSC IRB.

2.12.4 Children and Minors

In Texas, the age of majority is 18. The information in this section applies to minors under the age of 18 who are not considered legally emancipated.

The IRBs will follow 45 CFR 46 subpart D, which provides special safeguards for children and minors when they are subjects in research studies. In addition, the IRBs adopt all Food and Drug Administration regulations found in 21 CFR 56 subpart D when the research is regulated by the FDA

When children or minors are research subjects, researchers must obtain both the consent/permission of the parent or representative and the assent of the child if he/she is 7 years or older. Mere failure to object is not assent. In certain cases, the IRB can waive or modify the assent requirement. Investigators wishing to waive or modify the assent requirement should submit their request to the IRB either as part of the initial application or in an amendment for previously approved studies. Note that consent/permission of the parent or representative may not be waived for FDA regulated research.

2.12.4.1 Additional Required Determinations

Minimal risk is defined as follows: 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 and or psychological examinations or tests. This standard is indexed to the lives of healthy children.

The IRB can approve non-exempt research involving children only if it falls into one of the following categories which differ according to assigned risk and potential for direct benefit to the child. The chosen category (45 CFR 46.404-407; 21 CFR 50.51-54) will be documented in the IRB meeting minutes.

- Research presenting no greater than minimal risk to children (45 CFR 46.404/21 CFR 50.51).
  - Where parental permission (consent) is to be obtained, permission from both parents is preferable. However, the IRB may find that the permission of one parent is sufficient for research to be conducted.
- Research involving greater than minimal risk of children that offers the prospect of direct benefit or may contribute to the well-being of the individual child (45 CFR 46.405/21 CFR 50.52).
  - Where parental permission (consent) is to be obtained, permission from both parents is preferable. However, the IRB may find that the permission of one parent is sufficient for research to be conducted.
- Research involving only a minor increase over minimal risk yet does not offer any, prospect of direct benefit or contribute to the well-being of the child (45 CFR 46.406/21 CFR 50.53).
  - When parental permission is to be obtained, both parents must give their permission unless one parent is deceased, unknown, incompetent, or

not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.
- Federally funded research that does not fit into one of these categories must either be disapproved or referred to the Secretary of the Department of Health and Human Services (DHHS).

2.12.4.2 Placebo Controls

Placebo groups are not specifically prohibited in research involving children, but they may be used only in studies where there is no proven prophylactic, diagnostic, or therapeutic treatment in existence. The IRB must consider the risks and benefits to the child of the study without concern for the success or failure of the study.

2.12.4.3 Wards

Children who are wards of the State of Texas or any other agency, institution, or entity can be included in research approved under applicable federal regulations only if such research is:

- related to their status as wards; or
- conducted in schools, camps, hospitals, institutions, or
- similar settings in which the majority of children involved as subjects are not wards

If the research is approved, the IRB shall require appointment of an advocate for each child who is a ward, in addition to any other individual acting on behalf of the child as guardian or in loco parentis. One individual may serve as advocate for more than one child. The advocate shall 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.

2.12.5 Employees as Participants

No researcher may give an indication that an employee is required to participate as a research subject. No coercion or inference that employment status could be affected with respect to participation in research activities is allowed. TTUHSC employees who are paid for their participation in a research project should be informed that the compensation may be considered to be “additional compensation” from TTUHSC and will be taxed accordingly. Further information regarding payment of employees as research participants can be found in TTUHSC OP 72.19 Payment to Research Participants/Patient Studies.

2.12.6 Students as Participants

Students must always be informed if participation in research is a course requirement and they must be offered an alternative activity if they choose not to participate. The syllabus shall clearly describe proposed participation in research activities for course credit and the alternative means of earning the course credit, which must require an equivalent amount of time and effort. The IRB shall review:

- that consent for participation is sought only under circumstances which minimize the possibility of coercion or undue influence,
- that methods used to maintain confidentiality are clearly identified, and
- that genuinely equivalent alternativesto participation are available

Any IRB concerns regarding the use of students should promptly be forwarded to the research compliance officer or to the SVPR.

2.12.7 Participants with Impaired Decision-Making Capacity

Individuals likely to have diminished decision-making capacity include those legally determined to be incompetent or incapacitated as well as mentally handicapped or cognitively impaired. Cognitive impairment may be permanent (late-stage dementia) or temporary (ex: in emergency situations).

The following questions must be found to be satisfactory prior to approval of individuals with diminished decision-making capacity in the research.

- Does the research question focus on an issue relevant to the population being considered? The research should bear some direct relationship to the population's condition or circumstances.
- Is it feasible to use a non-decisionally impaired population instead?
- Are there sufficient plans to assess mental capacity initially and in an ongoing fashion, if necessary, such as in cases of temporary cognitive impairment? If a subject's temporary cognitive impairment resolves, are there specific and clear plans to obtain the subject's consent to continue on the research?
- If the subject lacks the mental capacity to offer their informed consent, are there adequate plans describing the assent process.
- Are there clearly defined processes to determine the legally authorized representative to offer consent for participation in the research?
- Are additional protections necessary/ included to protect this population?

The IRB will review all study material(s) submitted for information regarding protections provided to decisionally impaired participants, regardless of the cause of the impairment. Particular attention will be paid to the material(s) provided to the participant(s) and the investigator's provisions for ensuring the participants understanding of the material.

The IRB review process will include evaluation of any additional safeguards that may be required as part of the informed consent process in order to address the challenges inherent in obtaining informed consent from persons with decisional impairment. Information to be evaluated will include:

- Assessment of consent capacity of potential subjects and the investigator's plan for assessment of this capacity (for example through use of an independent qualified professional) to ensure that it is adequate.
- If the consent assessment reveals the subject is unable to offer consent, a plan for determining the capacity of the potential subjects' ability to offer ***assent*** must be clearly stated and adequate.
- Whether a waiting period is provided in the decision-making process to allow additional time for decision-making.
- Whether methods are used to enhance consent/assent capacity. For example, simplification/repetition of information; use of a subject advocate or trusted ally of the person to assist when sharing information about the study.
- What plans are used to assess subject's understanding of the information after it has been shared.

If the project is required to meet ICH-GCP (E6) and is a non-therapeutic clinical trial (i.e. a trial in which there is no anticipated direct clinical benefit to the participant).

Except as described below, a non-therapeutic trial should only be conducted in subjects who personally give consent and who sign and date the written informed consent form.

Non-therapeutic trials may be conducted in subjects with consent of a legally acceptable representative provided the following conditions are fulfilled:

(a) The objectives of the trial cannot be met by means of a trial in subjects who can give informed consent personally.
(b) The foreseeable risks to the subjects are low.
(c) The negative impact on the subject's well-being is minimized and low.
(d) The trial is not prohibited by law.
(e) The opinion of the IRB is expressly sought on the inclusion of such subjects, and the written opinion covers this aspect.

Such trials, unless an exception is justified, should be conducted in patients having a disease or condition for which the investigational product is intended. Subjects in these trials should be particularly closely monitored and should be withdrawn if they appear to be unduly distressed.

When providing information, t he available nonclinical and clinical information on an investigational product is adequate to support the proposed clinical trial

2.12.8 Other Vulnerable Populations

Other groups may be considered vulnerable research participants . When the IRB reviews any project involving subjects deemed to be vulnerable (terminally ill, economically disadvantaged, etc) the special needs of the particular population will be considered and addressed. A reviewer checklist will address additional safeguards to protect the rights and welfare of the subject population deemed to be vulnerable.

2.13 Health Insurance Portability and Accountability Act (HIPAA)

The HIPAA Authorization form or a request for a Waiver of Authorization shall be included in initial IRB applications for any project which utilizes protected health information. Once the HIPAA documentation has been reviewed for compliance with TTUHSC policy, it does not need to be re-submitted for the duration of the study, unless there are changes required that affect the HIPAA form. Further information regarding HIPAA compliance, including approved forms, can be found at the TTUHSC HIPAA website.

2.13.1 HIPAA Authorization

Each TTUHSC PI shall present subjects with an "Authorization to Use and/or Disclose Your Protected Health Information for Research Study" before using or disclosing protected health information (PHI). Such authorization shall satisfy the requirements of 45 CFR 164.508, except that the authorization may state that there is no expiration date or that the authorization continues in effect until the end of the research study. If there is any question as to whether PHI is being collected, contact your IRB administrator. Requests to alter HIPAA documents shall be submitted to the local TTUHSC HIPAA Privacy Officer.

Principal Investigators who are members of unaffiliated organizations that have designated TTUHSC as their Privacy Board may use the TTUHSC HIPAA authorization form that is found in Cayuse. All references to TTUHSC should be deleted except as it pertains to the IRB stamp. This policy does not prohibit organizations from using their

own HIPAA Authorization Form in additionto the TTUHSC HIPAA Authorization Form, should they so wish.

Procedure for Tracking Research-Related PHI Disclosures
The TTUHSC Office of Research and Innovation shall coordinate with Institutional Compliance to implement a process for identifying, monitoring, and tracking research-related disclosures of PHI. The process shall ensure compliance with applicable accounting of disclosure requirements and require documentation and retention of disclosure information. When a Principal Investigator indicates within the electronic IRB system that PHI will be disclosed to an external entity, the Research Compliance Officer shall coordinate with the investigator and appropriate institutional offices to ensure the disclosure is appropriately reviewed, required agreements are executed, and safeguards are implemented to protect PHI

2.13.2 HIPAA Waiver Request to Privacy Board

Principal Investigators may request to use and disclose specified PHI without an individual's specific authorization and/or without the necessity for an opportunity for the individual to agree or object for research purposes provided that the criteria required by 45 CFR 164.512(i) are satisfied. These criteria include:

- The intended use and/or disclosure of the Protected Health Information (PHI) involve no more than a minimal risk to the privacy of the individuals.
- The research could not practicably be conducted without the waiver.
- The research could not practicably be conducted without access to and use of the protected health information.

HIPAA Waiver questions included in the IRB Application Form in Cayuse are to be completed by investigators who wish to request a waiver of HIPAA Authorization. Responses to the questions associated with a request for a HIPAA Waiver will be reviewed by a member of the Institutional Privacy Board and will be acknowledged as part of the IRB review process.

For purposes of HIPAA, the TTUHSC IRBs will act as Privacy Boards as defined by 45 CFR 164 .512(i). IRB administrators shall verify Privacy Board Agreements with affiliated Entities are in place prior to a Privacy Board Review. The local IRB administrators/coordinators and the Assistant Vice President - Research Integrity are members of the Privacy Board and may acknowledge HIPAA waiver requests.

2.14 Recruitment Methods

2.14.1 Subject Identification

Investigators are required to provide a detailed description of subject identification and recruitment methods as part of the IRB application. If the investigator/study personnel have no direct patient care relationship with a potential research subject t hey should include a clearly written description of how subjects will be identified and/or approached in a manner that protects their privacy and confidentiality.
Acceptable recruitment strategies might include: a) advertisements, b) notices and/or media announcements, c) a letter describing the project with research personnel contact information provided to colleagues for general distribut ion to their patient population so that interested persons may then self-refer, or d) study personnel may recruit from within their own patient population by describing the project and reviewing the informed consent document with potentially eligible subjects.

Unacceptable recruitment methods might include: a) Study personnel with no professional relationship with the potential research subject searching through medical records or existing databases (e.g., registries) for qualified subjects and subsequently contacting those patients directly; b) Presenting the research immediately prior to sensitive or invasive procedures (e.g., cardiac surgery) when the person is potentially distracted/nervous, medicated and/or temporarily decisionally impaired; or c) retaining sensitive information obtained at screening - without the consent of those who either failed to qualify or refused to participate- for possible future study participation.

2.14.2 Advertisements/Recruitment Materials

Advertising for recruitment is considered to be the beginning of the informed consent process, therefore all recruiting and advertising materials must be approved by the IRB prior to use. An expedited review may be used for approval, but advertising may also be referred for full board review at the reviewer's discretion.

The IRB defines advertisement/recruitment materials any research-related information that will be seen or heard by a potential subject before he or she has signed a consent form for the study. This means recruitment materials may include:

- printed items in newspapers, magazines, flyers, posters, and so forth;
- radio, TV, video scripts and recordings;
- internet postings;
- web pages;
- informational brochures;
- letters to potential subjects;
- imprinted items (notebooks, bags, and so forth)

TTUHSC IRBs use information from the FDA Information sheet, Recruiting Study Subjects, to determine acceptability of advertising methods.

The information that is permissible includes:

- name, address of investigator and research facility;
- condition under study and/or purpose of the research;
- summary of inclusion / exclusion criteria;
- brief list of procedures involved;
- time commitment required;
- compensation/reimbursement;
- location of research and contact person for further information.

Additional guidelines to be followed should be very clear that research participation is being solicited.

The following information is not permissible and should not be included in posted notices or recorded descriptions of the research:

- claims, either explicit or implicit, that the drug, biologic, device or other type of intervention is safe or effective for the purposes under investigation;
- catchy words like "free" or "exciting";
- claims, either explicit or implicit, that the test article is known to be equivalent or superior to any other drug, biologic, device or intervention;
- terms such as "new treatment," "new medication" or "new drug" without explaining that the test article is investigational, meaning non-FDA-approved;

- promise of "free medical treatment," when the intent is only to say that participants will not be charged for taking part in the investigation;
- an emphasis on the payment or the amount to be paid, by such means as larger or bold type. The IRB has the authority to approve whether compensation information shall be included in the advertisement.

2.14.2.1 Additional Approval

Formal approval at the facility where any advertisement is to be posted may be required. For example, advertisements posted at TTUHSC must comply with TTUHSC OP 61.03 Posting of Notices on TTUHSC Property. Non-TTUHSC facilities may have their own specific requirements.

2.15 Payment to Subjects

Payment to research subjects for participation in studies is not considered a benefit. Rather, it shall be considered compensation for time and inconvenience. The amount and schedule of all payments shall be presented to the IRB at the time of initial review. The IRB shall review both the amount of payment and the proposed method and timing of disbursement to determine whether the payment is an undue inducement of the subject to participate in the research or to continue beyond where they would have otherwise withdrawn.

2.15.1 Timing of Payments

Payment(s) shall be made to the subject in proportion to the portion of the study completed and shall not be contingent upon the subject completing the entire study. A schedule for the amount to be paid for each activity will not suffice; a timetable for the payments themselves must be submitted, approved, and presented to every subject as part of the Informed Consent process.

2.15.2 Method of Payments

The informed consent document must clearly establish the frequency and amount of payment associated with research participation. Persons who receive more than $25 for participating in a research study must provide a social security number. Persons who are unable or unwilling to provide a social security number may be paid through the approved TTUHSC payment system, but the compensation will be subject to withholding. This information must be provided to the potential participant as part of the consent process. The description must also inform the subject if any money received will be reported to the Internal Revenue Service (receipt of $600 or more per year must be reported to the IRS). Additional details regarding acceptable methods of payment and income tax information can be found in TTUHSC OP 72.19 Payment to Research Participants/Patient Studies and TTUHSC OP 72.12 Payments to Nonresident Aliens. The IRB will consider lottery-style payment plans (whereby only some subjects receive payment, by chance) on a case-by-case basis.

2.15.3 Alterations in Payments

Any alterations in previously approved amount(s) or timing of human research subject payment or revisi on of the payment schedule must be submitted to the IRB as an amendment prior to implementation. A document to be sent to the subjects informing them of payment changes must be part of this submission.

2.15.4 Documentation

The PI must keep documentation of payment(s) made to each subject in study files and for three years after the study is completed. All records shall be made accessible for inspection and copying by authorized TTUHSC representatives, including TTUHSC Accounting and Research Compliance personnel, TTUHSC auditors, the SVPR, and federal regulatory officials. Additional details can be found in TTUHSC OP 72.19 Payment to Research Participants/Patient Studies

2.15.5 Finder Fees

Due to the conflict of interest created by offering such incentives, the TTUHSC IRBs will not allow the use of any form of compensation to study personnel who identify and/or recruit subjects for participation in a research study. TTUHSC also prohibits an payments to study personnel designed to accelerate the recruitment rate and that are tied to the rate or timing of enrollment (bonus payment). Furthermore, physicians who recruit their own patients to serve as research subjects are ethically obligated to inform patients that they are in no way obligated to participate in the physician's research projects.

Payments to subjects for referring other potential subjects may be considered by the IRB on a case-by-case basis. If such payments are approved they will be subject to taxation as described above in methods of payment.

2.16 Investigational Drugs/Devices

The use of an unapproved investigational drug, device or biologic requires an FDA investigational new drug application (IND) as detailed in 21 CFR 312 or an FDA investigational device exemption (IDE), detailed in 21 CFR 812.

2.16.1 Investigational Article Accountability

The principal investigator is directly responsible for the accounting of all investigational articles provided by a study sponsor as indicated in the FDA Form 1572. Regulations allow investigators to delegate these procedures to qualified pharmacist/individual health care provider. However, the physician/investigator is still ultimately responsible and should maintain internal controls to ensure guideline compliance.

The investigator must designate a single, centralized location as custodian to receive and manage the investigational articles (that would be the shipping address).

The principal investigator, pharmacist, or other designated individual will maintain records of the product's delivery to the trial site, the inventory at the site, the use by each participant, and the return to the sponsor or alternative disposition of un used products. These records will include dates, quantities, batch/serial numbers, expiration dates (if applicable), and the unique code numbers assigned to the investigational products and trial participants. Researchers should maintain records that docu ment adequately that the participants are provided the doses specified by the protocol and reconcile all investigational products received from the sponsor.

2.16.2 IND Application

Before submitting an application to the IRB that involves an investigational new drug or biologic, the PI must secure an IND number and approval from the FDA or correspondence from the FDA waiving this requirement. In order to confirm the test article has an IND and that the IND number is valid, the IRB staff and/or reviewer will

verify the IND number on the FDA correspondence matches the IRB application and/or protocol document.

If the IRB has any question as to the need for an IND, the PI will be required to contact the FDA and provide written correspondence from the FDA regarding the need for an IND or an exemption from this requirement. This FDA number or letter waiving the requirement for an FDA number shall be included in the submission to the IRBPlease see the guidance document here for more information on IND applications, expanded access, compassionate use, or emergency use (please also see the emergency use section of the HRPP manual below).

2.16.3 IDE Application

The IDE regulations specify that there are two different types of device studies, “significant” risk (SR) and “nonsignificant" risk: (NSR). The determination is initially made by the device manufacturer and must be made based on the proposed use of a device in and investigation, not just on the device alone. The IRB must review the risk level. The IRB minutes must document the rationale for SR/NSR and subsequent approval or disapproval decisions for clinical investigations.

Before submitting an application to the IRB that involves an investigational new drug or biologic, the PI must secure an IDE number and approval from the FDA or correspondence from the FDA waiving this requirement. In order to confirm the test article has an IDE and that the IDE number is valid, the IRB staff and/or reviewer will verify the IDE number on the FDA correspondence matches the IRB application and/or protocol document.

If the IRB has any question as to the need for an IDE, the PI will be required to contact the FDA and provide written correspondence from the FDA regarding the need for an IDE or an exemption from this requirement. This FDA number or letter waiving the requirement for an FDA number shall be included in the submission to the IRB.

2.16.3.1 Humanitarian Use Device (HUD)

A HUD is a device that is intended to benefit patients in the treatment and diagnosis of diseases or conditions that affect or are manifested in less than 8,000 individuals in the United States per year. The U.S. Office of Orphan Products Development (OOPD) determines if a device meets specific requirements, including scientific rationale and population prevalence, for designation as an HUD.

The IRB recognizes humanitarian device exemption (HDE) approval by the FDA is based on safety and probable benefit of a designated Humanitarian Use Device (HUD). All uses of a HUD require IRB approval.

Please see the guidance document regarding HUD use at TTUHSChere.

2.16.3.2 Significant Risk (SR) Studies

An SR device study is defined as a study of a device that presents a potential for significant risk to the health, safety, or welfare of a subject and 1) is intended as an implant; or 2) is used in supporting or sustaining human life; or 3) is of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health; or 4) otherwise presents the potential for serious risk to the health, safety, or welfare of a subject.

Determination of SR is made by sponsor; must be reviewed by the IRB; and is governed by Investigational Device Exemption (IDE) regulations (21 CFR 812).

Both IRB **and** FDA must approve the investigation; IRB should consider information including results of prior investigations using device, proposed investigational plan, subject selection criteria, and monitoring procedures; sponsor must furnish the IRB with a risk asse ssment and the rationale for making the determination [21 CFR 812.150(b)(10)].

2.16.3.3 Nonsignificant Risk (NSR) Studies

An NSR study investigation is one that does not meet the definition of a serious risk study. Both SR and NSR studies require initial and continuing IRB approval and informed consent. Determination of NSR is made by the sponsor.

The IRB acts as an FDA surrogate because sponsors are not required to report NSR device study approvals to the FDA.

2.16.3.4 IRB Risk Determination

The IRB may agree or disagree with sponsor's NSR designation.

If IRB agrees and approves study, it may begin without submission of an IDE application to the FDA.

If IRB disagrees, the IRB will notify the sponsor who must notify the FDA that an SR determination has been made and apply for approval of an IDE application.

2.16.4 Emergency Use of Investigational Drug/Device

Emergency use is defined as the use of an investigational drug or biological product or investigational medical device for which an IND/IDE has been issued with a human subject in a life -threatening situation in which no standard acceptable treatment is available. Sometimes there is not sufficient time to obtain IRB approval [21 CFR 56 102(d)]. This is sometimes referred to as "compassionate use."

Requests to administer emergency use investigational drugs/devices will only be considered by a TTUHSC IRB if the physician responsible for the investigational drug/device is full-time faculty at TTUHSC. In limited circumstances, physicians who are credentialed through an affiliated entity may also submit a request for a single emergency use of an investigational drug/device. In these cases, the affiliated entity must first agree in writing to assume t he responsibility for ensuring that all FDA requirements found in 21 CFR 56.104 (c) are met.

The emergency use provision in the FDA regulations [21 CFR 56 104(c)] permits an exemption from prior review and approval by the IRB. The exemption, which may not be used unless all of the conditions described in 21 CFR 56 102(d) exist, allows for one emergency use of a test article without prospective IRB review. FDA regulations require that any subsequent use of the investigational product at the institution have prospective IRB review and approval. The FDA acknowledges, however, that it would be inappropriate to deny emergency treatment to a second individual if the only obstacle is that the IRB has not had sufficient time to convene a meeting to review the issue.

Some manufacturers will agree to allow the use of the test article, but their policy requires "an IRB approval letter" before the test article will be shipped. If it is not possible to convene a quorum of the IRB within the time available, some IRBs have sent to the sponsor a written statement that the IRB is aware of the proposed use and considers the use to meet the requirements of 21 CFR 56 104(c). Although this is not

an "IRB approval," the acknowledgment letter has been acceptable to manufacturers and has allowed the shipment to proceed.

Life-threatening, for the purposes of section 21 CFR 56 102(d), includes the scope of both life-threatening and severely debilitating, as defined below. Life-threatening means diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes, where the end point of clinical trial analysis is survival. The criteria for life-threatening do not require the condition to be immediately life-threatening or to immediately result in death. Rather, the patient must be in a life-threatening situation requiring intervention before review at a convened meeting of the IRB is feasible.

Severely debilitating means diseases or conditions that cause major irreversible morbidity. Examples of severely debilitating conditions include blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke.

When possible, physicians will be asked to notify the IRB in advance when a situation arises that calls for the emergency use of a test article. The notification should include the following information:

- physician's name, contact information and affiliation with TTUHSC
- the patient's initials and diagnosis
- name of the test article to be used
- date the test article was (will be) administered
- a complete description of the patient's condition and an explanation of why the emergency use of the test article is (was) required; that is,
    a. the patient is (was) in a life-threatening situation;
    b. there is (was) no standard acceptable treatment available;
    c. there is (was) not sufficient time to obtain IRB approval
- a description of the anticipated consent process including the method of documentation.

This notification will be reviewed by the IRB chairperson or designee and a written response will be provided to the physician. The IRB response should not be construed as an IRB approval. The date of the IRB response letter will initiate the tracking date to verify that the physician files a report within the 5-day timeframe required by 21 CFR 56 104(c).

This physician summary report must be submitted within five days of the emergency use. The summary report should include the following:

- Physician's name
- Patient's Initials, Age and Diagnosis
- Name of Drug/Biologic/Device
- Date the test article was administered/utilized
- Brief description of the results of the emergency use, including patient outcome, if known, any serious adverse events or unanticipated problems

Templates for the notification and response letters can be obtained from the local IRB office.

DHHS and the FDA prohibit the data obtained from emergency use situation to be classified as research or the recipient to be classified as a research participant. Therefore, the physician should evaluate the likelihood of needing to use the test article

again. If additional use is ever anticipated, future use of this drug/device is deemed to be human research and required to comply with all human research requirements.

Any physician who fails to notify the IRB of the emergency use within five days will be required to notify both the sponsor and the FDA of their failure to follow the FDA regulations found in 21 CFR 56 104(c). The TTUHSC IRB should receive a copy of the report to the FDA and sponsor as well as any follow -up information received. Please see the guidance document here for additional resources and information.

2.16.5 Planned Emergency Research

TTUHSC does not intend to conduct planned emergency research. However, in very limited circumstances, the TTUHSC IRBs will consider approval of "planned emergency research" as described in 21 CFR 50.24. The federal requirements for conduct and IRB approval of this type of research are varied and complex. Investigators considering conducting planned emergency research should carefully review the federal requirements and plan to meet with TTUHSC HRPP re presentatives prior to protocol development or receiving a protocol from an external sponsor.

2.17 Human Biological Specimens

All prospective collection of human specimens for research requires prior written IRB approval and informed consent from the subject unless consent is waived by the IRB as described elsewhere in this document.

The secondary use of existing human specimens for research purposes can be permitted under certain circumstances. Some types of secondary use require IRB review and may require informed consent from subjects.

2.17.1 Prospective Collection and Use of Human Specimens for Research Purposes

IRB review is required for the prospective collection and research use of human specimens obtained explicitly for research purposes. Examples include extra blood taken for a research project at the time of a clinical blood draw, or additional biopsies performed for research purposes during a clinically indicated procedure. IRB review is required even if the work is being done off campus, for example, if an investigator travels to a remote site to collect the specimens. The IRB will typically require written consent/ authorization of each research participant.

Use of EXISTING Human Specimens for Research Purposes

2.17.1.1 De-identified Commercially-Available Human Cells or Cell Lines

IRB review is **not** required for laboratory research on human cells obtained from commercial or governmental entities because the release of these samples to investigators does not meet the regulatory definition of *human subjects research*. When human cells are obtained from one of these repositories, investigators are reminded to review the contract or purchase agreement carefully to ensure that the planned use of the specimens will be in accordance with the vendor's or supplier's terms a nd conditions. Exception: permission is required for use of human embryonic stem cells, regardless of source.

2.17.1.2 Fee-for-service Analyses of Human Cells or Cell Lines

TTUHSC IRB review is **not** required for activities limited to the performance of analyses on human specimens as a commercial or genuinely non -collaborative service. For example, appropriately qualified laboratory staff may perform analyses of blood samples for investigators outsid e of TTUHSC solely on a commercial (non-collaborative) basis.

2.17.1.3 Identifiable Commercially Available Human Cells or Cell Lines

IRB review and approval **are required** for laboratory research on identifiable human specimens obtained from commercial or governmental entities. Depending on the nature of the research, these types of projects may be classified as exempt from formal IRB review but the IRB, not the investigat or, will make this determination.

2.17.1.4 Identifiable Human Cells or Cell Lines Obtained from Collaborators Outside of TTUHSC

IRB review **is required** for research involving identifiable human specimens obtained from collaborators outside of TTUHSC. Depending on the nature of the research, these types of projects may be classified as exempt from formal IRB review but the IRB, not the investigator, will make this determination.

2.17.1.5 Secondary Use of Identifiable Previously -Collected Excess (i.e. otherwise discardable) Clinical Specimens from Within TTUHSC or Its Affiliates

IRB review **is required** for any proposed research use of excess clinical specimens obtained from Pathology or from related services within TTUHSC and its affiliates. Examples include specimens collected for diagnostic purposes or during surgery in the clinical laboratories (inc luding pathology) or in clinical care areas, such as the operating suites.

2.17.1.6 De-identified C ommercially-Available Human Cells or Cell Lines

IRB review is **not** required for laboratory research on human cells obtained from commercial or governmental entities because the release of these samples to investigators does not meet the regulatory definition of *human subjects research*. When human cells are obtained from one of these repositories, investigators are reminded to review the contract or purchase agreement carefully to ensure that the planned use of the specimens will be in accordance with the vendor's or supplier's terms a nd conditions. Exception: permission is required for use of human embryonic stem cells, regardless of source.

2.17.1.7 Fee-for-service Analyses of Human Cells or Cell Lines

TTUHSC IRB review is **not** required for activities limited to the performance of analyses on human specimens as a commercial or genuinely non -collaborative service. For example, appropriately qualified laboratory staff may perform analyses of blood samples for investigators outsid e of TTUHSC solely on a commercial (non-collaborative) basis.

2.17.1.8 Identifiable Commercially Available Human Cells or Cell Lines

IRB review and approval **are required** for laboratory research on identifiable human specimens obtained from commercial or governmental entities. Depending on the nature of the research, these types of projects may be classified as exempt from formal IRB review but the IRB, not the investigator, will make this determination.

2.17.1.9 Identifiable Human Cells or Cell Lines Obtained from Collaborators Outside of TTUHSC

IRB review **is required** for research involving identifiable human specimens obtained from collaborators outside of TTUHSC. Depending on the nature of the research, these types of projects may be classified as exempt from formal IRB review but the IRB, not the investigator, will make this determination.

2.17.1.10 Secondary Use of Identifiable Previously-Collected Excess (i.e. otherwise discardable) Clinical Specimens from Within TTUHSC or Its Affiliates

IRB review **is required** for any proposed research use of excess clinical specimens obtained from Pathology or from related services within TTUHSC and its affiliates. Examples include specimens collected for diagnostic purposes or during surgery in the clinical laboratories (including pathology) or in clinical care areas, such as the operating suites.

2.17.2 Special Categories of Biological Specimens

2.17.2.1 Human Embryonic Stem Cells (hESC)

Research use of hESC tissue requires TTUHSC Embryonic Stem Cell Research Oversight Committee (ESCRO) approval.

Additional review is not required by the IRB unless the research involves introduction of the hESC or their derivatives into patients or the possibility that the identity of the donors of the blastocysts, gametes, or somatic cells is readily ascertainable or might become known to the investigator.

TTUHSC will comply with the most current version of NIH Guidelines and state law relating to hESC research.

2.17.2.2 Fetal Tissue Specimens

IRB review is required for research on fetal tissue. Note: federal law prohibits the sale of fetal tissue for profit.

2.17.2.3 Whole Genome Sequencing

If the research might include whole genome sequencing (i.e.: sequencing of a germ line or somatic specimen with the intent to generate the genome or exome sequence of that specimen) a statement to this effect must be included in the informed consent document.

2.17.2.4 Transfer of Samples to Research Collaborators Outside of TTUHSC

The IRB must review any plan to transfer human specimens that were collected for research purposes (generally as part of a TTUHSC IRB-approve tissue repository) to outside collaborators for research. In addition, a Materials Transfer

Agreement (MTA) may be required with the recipient entity. For more information, please contact the TTUHSC Office of Sponsored Programs. Note**:** The transfer of **non-identifiable** human specimens from an IRB -approved TTUHSC Tissue Repository to another investigator, if approved by the IRB as one of the procedures of the tissue bank, does NOT require separate IRB review and approval. This is because the IRB already will have reviewe d and approved the procedures of the Tissue Repository, which describe such transfers.

2.18 Genetic Research

Genetic information must be carefully maintained in order to protect against stigmatization, discrimination, or significant psychological harm to the subject. In general, genetic research is defined as an analysis of human DNA, RNA, chromosomes, proteins, or metabolites that detect genotypes, mutations, or chromos omal changes. Routine tests that do not detect genotypes, mutations, or chromosomal changes, such as complete blood counts, cholesterol tests, and liver enzyme tests, are not typically considered genetic tests. Also, genetic tests do not include analyses o f proteins or metabolites that are directly related to a manifested disease, disorder, or pathological condition that could reasonably be detected by a health care professional with appropriate training and expertise in the field of medicine involved.

When reviewing genetic research, the IRB will consider the following issues in both the application and the informed consent document, as applicable:

- Information that can be obtained from DNA samples in general, and the specific questions to be addressed in this study.
- The extent of subject and sample confidentiality if the sample and subsequent information will be part of a registry or database (see information on GINA, below).
- The rights and limitations of subjects to request destruction or removal of their sample and/or associated data at a future date. The rights and limitations of subjects to request that their sample and or associated data be stripped of any identifying information.
- Identifying information available to other researchers if their sample and/or associated data are part of a registry or database.
- Mechanisms for maintaining confidentiality in long -term studies, registries, or databases.
- Potential for commercial profit by the entity, PI or sponsor from information gathered in this study.
- A clear statement of financial benefit to subject in tissue bank consent documents using IRB approved financial benefit language.
- The availability or access to genetic counseling in cases where a study may reveal genetically important information (i.e. possessing genetic defects which could be passed on).
- A clear statement that the sample/data, any cell lines, profits from data etc., are the property of TTUHSC or the entity sponsoring the research.
- If genetic information will be disclosed to the subject or another party, the PI disclosing the information must be named and the specific genetic information being disclosed must be stated.
- Information disclosed must be in a manner consistent with the recipient's level of knowledge, e.g., information would be phrased differently when disclosed to a lay person versus a physician.
- Subjects must have the right to decline receiving genetic information.

In the absence of a specific authorization to maintain a DNA sample, DNA samples collected and stored or analyzed in connection with a research project shall be destroyed upon completion of the project or withdrawal of the individual from the project. Thi s information must be clearly stated in the informed consent document.

2.18.1 Minors

For genetic research involving minors, the informed consent document must give parents/guardians the option of whether or not they want the results (if available) of the genetic analysis disclosed to them. Whenever appropriate, the minor's assent shall be solicited. When minors reach maturity, they shall be re -consented if identifiers are taken.

2.18.2 Genetic Relationships

In some cases, it may be possible to determine that some members of the family are not genetic relatives. Issues of genetic relationships (paternity or maternity, as could be hidden by adoption or donor fertilization) and other incidental information shall not be revealed to the subject.

2.18.3 Genetic Information Nondiscrimination Act (GINA)

The following information should be included in TTUHSC informed consent documents when genetic testing is part of the research protocol.

A Federal law, called the Genetic Information Nondiscrimination Act (GINA) generally makes it illegal for health insurance companies, group health plans and most employers to discriminate against a research subject based on genetic information. This law generally will protect research subjects by prohibiting health insurance companies and group health insurance plans from requesting genetic information that is collected in a research study. Health insurance companies and group health plans are also prohibited from using genetic information when making decisions regarding eligibility or premiums. Employers with 15 or more employees may not use genetic information obtained from research when making a decision to hire, promote or fire an employee or in setting conditions of employment.

All health insurance companies and group health plans must follow this law by May 21, 2010. All employers with 15 or more employees must follow this law as of November 21, 2009.

This Federal law does not protect against genetic discrimination by companies that sell life, disability, or long-term care insurance.

More information about the impact of GINA on research can be found in the OHRP Guidance document.

2.19 Research Compliance

The TTUHSC Institutional Review Boards are authorized to monitor research involving human subjects approved by the IRB pursuant to the responsibilities and assurances made by TTUHSC under federal regulations (FWA 00006767) and TTUHSC Policy (TTUHSC OP 73.06 Research Involving Human Subjects and TTUHSC OP 73.14 Research Compliance). The Research Integrity Office shall be responsible for compliance activities on behalf of the IRB and SVPR, including audits and monitoring of IRB approved research.

The IRB has the authority to inspect research facilities, obtain records and other relevant information relating to the use of human subjects in research. The IRB takes such actions

that are in its judgment necessary to enforce compliance with applicable federal and state law, regulations, or guidelines, including action to suspend/terminate approval of research that is not being conducted in accordance with IRB requirements or that has been associated with unexpected serious harm to subjects.

2.19.1 Definitions

2.19.1.1 Non-compliance

A situation, event or process in research involving human subjects that is inconsistent with:

- the ethical principles of human subjects research as described in the Belmont Report, or
- Federal, state, and/or local regulations applying to human subjects research under the jurisdiction of the TTUHSC IRB, or
- TTUHSC policies and procedures governing human subjects research, or
- the research activities as approved by the TTUHSC IRBs.

Note: Data collected by activities determined to be in "non-compliance" cannot be described in publications or presentations as having been obtained with IRB approval.

2.19.1.2 Minor Non-compliance

Non-compliance that is neither serious nor continuing.

2.19.1.3 Serious Non-compliance

Non-compliance which could significantly:

- Increase risks to, and/or
- jeopardize the safety, welfare, or rights of subjects or others, and/or
- decrease potential benefits (the scientific integrity of the research)

Note: Conducting a research study without prospective IRB approval is always considered serious non-compliance.

2.19.1.4 Continuing Non-compliance

A pattern of repeated non-compliance which continues:

- after initial discovery and
- after IRB approval of corrective action plan and
- suggests that non-compliance will continue if there is no intervention, or
- increases the risk of serious non-compliance, or
- if continued, could significantly increase risks to, or jeopardize the safety, welfare, and/or rights of subjects or others, or
- if continued, could decrease potential benefits (the scientfic integrity of the research)

2.19.2 Reporting Non-compliance

The Research Integrity Office encourages the reporting of non-compliance by the principal investigator, members of the research staff, research participants or others. Reports of non-compliance can include but are not limited to, protocol deviations, unanticipated events involving risks to subjects or others, complaints from participants or others regarding treatment by research staff, reimbursement issues, issues of data integrity, or any other compliance concerns. When a report of non-compliance is made by someone other than the principal investigator, effort will be taken to maintain

confidentiality. The name of the reporter will not be disclosed to the individuals involved in the complaint, unless disclosure is required to reconcile the situation. If a translator is necessary for participants to state the allegation(s), arrangements for a translator will be made.

The research compliance officer in the Research Integrity Office may receive an allegation of non-compliance by any means including, but not limited to:

- voluntary notification by the principal investigator or research staff, through Cayuse or direct communication with the research compliance officer or research integrity office staff
- information given by other staff of the institution,
- information given by other members of the research staff,
- monitoring reports provided by the study sponsor,
- anonymous reports to EthicsPoint as stated in each consent document

As indicated in TTUHSC OP 52.04, Report & TTUHSC Internal Investigation of Alleged Violations, Non-Retaliation, employees and TTUHSC affiliates have a duty to promptly report known or suspected violations to minimize risk to TTUHSC and its operations. This duty extends to known or suspected non-compliance related to the HRPP. The TTUHSC HRPP defines prompt reporting of suspected violations to be no more than 30 days after the recognition of a reportable event.

Initial assessment of the validity of an allegation will be made by the research compliance officer in consultation with the Assistant Vice President - Research Integrity, the IRB chairperson, and/or the IRB administrator. This initial assessment will generally be conducted within one business day. The initial assessment depends on the nature of the allegation and may include, but is not limited to, a review of the approved consent document, speaking with study staff, or a review of financial records associated the study fund.

If the initial assessment indicates that the allegation has no basis in fact or cannot be adequately investigated given the information received, the research compliance officer will create a personal “Note to File” and no further action will be taken.
If the allegation does have a basis in fact, and a suitable corrective action has not already been implemented by the principal investigator, a “for cause” regulatory compliance audit may be initiated by the research compliance officer as described below.

2.19.3 Regulatory Compliance Audits

The research compliance officer conducts regulatory compliance audits on research approved by the TTUHSC IRB. These audits are conducted based upon allegations reported to the Research Integrity Office or on a routine basis. The process of this audit is the same for both “for-cause” audits and those audits selected on a routine basis.

The trials that are audited on a routine basis are selected based on the following but are not limited to these criteria:

- new investigators to the institution
- new coordinators to the institution
- research in departments which have had previous compliance concerns
- research conducted by investigators with previous compliance concerns
- research involving new sponsors to the institution
- research new to the institution

Trials audited on a for-cause basis are done so based upon the receipt of an allegation or a request from the IRB to review the research.

The following is a non-exhaustive list of documents and activities that may be reviewed as part of a regulatory compliance audit:

- regulatory file for required elements including the presence of required documentation, protocol and amendments
- study personnel training
- approved consent forms and IRB documentation
- subject eligibility
- informed consent documentation
- unanticipated and serious adverse event reporting
- accuracy and completeness of data collection sheets
- confidentiality of records
- drug and device handling and accountability
- laboratory data
- study progress reports
- contacting of research subjects
- study advertisements and recruiting information
- any additional information determined necessary by the research compliance officer.

The principal investigator is generally notified of the audit at least a week in advance. An audit report is generated from each audit investigation and is submitted to the principal investigator, the Executive Vice President for Research and Innovation - Research Integrity, the IRB chairperson, and the IRB administrator. If applicable, the audit report can include a list of findings as well as recommendations to the IRB regarding the findings and the nature (minor or serious/continuing or non-continuing) of the non-compliance.

The audit report recommendations will include possible corrective actions that the principal investigator, study staff, and/or the IRB might take to correct any problems reported in the findings. Possible corrective actions recommended may include, but are not limited to:

- request for more information before a final decision can be made;
- protocol or informed consent document changes;
- changes to, or outside monitoring of the informed consent process;
- suspension or termination of IRB approval of the study;
- more frequent review by the IRB;
- follow-up audits to be conducted on a regular basis for a specified period of time;
- additional training or certification of the PI and the research staff;
- disqualification of the PI or members of the research staff from conducting research at TTUHSC;
- disallowance of research use of data collected;
- notification of current and/or past research participants regarding study problems;
- re-consent of current study participants;
- notification of other TTUHSC committees or administrators; or
- notification of outside entities (DHHS, FDA, study sponsor) of the compliance issues.

2.19.4 IRB Review of Audit reports

Audit reports will be generated for each audit investigation and will be distributed to the principal investigator, the SVPR, the Assistant Vice President - Research Integrity, the IRB chairperson and the IRB administrator. For routine audits, the IRB chairperson or designee will conduct an initial review of the audit report. If both the research compliance officer and IRB chairperson/designee agree that the audit report contains no findings related to serious or continuing non-compliance, the audit report can be accepted as written on behalf of the IRB. A copy of the audit report may be placed on the next agenda for IRB members to review for informational purposes.

The research compliance officer will work with the principal investigator, if requested, to implement any recommendations that were included in the audit report. Failure by the principal investigator to communicate with the research compliance officer regarding implementation of recommendations may lead to a "for cause" audit or could be reported to the IRB as continuing non-compliance.

All audit reports that result from "for cause" audits, regardless of the findings, and any audit reports that either the research compliance officer or the IRB chairperson/designee (or both) determine to include findings of serious or continuing non-compliance will be placed on the next IRB agenda for review at a convened meeting of the IRB. Audit reports will be available for review by all IRB members. At the convened IRB meeting, the audit report, findings, and recommendations will be reviewed. The Board will make a final determination as to whether the findings meet the definition of serious and/or continuing non-compliance. The Board will either accept the recommendations of the research compliance officer or may require different or additional aspects of the corrective action plan.

Following the IRB's review of the audit report and any additional determinations that they have made, the principal investigator will be notified (via Cayuse) of the outcome of the review. If the IRB offers a plan of correction, the specific changes to be implemented will be communicated, as well as a time frame for implementing the changes. If the IRB has determined that the project is to be suspended or terminated, this information will be communicated to the principal investigator as well. See information regarding Study Suspension and Study Termination.

The SVPR and Assistant Vice President - Research Integrity will be notified of any IRB determinations of serious or continuing non-compliance and any decision to suspend or terminate a research project. The SVPR will be responsible for notifying DHHS and/or the FDA (if necessary) or any other oversight or sponsoring agency. The Department Chairperson of the principal investigator will also be notified of these decisions by the IRB.

3 RESEARCHER AND RESEARCH STAFF INFORMATION

3.1 Introduction

The purpose of this chapter is to provide guidance to research investigators and personnel on the protection of human research participants in accordance with applicable laws, regulations and Texas Tech University Health Sciences Center (TTUHSC) policies and procedures.

All research involving human subjects conducted at or in affiliation with TTUHSC must be reviewed and approved by a TTUHSC Institutional Review Board (IRB) prior to beginning the study.

The Research Integrity Office (RIO) provides administrative support to the TTUHSC IRBs, provides education regarding the protection of human research participants, and monitors human research approved by the IRB through routine and for-cause audits.

In addition to the information found in this Manual, investigators and research staff or those who wish to learn more about the TTUHSC Human Research Protection Program can find more information at the TTUHSC Human Research Protection Program website. Contact information for IRB administrators, current IRB rosters, IRB deadlines and meeting dates, as well as links to other helpful information can be found at the site. Questions or suggestions about the TTUHSC HRPP can be sent through the SuggestionBox on the site or by sending an email to ttuhscresearch@ttuhsc.edu.

3.2 Ethical Principles

The IRBs are guided by ethical principles applicable to all research involving human subjects as set forth in the report of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research known as the Belmont Report. The ethical principles are:

- Respect for Persons: Recognition of the personal dignity and autonomy of individuals and special protection of those persons with diminished autonomy
- Beneficence: Obligation to protect persons from harm by maximizing anticipated benefits and minimizing possible risks of harm
- Justice: Fairness in the distribution of research benefits and burdens.

3.3 Federal Regulations

Applicable federal regulations include, but are not limited to:

- 45 CFR 46, generally known as the Common Rule, and subparts B, C, and D
- 21 CFR 50, Human Subject Protection (Informed Consent)
- 21 CFR 56, Institutional Review Boards,
- 21 CFR 312, Investigational New Drug Application,
- 21 CFR 812, Investigational Device Exemptions.

3.4 Prerequisites for all personnel involved in human research

All Principal Investigators, all Co-Investigators, and all research staff are required to receive training regarding the protection of human subjects research and financial conflict of interests ***prior to*** beginning any human research-related activities. This training will be verified ***prior to*** Cayuse access being granted (if a new Cayuse account is needing to be set up). Initial

approval of IRB submissions will be withheld until all study personnel have been verified as having current completed training and financial disclosure reports. Detailed instructions for completing all required training can be found on the IRB Education and Training webpage.

3.4.1 Human Subject Protection Training (CITI)

Each person conducting or assisting in the conduct of a research project that involves human participants is first required to complete training on ethical and regulatory issues. The web-based course currently required by TTUHSC is the CITI Biomedical Investigator Training Course (or any version of this training from the Human Subjects Research series-Biomedical in CITI, completed at any institution).

FOR CRAs and PIs : In special circumstances, Clinical Research Coordinators and Principal Investigators may be permitted to substitute pre-approved CITI courses and/or recognized certifications in place of the CITI Biomedical Investigator Course. The IRB Staff may be contacted for more information.

Renewal: All investigators and research staff are required to renew their Biomedical Investigator Training every 3 years (or the approved certificate or CITI course). Lapsed training will be reported as a finding requiring correction on any routine or for-cause audits conducted in accordance with Section 2.19 of this Manual.

3.4.2 Conflict of Interest Training/Financial Disclosure (COIC)

All TTUHSC investigators and study personnel are bound to the policies set forth in TTUHSC OP 52.06 Standards of Conduct and Ethics, TTUHSC OP 10.05 Conflicts of Interest and Commitment and TTUHSC OP 73.09 Financial Conflicts of Interest in Research.

In accordance with the TTUHSC Conflict of Interest in Research Policy, all research personnel are required to disclose any financial conflicts of interest as outlined in the policy. These disclosures are to be made at least annually and are to be updated within thirty (30) days of a change in significant financial interests. Lapsed COIC training/disclosures will be reported as a finding requiring correction on any routine or for-cause audits conducted in accordance with Section 2.19 of this manual.

3.4.3 Cayuse Access

All submissions to a TTUHSC IRB must be submitted using the web-based Cayuse software system (Human Ethics module). TTUHSC employees and residents have already been given Cayuse accounts, and new employees will be automatically set up with a Cayuse account (through HRConnect). Users without an eRaider (i.e. Outside Collaborators) will need to request a Cayuse account. Prior to approval of a Cayuse account, the user must have completed the CITI and COIC requirements . Cayuse account requests can be submitted through the online request form OR by contacting an IRB Staff member.

3.5 Individual Conflicts of Interest

In order to minimize the actual or potential conflicts of interest in Human Research, the IRB requires that all individuals involved in the design, conduct, or reporting of the research disclose financial interests related to the research. Of note, in addition to the PI and coinvestigators, individuals involved in the design, conduct, or reporting of the research may include study coordinators, research nurses, data coordinators, and other support staff . Unaffiliated investigators may also be bound to these policies if their own institutions do not

have internal conflict of interest policies. Failure of any PIs and their research personnel to comply with these policies may result in suspension of submission privileges.

If a project is submitted for IRB review and it is determined that a financial conflict of interest exists, the issue must be referred to the Conflict of Interest in Research Committee (COIRC) established by TTUHSC OP 73.09 Financial Conflicts of Interest in Research. The IRB will not continue the review of the submission until the COIRC has met and made its recommendations and these recommendations have been adequately addressed by the investigator. Affiliated entities should submit documentation to the IRB specifying the identified conflict of interest and how it will be managed.

A financial conflict of interest in research is any financial interest related to the research. This can refer to, but is not limited to, any of the following interests in the sponsor, product or service being tested, or competitor of the sponsor held by the individual or the individual's immediate family (spouse, unmarried domestic partner, dependent children):

- Ownership interest of any value including but not limited to stocks and options.
- Compensation of any amount including, but not limited to honoraria, consultant fees, royalties, or other income (TTUHSC salary paid by a sponsor is excluded).
- Proprietary interest of any value including, but not limited to, patents, trademarks, copyrights, and licensing agreements.
- Board or executive relationship, regardless of compensation.
- Reimbursed or sponsored travel by an entity other than a federal, state, or local government agency, higher education institution or affiliated research institute, academic teaching hospital, or medical center.

With regards to intellectual property, patents, technology development, proprietary ownership, commercial or manufactured products, etc., the IRB recommends disclosure of intent to commercialize or license intellectual property, as it relates to the research, in the consent documents. This disclosure should include plans for any development, licensure, commercialization, and/or patentability of any intellectual property, technology, commercial or manufactured products, etc., and indicate how participant identifiers are used in this process, if at all. The disclosure should include a statement about if/when the PI would profit or benefit financially and indicate what additional compensation will be awarded to participants, if any, if/when the intellectual property results in commercialization.

Non-financial conflicts of interest (conflicts of commitment, nepotism, etc.) may also interfere with objective conduct of research activities. Such conflicts will be addressed as indicated in TTUHSC OP 10.05 Conflicts of Interest and Commitment and TTU System Regents' Rules, Chapter 10.

3.6 Who can be a TTUHSC Principal Investigator?

Faculty status is required for all principal investigators. Exceptions may be granted on a case-by-case basis by the Assistant Vice President for Research Integrity, or designee. TTUHSC PI must meet requirements of, TTUHSC OP 73.08 Requirements for Principal Investigator Status, exceptions may be granted on a case-by-case basis by the Assistant Vice President for Research Integrity, or designee.

3.7 Who can be a Principal Investigator from an affiliated entity?

Employees of entities affiliated with TTUHSC may be designated as Principal Investigator in a research study if **all** of the following conditions are met:

- Affiliated entity has a Federal Wide Assurance (FWA) approved by DHHS;
- Affiliated entity has a current IRB Agreement/Memorandum of Understanding with TTUHSC;
- Affiliated entity has existing policies regarding the institutions protection of human research participants;
- Affiliated entity has a named human research protection administrator;
- PI submits application and protocol in accordance with federal regulations and TTUHSC policy with signature of authorized official from the affiliated entity. The signature of the authorized authority from the affiliate entity signifies that the affiliated entity (1) approves of the research; (2) has sufficient resources to conduct the research and (3) agrees that the PI has the appropriate education and experience to conduct the research.
- The PI Agrees to comply with the compliance requirements of TTUHSC;
- Affiliated entity agrees to pay IRB fees upon receipt of invoice per the IRB agreement/Memorandum of Understanding with TTUHSC.

Collaborators from institutions that are not affiliated with TTUHSC may not be Principal Investigators on TTUHSC IRB applications and, if listed as participants in the study project, must comply with all TTUHSC policies and procedures.

3.8 Principal Investigator Responsibility for Research Activities

The Principal Investigator retains ultimate responsibility for the conduct of **all** research activities as specified in the IRB -approved protocol and for submission of all required documents including the application, protocol, forms, responses to stipulations, revisions, reports, and any other documentation, including those made by auth orized research personnel in accordance with TTUHSC IRB Policies and Procedures. Ensuring that prompt and proper payment of participants in accordance with information in the signed informed consent document is also the responsibility of the principal investigator. While duties related to the conduct of the research may be delegated to other members of the research team, the authority for and conduct of research remain with the principal investigator.

3.8.1 Notice of Absence

Principal investigators shall notify the IRB in writing as soon as possible prior to any employment change, extended absence, or faculty development leave during which the PI will be engaged in research. (SeeTTUHSC OP 60.02 Faculty Development Leaves of Absence) PI shall submit information and/or an amendment to the IRB designating an investigator responsible for any active research study during PI's absence. Notice and/or amendments shall be made in accordance with local IRB submission requirements.

3.9 Preparing the IRB Submission

The TTUHSC IRBs use the web-based Cayuse software program (Human Ethics module) to review and track research study information. Principal Investigators and research personnel **must use** this software to submit study-related information to the IRB. TTUHSC employees and residents have already been given Cayuse accounts, and new employees will be automatically set up with a Cayuse account (through HRConnect). Users without an eRaider (i.e. Outside Collaborators) will need to request a Cayuse account. Prior to approval of a Cayuse account, the user must have completed the CITI and COIC requirements . Cayuse account requests can be submitted through the online request form OR by contacting an

IRB Staff member. Once your Cayuse account/access is granted, you will return to the Cayuse website and login using your user ID and password.

Delays in the approval of initial applications include the absence of adequate detail for the IRB to evaluate the study's purpose and/or procedures. Investigators are required to provide specific information on how potential subjects are initially identified, the entire consent process and detailed list of all research procedures clearly delineating standard of care from research. There is no such thing as too much detail when describing study procedures! The more complete the initial description, the less likely that time will be spent with correspondence back and forth between the principal investigator and the IRB. Staff in the IRB office is available to respond to questions by email or phone.

Studies for which no scientific review outside of the Signatory Authority's signature has taken place will receive a scientific review by IRB as part of the initial review process. The scientific review will address the following issues:

- Has a literature search supporting study rationale been conducted?
- Will testing the hypothesis provide important knowledge for the field?
- Are the hypotheses/specific goals and aims clearly stated?
- Are the outcomes clearly stated and defined?
- Is the study design appropriate?
- Will the proposed tests/measurements address the hypotheses?
- Are all of the proposed tests/measures required/related to at least one proposed outcome?
- Are the validity/reliability of measures established?
- Are the proposed statistical methods clearly stated/correlate with study design?
- Is the proposed sample size adequately justified?
- Is the Principal Investigator appropriately qualified, knowledgeable and experienced to perform the procedures?

The following should be submitted to the IRB during the initial review process:

- Complete IRB application form;
- Full protocol;
- Investigational New Drug (IND) or Investigational Device Exemption (IDE) number (if applicable)
- Investigator's Brochure (if the study involves an investigational drug or device);
- Proposed informed consent document using TTUHSC IRB-approved format (required for all non-exempt studies);
- Authorization to Use and Disclose PHI for Research (HIPAA authorization) and/or HIPAA waiver request;
- Copies of letters of assurance or cooperation with research sites (as applicable);
- Data collection forms;
- Recruitment materials (if any will be used);
- Surveys, questionnaires, or videotapes (if any will be used);
- Documentation of approval by other TTUHSC institutional committees as applicable;
- Curriculum Vitae of Principal Investigator.

Materials for initial review shall be submitted by the established deadlines (see the IRB website for current deadlines at https://www.ttuhsc.edu/research/divisions/integrity-office/review-board/default.aspx.

3.9.1 Relation to Other Committees

The TTUHSC IRB functions independently of, but in coordination with other TTUHSC research compliance committees, including but not limited to:

- **Conflict of Interest Research Committee** (COIRC)
- **Institutional Biosafety Committee** (IBC)
- **Radiation Safety Committee** (RSC)
- **Quality Improvement Review Board** (QIRB)
- **Embryonic Stem Cell Research Oversight Committee** (ESCRO)

The IRB may request that approval from any of these, or additional, committees be obtained prior to TTUHSC IRB approval IRB. For detailed information refer to TTUHSC OP 73.14 Research Compliance.

3.10 IRB Fee Policy for Commercially Sponsored Research

All commercially sponsored applications submitted to the IRB for initial review will be assessed a fee for new applications and continuing review applications requiring full board review. The IRB fee and payment schedule shall be determined by the RIO and established during contract negotiations with sponsors and in IRB Agreements with affiliated entities.

Currently, the fee for commercially sponsored initial reviews is $ 3,000.
Currently, the fee for commercially sponsored continuing reviews is $ 1,000.
Currently, there is no fee for reviews of amendments to the protocol or unanticipated events.

If an application is received and is not designated as having a commercial sponsor but is later determined by the IRB to have a commercial sponsor, an invoice will be sent to the sponsor or affiliated entity. The invoice shall contain a request for billing information and will clearly show a description of the charge and the amount being assessed.

IRB applications supported by State, Federal, non-profit foundation, or internal funds are generally excluded from this charge.

3.10.1 Waiver of IRB Fees

There may be extenuating circumstances where charging IRB fees would be unwarranted. PIs may send a written letter requesting waiver of IRB fees to the Assistant Vice President – Research Integrity, who has discretion and makes the final decision to waive fees.

3.10.2 Indirect cost Rate for Industry Sponsored Clinical Trials

For corporate and industry sponsored clinical trials with an effective or start date prior to June 1, 2017, the TTUHSC's minimum June 1, 2017, the minimum rate is 25% of total direct costs. For new clinical trials after June 1, 2017, the minimum rate is 12% of total direct costs. This rate is applied to total per patient/subject amount of the budget; this includes subject stipends. When funds are expended for clinical trial procedures, salaries, service, etc., the indirect rate is applied to each transaction. IRB fees are not subject to the indirect rate; no other budgeted item is excluded from the application of indirect.

Because reductions in the recovery of indirect costs require the campus to use other funding sources for research infrastructure expenses, a limited number of requests to

reduce or waive overhead recovery may be approved. The TTUHSC Executive Vice President for Research and Innovation retains authority to approve exceptions to the indirect rate with approval from the relevant Department Chair.

3.11 Compensation for Research Related Injury

Federal regulations [45 CFR 46 .116(b)(6); 21 CFR 50 .25(a)(6)] require that potential participants in studies considered to be greater than minimal risk be informed as to whether compensation or medical care for research-related injuries is available, and, if it is available, the nature of the compensation or care. While TTUHSC does not maintain a specific fund for compensating participants in cases of research-related injury, the institution requires that private sponsors (generally, pharmaceutical companies) who enter into a contract with TTUHSC to conduct greater than minimal risk research make provisions for the coverage of all costs of necessary treatment for any injury, illness,serious adverse event or complication that arises from medications, devices, interventions, procedures, or tests that a subject would not have been exposed to had he or she not volunteered to participate in a research study. Details of the TTUHSC requirements can be found in TTUHSC OP 73.17, Research Related Injury in Privately Sponsored Research Studies.

3.12 Clinical Trial Registration

The sponsor of any clinical trial must register the study on a publicly accessible trial registration site prior to enrolling the first subject. ClinicalTrials.gov is a directory of federally and privately supported research trials designed to test the effect of experimental drugs, devices and procedures for many diseases and conditions. The FDA mandates the registration of clinical trials on the website prior to en rollment of the first participant. Other entities, including NIH, have similar requirements for registration of applicable clinical trials. If an IRB-approved study is a clinical trial which has not been registered by the study sponsor, it may be the Prin cipal Investigator's responsibility to register the trial. The Protocol Registration and Results System website provides specific information regarding how to register a new trial. The Research Compliance Officer serves as the TTUHSC administrator for registration at ClinicalTrials.gov and should be contacted for account set-up.

In addition, FDA regulations (21 CFR 50 .25c) requires the following statement in informed consent documents for all applicable clinical trials overseen by the agency: "*A description of this clinical trial will be available on http://www.ClinicalTrials.gov as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time*". The statement is included in the TTUHSC biomedical informed consent template.

3.13 Informed Consent

Except in the limited circumstances, no investigator may involve a human being as a subject in research covered by these policies unless the investigator has obtained the legally effective informed consent of the subject or the subject's authorized represe ntative. Authorized study personnel shall seek such consent only under circumstances that provide the prospective subject or the representativesufficient opportunity to consider whether or not to participate and to minimize the possibility of coercion or undue influence. Information regarding the study shall be provided to the subject or representative in language that is understandable to the subject or representative. The process of obtaining informed consent may never include language through which the subject or repres entative is made to or appears to waive any of his/her legal rights or releases or appears to release the investigator, the sponsor of the study, TTUHSC or its agents from liability for negligence. Investigators

should strive to write consent documents in language that would be understandable to a reader with a 7th grade education.

All TTUHSC research studies shall utilize one of the TTUHSC Informed Consent templates found in Cayuse. These templates include all of the necessary elements of a consent document outlined in 45 CFR 46.116 and 21 CFR 50.25. A copy of the consent shall be given to the person signing the form. The Principal Investigator shall maintain all original consent documents. Original paper documents, once scanned into the electronic health record, become the source document. After scanning into the electronic medical record, the paper document may be destroyed.

3.13.1 Written Consent Form Signed by Subject or Representative

The PI or designee must provide the opportunity to discuss the informed consent with the subject, reviewing all of the elements, preferably during a face-to-face presentation to the subject or the subject's representative. The PI shall allow the subject or the representative adequate opportunity to read, review and consider the consent document before it is signed. A signed and dated copy of the document shall be given to the person signing the form , unless the investigator has requested and received approval from the IRB to waive this requirement. The requirement that the consent be signed may be waived by the IRB on a case-by-case basis following a written request and justification by the investigator.

3.13.2 Subjects Who Do Not Speak English

These subjects will be presented with an informed consent document written in a language understandable to them. The foreign language version should be a certified translation of the IRB approved English version of the informed consent document. It is, therefore, submitted after the IRB has approved the English version. Certified translations of informed consent documents should be submitted with a certificate verifying the translation was provided by a certified translation service. Certified translations will be acknowledged and stamped by an IRB member or a designee. In cases where a certified translation of the informed consent document has not been provided, the author of the translation and his/her qualifications should be stated/described. Non-certified translations submitted to the IRB may require back-translation. Submission of a non-certified translation may delay the approval.

In circumstances where a potential participant is identified whose native language is not frequently encountered and no certified translation of the informed consent document is available, the use of a short form of the consent document and/or oral presentation of the informed consent can be conducted as described elsewhere in this manual.

3.13.3 Approval Date

IRB-approved Informed Consent documents will have the TTUHSC seal and approval affixed to the document.

Approval Date - The date of approval of the informed consent document will be determined based on the type of submission to the IRB. The approval date will be the date of final approval by the IRB for new studies, the date of continuing review approval for ongoing stud ies, or the date of approval of a change to the informed consent document.

Note that approved informed consent documents may be used to document the informed consent process on the expiration date of the study (if expiration date applicable).

3.14 Recruitment and Advertising

All research studies are approved to recruit only the number of participants indicated on the IRB approval letter. If the Principal Investigator finds that actual recruitment is approaching that limit, an Amendment should be submitted requesting an increase in the number of participants to be enrolled in the study. Over-enrollment should be reported to the IRB as an Unanticipated Event (See Section 2.10.4).

Recruitment methods and advertising materials must be approved by the IRB prior to implementation.

When advertising is to be used, the IRB must review the information contained in the advertisement and the mode of its communication to determine that the procedure for recruiting participants is not coercive and does not state or imply a certainty of favorable outcome or other benefits beyond what is outlined in the consent document and the protocol. An expedited review may be used for approval, but all advertising may be referred for full board review at the reviewer's discretion. Any advertisement to recruit participants shall be limited to the information the prospective participants need to determine their eligibility and interest.

Advertising materials shall not include the following:

- claims, either explicit or implicit, that the drug, biologic, device or other type of intervention is safe or effective for the purposes under investigation;
- claims, either explicit or implicit, that the test article is known to be equivalent or superior to any other drug, biologic, device or intervention;
- terms such as "new treatment," "new medication" or "new drug" without explaining that the test article is investigational, meaning non-FDA-approved;
- promise of "free medical treatment," when the intent is only to say that participants will not be charged for taking part in the investigation;
- an emphasis on the payment or the amount to be paid, by such means as larger or bold type. The IRB has the authority to approve whether compensation information shall be included in the advertisement.

3.14.1 Finder's Fees

The IRB does not allow the use of **any form** of additional compensation to individuals (including faculty, residents, staff, students, family members, etc.) who identify and/or recruit participants for participation in a research study.

3.15 Payments to Subjects

Payment to research subjects for participation in studies is not considered a benefit. Rather, it shall be considered compensation for time and inconvenience. The amount and schedule of all payments shall be presented to the IRB at the time of initial review. The IRB shall review both the amount of payment and the proposed method and timing of disbursement to determine that neither are coercive nor present undue influence.

3.15.1 Timing of Payments

Payment(s) shall be made to the subject throughout the study's progression and shall not be contingent upon the subject completing the entire study. A schedule for the

amount to be paid for each activity will not suffice; a timetable for the payments themselves must be submitted, approved, and presented to every subject as part of the Informed Consent Process.

3.15.2 Method of Payments

The method of payment to subjects must be described in the IRB Application and be reviewed and approved by the IRB. Subjects must be informed of IRS 1099 -MISC reporting requirements and that their social security numbers will be collected for payments greater than $25. Payments processed through TTUHSC must comply with TTUHSC OP 72.19 Payment to Research Participants/Patient Studies and TTUHSC OP 72.12 Payment to Nonresident Aliens

3.15.3 Disclosure of Payments

All information concerning payment, including the amount and schedule of payment(s) shall be set forth in the informed consent document.

3.15.4 Alterations in Payments

Any alterations in human research subject payment or revising of the payment schedule must be approved by the IRB prior to implementation as an amendment. A document must be sent to the subjects informing them of payment changes and must be included in the amendment.

3.16 Investigational Drugs/Devices

3.16.1 IND/IDE Application

The use of an unapproved investigational drug, device or biologic requires an FDA investigational new drug application (IND) as detailed in 21 CFR 312 or an FDA investigational device exemption (IDE), detailed in 21 CFR 812.

Before submitting an application to the IRB that involves an investigational new drug, device, or biologic, the Principal Investigator must secure an IND or IDE number from the FDA or correspondence from the FDA waiving this requirement. This FDA number or letter waiving the requirement for an FDA number shall be included in the submission to the IRB. If the IRB cannot verify the IND/IDE number the PI will be requested to provide documentation from thesponsor or FDA than an IND/IDE is not required.

The IND/IDE goes into effect 30 days after the FDA has received the application, unless the FDA notifies the sponsor-investigator that the investigation is subject to a clinical hold. ***NOTE: In addition to having the IND go into effect, IRB written approval must be received before your study may begin , this includes recruiting, obtaining consent and screening participants for the specific study subject to the INDThe TTUHSC IRB will not approve a project until a valid IND is in effect.***

3.16.2 Emergency Use

An emergency exists when (a) a patient/subject meetsthe requirements for emergency use established by the FDA (21 CFR 812); **and** (b) an IND/IDE exists for an investigational drug/device, but there is no IRB approved study at TTUHSC.

After Emergency Use of Investigational Drug/Device Procedures the use of drug/device must be reported to the IRB within **5 business days** of its use. This report must contain a description of the investigational drug/device and include rationale for its use. The

likelihood of similar need for the investigational drug/device must be evaluated and an IRB application initiated immediately if subsequent use appears likely.

3.16.3 Storage, Handling, and Dispensing of Investigational Agents

The principal investigator is directly responsible for the accounting of all investigational articles provided by a study sponsor as indicated in the FDA Form 1572. Regulations allow investigators to delegate these procedures to qualified pharmacist/individual health care provider. However, the physician/investigator is still ultimately responsible and should maintain internal controls to ensure guideline compliance.

The investigator must designate a single, centralized location as custodian to receive and manage the investigational articles (that would be the shipping address!). Regardless of where the investigational agent is retained, the principal investigator, pharmacist, or other designated individual will maintain records of the product's delivery to the trial site, the inventory at the site, the appropriate storage requirements are met (for example: refrigerator temperature logs, locked cabinet site), the use by each participant, and the return to the sponsor or alternative disposition of unused products. These records will include dates, quantities, batch/serial numbers, expiration dates (if applicable), and the unique code numbers assigned to the investigational products and trial participants. Researchers should maintain records that document adequately that the participants are provided the doses specified by the protocol and reconcile all investigational products received from the sponsor.

Inclusion/exclusion criteria for each study subject are verified by the principal investigator and/or study personnel *prior to* dispensing any investigational agent to a subject.

If the investigational agent is stored in a pharmacy and dispensed by a pharmacist, the principal investigator will ensure a copy of the current protocol is provided prior to dispensation of any investigationalagent. Further, the principal investigator will ensure the pharmacist has access to the informed consent document to verify that the investigational agent is being dispensed only to an approved study subject.

If the investigational agent is stored at a site other than a pharmacy it will be dispensed by approved, licensed study personnel who have a copy of the currently approved protocol, informed consent document for each subject and have verified the study subject has met all inclusion/exclusion criteria.

3.16.4 Packaging and Shipment of Infectious Materials

The Principal Investigator is responsible for overseeing training and ensuring that all specimens packaged and shipped from TTUHSC complies with TTUHSC OP 75.13 Shipment of Hazardous or Infectious Materials

3.17 Recordkeeping and Confidentiality

3.17.1 Recordkeeping

Every Principal Investigator is required by TTUHSC and federal regulations to maintain paper and/or electronic records of all correspondence relating to the use of human subjects in research. Correspondence with the IRB, notices of approval, and original signed Informed Consent Documents or an electronic copy must be maintained in the Principal Investigator's records.

All records of human subject research are subject to inspection by federal authorities, TTUHSC officials, including but not limited to RIO and Compliance Officers, SVPR and the IRB. Research records (including data) are the property of TTUHSC and shall not be transferred to another entity without prior approval of the SVPR. All research records (including consent documents) must be kept for a minimum of three years after the close of the study at the local research site. Studies that involve drugs or devices seeking FDA approval must be kept for two years after the FDA has taken final action on the marketing application, or as directed by the Clinical Trial Agreement.

3.17.2 Confidentiality

An issue of primary importance is the protection of subject confidentiality. The Principal Investigator must have sound plans to protect the subject's identity as well as the confidentiality of the research records.

Care should be taken to explain the mechanisms that have been devised to protect confidentiality, for example, the use of encrypted data coding systems or safely locked files in private offices. Furthermore, the Principal Investigator should describe who has access to the data and under what circumstances a code system may be broken. Without appropriate safeguards, problems may arise from long-term retention of records.

Video or taped data and photographs provide additional potential means for subject identification. Principal Investigators must secure subject consent explicitly mentioning these practices. They should also explain plans for final disposition or destruction of such records.

The conditions for maintaining confidentiality of the subjects and the research records are required for the life of the data. These rules apply equally to any and all research conducted by faculty, staff, and students. Studies conducted with FDA regulated articles must be kept in accordance with current FDA regulations or life of the data, whichever is longer.

3.17.3 Certificate of Confidentiality

Data collection about sensitive issues (such as illegal behavior, alcohol or drug use, or sexual practices or preferences) may require the protection of confidentiality beyond preventing accidental disclosures. Under federal law, an advance grant of confidentiality, known as a Certificate of Confidentiality is available. General information may be found at http://grants.nih.gov/grants/policy/coc/index.htm

A Certificate of Confidentiality provides protection for the researcher and the subjects against compelled disclosure of identifying information about subjects of biomedical, behavioral, clinical, and other research (Public Health Service Act 301(d), 42 U.S.C. 241(d)). Under this Act, the Secretary of HHS may authorize persons engaged in research to protect the privacy of subjects by withholding the names or other identifying characteristics of the subjects from all persons not connected with the conduct of the research. This means that researchers may not be compelled in any Federal, State or local civil, criminal, administrative, legislative, or other proceedings to identify their subjects.

The Confidentiality Certificate does not govern the voluntary disclosure of identifying characteristics of research subjects but only protects subjects from compelled disclosure of identifying characteristics by the researcher. Researchers, therefore, are not prevented from the voluntary disclosure of matters such as child abuse or a

subject's threatened violence to self or others. If an investigator intends to make such voluntary disclosures, however, the consent form shall clearly indicate this possibility to subjects. In order to seek a Certificate of Confidentiality, a PI shall identify the potential for compelled disclosure in the application. The consent document shall also include and describe possible disclosure situations. The IRB shall determine whether the risks to subjects are minimized, informed consent is appropriate, and privacy and confidentiality protections are adequate.

3.18 Useful Tools for Investigators

3.18.1 PI Responsibilities

The principal investigator promotes good clinical practices in the conduct of clinical investigations by assuring adherence to protocol requirements, protecting the rights and welfare of subjects, assuring the integrity of data generated at the site and directing the conduct of the clinical investigation according to federal and state regulations and guidance documents.

PROVIDES INVESTIGATOR QUALIFICATIONS AND AGREEMENTS BY:

- maintaining a current, up-to-date, signed and dated curriculum vitae
- maintaining current licensure to practice
- providing the sponsor and IRB with documentation of credentials as requested
- demonstrating the proper education, training and experience to conduct the clinical investigation
- assuming responsibility for the conduct of the clinical investigation
- signing the Form FDA 1572 or Investigator agreement as appropriate
- signing the protocol as required
- documenting the financial aspects of the trial as appropriate
- disclosing conflicts of interest as described in the regulations
- complete institutional mandated research training as required

ASSURES PROTOCOL COMPLIANCE BY:

- possessing a thorough understanding of the requirements of each protocol
- determining that inclusion/exclusion criteria are applicable to the study population
- assuring recruitment goals are reasonable and attainable
- assessing overall protocol feasibility following the trial's randomization procedures
- not implementing any protocol deviation or changes without agreement by the sponsor and prior review and approval by the IRB
- reviewing the inclusion/exclusion criteria, schedule of visits, end point criteria and investigational article use with the research team

ASSURES INITIAL AND ONGOING IRB REVIEW BY:

- providing the IRB with adequate information to initially review the study (i.e. protocol, investigator's brochure, informed consent form, recruitment advertisements and any written information to be given to subject(s)
- providing the IRB with documents for ongoing review (i.e. amendments to the protocol, serious adverse events, violations or new information)
- securing written IRB approval prior to initiating the study or instituting any changes to the protocol as approved
- providing written summaries of the trial status to the IRB annually, or as requested
- providing written information of premature termination or suspension of a trial
- providing the IRB with all documents subject to their review

DETERMINES ADEQUATE RESOURCES ARE AVAILABLE TO CONDUCT THE STUDY BY:

- having adequate number of qualified staff to conduct the study
- having adequate facilities to conduct the study
- assuring he/she has adequate time to conduct and supervise the study

MANAGES THE MEDICAL CARE OF SUBJECTS BY:

- assuring that a qualified physician (self or sub-investigator) is responsible for all trial-related medical decisions
- assessing subject compliance with the test article and follow-up visits
- assessing subject's response to therapy
- evaluating for adverse experiences
- ensuring that medical care is provided to a subject for any serious adverse event(s)
- informing a subject when medical care is needed to treat an intercurrent illness(es)
- informing the subject's primary physician about their participation in the trial

PROTECTS THE RIGHTS AND WELFARE OF SUBJECTS BY:

- reporting all serious adverse events immediately to the sponsor and IRB
- reporting new information that might affect adversely the safety of the subjects or the conduct of the clinical trial
- reporting any changes significantly affecting the conduct of the clinical trial or increasing the risk to subjects
- assuring that the informed consent form contains all the elements required by 21CFR 50 and 45 CFR 46
- obtaining a signed and dated informed consent from the subject or subject's authorized representative prior to initiating any study-related procedures
- informing the subject or authorized representative about all aspects of the clinical trial
- providing new information about the study or test article(s)
- ensuring subject confidentiality
- providing the subject or subject's authorized representative with a copy of the signed and dated informed consent form
- assuring that the informed consent form is in language that is understandable to the subject
- securing an impartial witness to the informed consent process when the subject or authorized representative is unable to read
- allowing ample time and opportunity for the consent process and answering questions about the trial to the satisfaction of the subject or authorized representative
- securing consent/assent from minors and mentally impaired subjects as appropriate
- following emergency use guidelines for waiver of consent in emergency situations as directed by the federal regulations and IRB policy and procedures
- acts in accordance with all applicable laws, regulations, and/or their professional licensing board in regards to protecting the rights and welfare of research participants during an emergency.

ASSURES VALIDITY OF THE DATA REPORTED TO THE SPONSOR BY:

- ensuring the accuracy, completeness, legibility and timeliness of case report forms
- ensuring that case report forms accurately reflect source documents
- explaining any discrepancies between source documents and case report forms
- endorsing changes or corrections to a case report form

ASSURES DOCUMENTATION OF STUDY-RELATED PROCEDURES, PROCESSES AND EVENTS BY:

- documenting deviations from the approved protocol
- documenting and explaining premature unblinding of the investigational product(s)
- documenting that informed consent has been obtained from the subject or authorized representative
- ascertaining the reason for a patient's premature study withdrawal
- documenting adverse experiences
- complying with written procedures to document changes to data and/or case report forms maintaining trial documents as required by the regulations and sponsor for the appropriate timeframe and under secure conditions
- providing study reports as requested by the sponsor, IRB and regulatory authority(ies)

ASSURES THE PROPER USE AND STORAGE OF INVESTIGATIONAL AGENTS BY:

- being thoroughly familiar with the use of the investigational product(s)
- reading the current investigator's brochure, product insert, or other source information
- assuming responsibility for the investigational product at the trial site
- ensuring the proper use, storage and documentation of the storage environment of the investigational product(s) at the trial site
- reviewing the proper use of the study article(s) by the subject(s) which includes verification that inclusion/exclusion criteria of each subject are met prior to dispensing the investigational agent
- if the investigational agent is stored and dispensed by a pharmacy, ensures that a current copy of the protocol and informed consent document are available to the pharmacist prior to dispensing the investigational agent.

DIRECTS SITE OPERATIONS BY:

- communicating effectively with subjects, research team, IRB and sponsor
- meeting regularly with the research team to discuss subject participation and protocol progress
- assuring that all research staff are informed about the protocol and investigational agents
- being knowledgeable about regulatory requirements and GCP standards
- preparing for and attending investigator and start-up meetings
- participating in monitoring visits and audits as appropriate
- permitting monitoring and auditing by the sponsor, institution, and regulatory authorities
- making available to monitors, auditors, IRB and regulatory authority(ies) all requested trial- related records
- delegating authority at the site appropriately
- assuring that all research staff are informed about their trial-related duties and functions
- maintaining a list of qualified persons and their corresponding trial-related delegated duties

MAINTAINS PROFESSIONAL AND TECHNICAL KNOWLEDGE BY:

- attending educational workshops
- reviewing professional publications
- participating in professional societies

3.18.2 Special Considerations for Clinical Trials That are Required to Follow ICH-GCP (E6)

Many federal and industry -sponsored multi -site clinical trials require trial sites to adhere to the standards outlined in the International Council for Harmonization -Good Clinical Practice Guidelines. These guidelines provide an international ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the participation of human subjects. Compliance with this standard provides public assurance that the rights, safety and well -being of trial subjects are protected, consistent with the principles that have their origin in the Declaration of Helsinki, and that clinical trial data are credible. (ICH Harmonised Tripartite Guideline: Guideline for Good Clinical Practice E6[R1])

TTUHSC investigators conducting trials that are required to follow ICH-GCP standards must adhere to the following considerations:

- The TTUHSC HRPP offers training on principles of ICH-GCP through the CITI Program Good Clinical Practice course (CITI Program). Choose the Good Clinical Practice course). Investigators and others required to provide evidence to sponsors of completion of ICH-GCP training may utilize this course with no fee, provided that the CITI sign-in is affiliated with TTUHSC.
- The informed consent document provided to participants must include the following: that the monitor, the auditor, the IRB, and the regulatory authority will be granted direct access to the participant's original medical records for verification of clinical trial procedures or data, without violating the confidentiality of the participant, to the extent permitted by the applicable laws and regulations and that, by signing a written consent form, the participant or the participant's legally acceptable representative is authorizing such access. The IRB will review the informed consent to determine this information is included.
- During and following a participant's participation in a clinical trial, the investigator must ensure that adequate medical care is provided to a participant for any serious adverse events, including significant laboratory values, related to the clinical trial. The research follows the clinical trial's randomization procedures, if any, and ensures that the code is broken only in accordance with the protocol. If the clinical trial is blinded, the researcher promptly documents and explains to the Sponsor any premature unblinding.
- The research er must inform the participant's primary physician about the participant's participation in the clinical trial if the participant has a primary physician and if the participant agrees to the primary physician being informed.
- Although a participant is not obliged to give his or her reasons for withdrawing prematurely from a clinical trial, the researcher makes a reasonable effort to ascertain the reason, while fully respecting the participant's rights.
- Essential documents must be retained until at least two years after the last approval of a marketing application in an ICH region and u ntil there are no pending or con templated marketing applications in an ICH region or at least two years have elapsed since the formal discontinuation of clinical development of the investigational product.
- The researcher must report all serious adverse events (SAEs) to the sponsor except for those SAEs that the protocol or other document (such as the investigator's brochure) identifies as not needing immediate reporting. The researcher follows regulatory requirements related to the reporting of

unexpected serious adverse drug reactions to the regulatory authority and the IRB.

- The researcher reports serious adverse events or laboratory abnormalities identified in the protocol as critical to safety evaluations to the sponsor according to the reporting requirements within the time periods specified by the sponsor in the protocol. If the researcher terminates orsuspends a clinical trial without prior agreement of the sponsor, the researcher informs the organization, sponsor and the IRB.
- If the IRB terminates or suspends approval of the clinical trial, the researcher promptly notifies the sponsor.
- Upon completion of the clinical trial, the researcher informs the organization, the IRB with a summary of the trial's outcome, and any regulatory authority with any reports required.

If the project is required to meet ICH-GCP (E6 [R1]) and is a non-therapeutic clinical trial, a non-therapeutic trial should only be conducted in subjects who personally give consent and who sign and date the written informed consent form.
Non-therapeutic trials (i.e. a trial in which there is no anticipated direct clinical benefit to the participant) may be conducted in subjects with consent of a legally acceptable representative provided the following conditions are fulfilled:

a. The objectives of the trial cannot be met by means of a trial in subjects who can give informed consent personally.
b. The foreseeable risks to the subjects are low.
c. The negative impact on the subject's well-being is minimized and low.
d. The trial is not prohibited by law.
e. The opinion of the IRB is expressly sought on the inclusion of such subjects, and the written opinion covers this aspect.

Unless an exception is justified, such trials should be conducted in patients having a disease or condition for which the investigational product is intended. Subjects in these trials should be particularly closely monitored and should be withdrawn if they appear to be unduly distressed.

3.18.3 Documentation of the Consent Process

Subject Identifier:_____

Protocol:_____

Principal Investigator:_____

☐The subject appears to meet all protocol inclusion criteria and have no protocol exclusion criteria.

The Informed Consent Document was explained and questions were discussed in

☐English ☐Spanish ☐Other_____.

An interpreter ☐was ☐was not used. If used, list name:

_____

The Informed Consent discussion took place at _____AM/PM on,___/____/_____ and before any research procedures were performed.

☐ Informed consent or assent was obtained using Good Clinical Practice Guidelines.

The consent discussion included: ☐subject ☐subject's family ☐legally authorized representative

☐ **Risks and benefits of this research**.
☐ **Alternative treatments or therapies**
☐ **All procedures included in the research protocol**
☐ **The subject's rights while participating in a research study**
☐ **Verbalized understanding of the study, the study procedures and study participant role.**
☐ **After all questions were answered, adequate time was allowed to consider participation prior to any study related procedures.**
☐ **Informed Consent or Assent was obtained voluntarilyand a copy of the consent document was provided to subject/legally authorized representative**
☐ The original signed and dated consent form is retained by the Principal Investigator

Printed name of person who obtained informed consent

_____

Name(s) of other individuals present during informed consent process:

_____

HIPAA Authorization Form signed: ☐ Yes ☐ N/A

_____

Printed name of person completing this form

3.18.4 Delegation of Authority

As Principal Investigator for the following study I have ensured that the individuals listed below are properly qualified and have received appropriate training. Based upon this, I have delegated authority to perform the following duties to the individuals named below, and assert that these duties will be performed under my direct supervision:

STUDY TITLE _____

AUTHORITY	***PERSONNEL***	***DATE***
Administration		
Contract and budget negotiations		
Fiscal management		
Strategic planning		
Performance tracking		
Quality assurance		
Project Management		
IRB submissions & communications		
Patient recruitment activities		
Sponsor, CRO contact		
Regulatory files creation and maintenance		
Data management/CRF completion		
Serious Adverse event reports		
Organizational tools		
Office staff training		
Storing, dispensing, accounting for study drug		
Overall study drug accountability		
Storing study documents		
Screening subjects for eligibility		
Obtaining informed consent		
Subject education		
Monitoring patient compliance		
Subject enrollment and follow-up		
Clinical assessments		
Serious Adverse event determination		
Source documentation		
Appointment scheduling		

3.18.5 Regulatory Files Binder Items

The following items are maintained in a regulatory binder(s) as needed for individual projects.

Investigator's Brochure
The most recent version of the Investigator's Brochure along with all previous versions.

Protocol and Case Report Forms
A copy of the complete final protocol for this study. If required by the sponsor, ensure that the protocol title page has been signed and dated by the principal investigator.

Protocol Amendments
Retain copies of any amendments to the original final protocol made by the sponsor or the investigator. Modifications may be in the form of new pages to be inserted in the protocol, an addendum to the protocol in the form of a letter or contained in the body of an amended protocol. Note that all protocol amendments must be reported to your Institutional Review Board (IRB). Also, protocol amendments that increase the risk to the subject in any way must receive IRB approval prior to implementation.

Form FDA 1572/Investigator Agreement
A copy of the signed original FDA Form 1572 or Investigator Agreement The form should list the name of the principal investigator and include any sub-investigators, if applicable. Any changes to the form/Agreement should be submitted to the sponsor and the IRB should be notified as well.

Investigator CVs
Copies of the current CVs for all personnel listed on the FDA Form 1572.

IRB Correspondence
All correspondence between the investigator and the IRB regarding this protocol. Examples of documents to retain are IRB approval letter(s), advertisements for the study approved by the IRB, yearly renewals of approval, site updates to the IRB, unanticipated event reports, or letters notifying the IRB of the completion of the study. The correspondence is available in Cayuse, and a separate file may not be required.

IRB-Approved Informed Consent Form
Has the original approved IRB consent form(s), as well as any amended or renewed consent forms. Signed informed consent documents may be scanned and stored in electronic form (in Cayuse or in the EHR, for example). Paper copies of consent documents which are stored securely andavailable electronically may be shredded.

Laboratory Certification
Obtain a copy of the most recent certificate issued showing the expiration date.

Range Of Normal Values For The Reference Laboratory
Contains a copy of the range of normal laboratory values used for this study. If the units or ranges differ from those previously supplied to the sponsor, these must be submitted to the sponsor and a copy retained. Retain the previous listing and ensure that the revised listing incorporates the effective date of change.

Unanticipated Event Reports (including UPIRSOs, ADEs, SAEs and Deviations)
All serious adverse events and UPIRSO's must be reported promptly to the sponsor

and to the IRB. Contains copies of all IND safety reports sent by the sponsor.

Investigational Product Accountability
Includes sponsor investigational drug shipping inventory, drug dispensing log, and return shipment documentation.

Monitoring Log
At each visit from the sponsor, the log sheet should be signed and dated by all sponsor personnel and the purpose of the visit noted.

Inclusion/Exclusion Log
A list of all subjects who signed the informed consent form and/or were screened for entry into the study.

Study Personnel Training Records
A list of all study personnel and the dates of completion/expiration of required training.

Signature List
Contains a list of the signatures of all study site personnel who entered, edited or deleted study data in the source documents and case report forms.

Final Study Report
Contains a copy of the final clinical study report provided by the sponsor.

General Correspondence
Contains all correspondence between the investigator and sponsor, between investigator and study team members or between study team members. Correspondence with l subjects may be filed in individual subject binders.

4 EMERGENCY PREPAREDNESS

4.1 Overview

Written procedures for initiating a response to an emergency impacting the TTUHSC Human Research Protection Program (HRPP) or HRPP operations.

An emergency may include but is not limited to natural disasters, weather events, man-made disasters, and public health crises.

This section establishes HRPP-specific emergency planning and is intended to supplement, not replace, emergency response planning by Institutional leadership and/or Institution-wide response measures. HRPP-specific emergency response planning and measures are limited only to those functions of the HRPP not otherwise covered by institution-level plans.

These procedures are invoked once the Institutional Official (IO) has indicated an emergency has occurred or preparations are needed for an imminent emergency, and human research at TTUHSC, including the HRPP or HRPP operations, is or is likely to be adversely impacted.

In addition to this HRPP manual and Institutional policies, PIs will be instructed, and will be expected, to act in accordance with all applicable laws, regulations, and/or their professional licensing board in regards to protecting the rights and welfare of research participants during an emergency.

4.2 Responsibility

4.2.1 Implementation of the Emergency Plan

The IO and designee; the Institutional Review Board (IRB) Chairs, Co-Chairs, and Vice-Chairs; Research Integrity Office (RIO) leadership; and the Safety/Compliance team are responsible for carrying out the procedures described in this section.

Periodic Evaluation of the Emergency Plan – The Senior VP for Research and Innovation (SVPRI) is responsible for evaluating the emergency preparedness plan and making changes, when appropriate. This evaluation shall occur at least annually.

Periodic Review of the Emergency Plan Educational Materials – The SVPRI is responsible for ensuring the educational materials are reviewed and updated as necessary, based on the outcome of the periodic evaluation of the emergency preparedness plan.

4.3 Procedures

4.3.1 Assessment

- **Assess the nature of the risk and the potential impact on the HRPP:** Once an emergency or imminent emergency is identified, determine the response based on the nature of the event. RIO leadership shall contact the IO or appropriate Institutional personnel to determine whether there are Institutional plans already in place to address the event. Refer to the TTUHSC Emergency Preparedness website for the current StatAlert status and the TTUHSC Emergency Management Plan. If these plans are activated, proceed in accordance with the TTUHSC OP 10.0 and determine whether communication with the research community is necessary to alert them to the activation of the emergency preparedness plan.

- **Assess whether the emergency may impact HRPP operations IRB Meetings:** If the emergency may prevent one or more IRB meetings from occurring, determine whether to cancel or reschedule the meetings, being certain to identify currently approved human research which may expire prior to IRB review. If research will expire, refer to section 2.10.2.10 of the TTUHSC HRPP Manual regarding extensions.
  RIO Staff protocol processing and review: If staff will be unable to complete protocol processing and review responsibilities, or if capacity will be limited, RIO leadership shall work with the staff to prioritize reviews. If research will expire, refer to the TTUHSC HRPP Manual, section 2.10.2.10, Submission of Continuing Review Materials after Expiration Date for guidance.
  Data and records: If electronic records are unavailable, consult with TTUHSC Information Technology (IT) support to implement alternative procedures to access backup data.
- **Assess whether the emergency may impact investigators' ability to conduct research:** In-person interactions with research subjects: If studies involve in-person interactions with research subjects, determine whether the studies may be conducted as written while adhering to emergency mitigation strategies.
  Sponsored research: When studies have an external sponsor, ensure coordination with each sponsor to confirm mitigation plans.
  Clinical care and/or research facility considerations: If the emergency impacts clinical care standards which may in turn impact research, clarify what does and does not require IRB review. For example, in the case of a public health crisis, screening procedures implemented by the health care system where a clinical trial is being conducted would not require IRB review/approval of the screening procedures. Conducting research procedures at an alternate clinical care location may require prospective IRB approval. Emergency response plans must be considered for each existing research location.

  Safety monitoring: If trial participants are unable to come to the investigational site for protocol-specified visits, alternative methods for safety assessments must be considered. This may include utilizing phone contact, virtual visits, and alternative locations for assessment (including local labs or imaging centers) to assure the safety of trial participants.

4.3.2 Action

- **Consider necessary actions to address the impact of the emergency** RIO Leadership, in consultation with the IO and IRB Chairs, as needed, shall define the actions to take during the emergency to avoid stopping all research activities.
- **Postpone new study implementation** : Consider not accepting submissions of new protocols for IRB review for research which is non-interventional in nature, or which presents no direct benefit to participants.
- **Suspending existing research:** The IRB may need to identify studies for which recruitment and/or enrollment should be suspended, but ongoing study interventions may continue.
- **Continuing studies via alternate mechanisms:** When possible, implement online or remote strategies for research procedures such as recruitment, consent, data collection, debriefing, and follow-up. Identify any additional research activities that can be completed via telephone, video conference, or via online mechanisms. If possible, alter the timing of visits and procedures.

- **Relying on another organization to provide IRB oversight:** Make arrangements (when possible, in advance of an emergency) as necessary to rely upon other organizations for IRB review. Identify the external IRBs and ensure reliance agreements are in place in accordance with the TTUHSC HRPP Manual section 1.9.3 Cooperative Research Activities Involving Other Entities.
- **Employ strategies to exercise flexibility in oversight:** When studies are not federally regulated, organizations may employ different but equivalent procedures in terms of protecting the rights and welfare of research participants. For example, for non-federal research, the IRB may consider extending continuing review dates during the emergency, and/or allowing minor changes in research to be reported to the IRB at the time of continuing review versus in advance of the change. Further, for most minimal -risk research regardless of funding, the IRB may consider the more widespread use of waivers of documentation of consent. This strategy may be considered particularly for notifying participants of changes to consent documents.
- **Triage the research that will be subject to the emergency mitigation strategies** Consider the types of research that may continue and the types of research that may need to be temporarily postponed. This consideration may include:
  - Studies that present a likelihood of direct benefit to participants (or conversely, studies that include study interventions that may be harmful to subjects if discontinued) and shall not be postponed, to the extent possible.
  - Research involving direct interactions or interventions but can continue those interventions via alternate mechanisms (such as remote visits) may continue.
  - Studies that may have an adverse impact on resources required to address the emergency shall be postponed, if possible.

4.3.3 Prevention

- **Develop education, training, and communications on expectations during an emergency**: Targeted communications and education/training shall be developed and distributed based on roles/responsibilities within the HRPP. In particular, researchers and research staff, IRB Chairs and IRB members, RIO staff, and departmental administrators may each have differing needs in regard to effectively responding to emergency mitigation strategies.

  Communications shall occur via standard communication routes, such as email and web-based platforms, if available. If the standard routes are not available, consult the institutional plans in place to address communications. Ensure the communications include instructions and expectations for impacted personnel.
- **Prepare and file necessary plans with the appropriate TTUHSC office** File an HRPP Emergency Plan with the Office of Safety Services. At least annually, review the HRPP Emergency Plan and update it as necessary. Following the review, communicate the plan to the research community, including RIO staff.

4.4 References

AAHRPP Element I.1.H
AAHRPP Tip Sheet – Emergency Preparedness and Response
Texas Tech University Health Sciences Center Office of the President OP 10.02
Texas Tech University Health Sciences Center Emergency Management Plan

5 DEPARTMENT OF DEFENSE

5.1 Overview

Research sponsored by the Department of Defense (DoD) involving collaboration with DoD or involving DoD facilities or personnel (military or civilian), is subject to additional requirements including special protections for research participants, as well as additional review and reporting requirements for investigators and IRBs. Investigators should review these requirements when planning a DoD -supported research project as they may add a significant amount of time to the review and approval process of research.

Each DoD component (e.g., Army, Navy, Air Force) may have additional requirements beyond those included in this document. Principal Investigators are advised to check with their sponsoring component program manager about any additional requirements.

The TTUHSC IRB reserves the right to require review by an external IRB on a case-by-case basis.

5.2 Definitions

Component: Any one of the military branches or organizational entities within the Department of Defense, including the Army, Marine Corps, Navy, Air Force, Space Force, Coast Guard, or National Guard.

DoD-Affiliated Personnel: Service members, reserve service members, National Guard members, DoD civilians, and DoD contractors.

Human Research Protection Official (HRPO): A federal employee designated by a DoD component or institution to conduct an administrative review of DoD -supported research in accordance with the requirements of the Defense Federal Acquisition Regulation Supplement (DFARS), or comparable requirement, and whose review of DoD -supported research is intended to ensure compliance with DoD human subjects research requirements.

Minimal Risk: The definition of minimal risk includes the phrase “ordinarily encountered in daily life or during the performance of routine physical or psychological examination or tests” must not be interpreted to include the inherent risks that certain individuals face in their everyday lives, such as those:

- Encountered by service members, law enforcement, or first responders while on duty
- resulting from or associated with high-risk behaviors or pursuits
- experienced by individuals whose medical conditions involve frequent tests or constant pain

Prisoner of War (POW) or Detainee: Individuals under the custody and/or control of the Department of Defense as defined in the Geneva Convention Relative to the Treatment of Prisoners of War of August 12, 1949, Articles 4 and 5. In particular, one who, while engaged in combat under orders of his government, is captured by the armed forces of the enemy. Note: Research involving a detainee or a POW as a human subject is prohibited.

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

5.3 Prohibited Research

The following categories of research are prohibited:

- Research with detainees or prisoners of war, except research with investigational new drugs or devices when the purpose is for diagnosis or treatment of a medical condition in a patient, with their informed consent, and where such treatment would also be offered to US military service members at the same location and with the same medical condition consistent with established medical practice.
- DoD Instruction 2310.01E defines a detainee as: "Any individual captured by or transferred to the custody or control of DoD personnel pursuant to the law of war. This does not include persons being held solely for law enforcement purposes, except where the United States is the occupying power. Detainees who are U.S. citizens or U.S. resident aliens will continue to enjoy all applicable rights and privileges under U.S. law and DoD regulations."
- Classified human subjects research.
- Human testing of chemical or biological agents, except for certain prophylactic, protective or peaceful purposes.
- Research involving "experimental subjects" – unless
    - the informed consent of the subject is obtained in advance; or
    - in the case of research intended to be beneficial to the subject, the informed consent of the subject or a legal representative of the subject is obtained in advance.
- Overseas DoD Research with overseas populations.
- Department of Defense research with protected populations as defined by 45 CFR 46 subparts, B, C, and D.
- Texas Tech University Health Sciences Center does not conduct or review survey research on Department of Defense Personnel.

5.4 Principal Investigator Responsibilities

- The PI must identify the research as sponsored or funded by a DoD component (as defined in DoD Directive 3216.02). The PI is responsible for identifying DoD component requirements specified in the grant application guidelines and for advising the OSP staff and applicable oversight committee/IRB of the requirements.
- Department of Defense requires a scientific review of the protocol. The PI shall obtain a comprehensive scientific review from his/her Department Chair or designee prior to submission of the application to the IRB. The Department Chair or designee is responsible for conducting the scientific review and signing the IRB application. The IRB considers the scientific merit of the study relative to human subjects protections. The IRB may rely on outside experts to provide an evaluation of the scientific merit.
- Civilian investigators attempting to access military volunteers should seek collaboration with a military investigator familiar with service-specific requirements.
- The PI shall confirm approval by the appropriate DoD component, including DoD component-level administrative review (CLAR), Security, Defense Offices of Human Research Protection (DOHRP), and Component Office of Human Research Protection (COHRP) when required, prior to research starting, including who is responsible and the process they go through.
- Additional DoD approval may be required for additional safeguards when:
    - Research involves those with cognitive impairment, mental illness, physical disability, or any other circumstance that might require special protections required by the DoD.

5.4.1 Educational Requirements

- Initial and continuing CITI Biomedical Investigator Training
- Conflict of Interest and Commitment Training and a Disclosure is required for all personnel who conduct, review, approve, oversee, support, or manage human subjects research.
- If there are specific DoD educational requirements or other certification requirements for study personnel, the PI is responsible for ensuring those requirements are met. See section 3.4 of the TTUHSC HRPP Manual.

5.5 Multi-Site DoD Research

At present, the TTUHSC IRB does not have the resources necessary to serve as the single/primary IRB of record when a TTUHSC investigator is the lead researcher of a multi-site study. If a single IRB review is required for this type of trial where a TTUHSC faculty member is the lead researcher, the TTUHSC Office of Research and Office of General Counsel will provide assistance as requested to develop a formal, written agreement with an external IRB to serve in this role.

5.5.1 Relying on TTUHSC

If a DoD institution is collaborating with TTUHSC (a non-DoD institution) and relying on the TTUHSC IRB for review, the following conditions shall be met:

- Each institution engaged in the non-exempt research must have a current federal assurance of compliance.
- The involvement of DoD personnel in the conduct of the research will be secondary to that of the TTUHSC personnel (non-DoD institution).
- A written agreement defining the responsibilities and authorities of each organization will be executed . This agreement must be approved by the DoD component prior to the engagement of the DoD institution in research.

5.6 Informed Consent

5.6.1 Informed Consent Requirements

- The informed consent must include (in addition to the basic and required consent disclosures):
  - A statement that the DoD or a DoD organization is funding the study unless the research involves no more than minimal risk. Note: The Secretary of Defense may grant an exception to this requirement on the grounds that providing this information could compromise intelligence sources or methods.
  - A statement that representatives of the DoD are authorized to review research records.
- The TTUHSC IRB will determine that the disclosure for research -related injuries follows the requirements of the DoD component.
- Funds appropriated to the Department of Defense may not be used for research involving a human being as an experimental subject unless
  - the informed consent of the subject is obtained in advance; or
  - in the case of research intended to be beneficial to the subject, the informed consent of the subject or a legal representative of the subject is obtained in advance.
- When the research meets the DoD definition of “Research Involving a Human Being as an Experimental Subject,” the IRB may not waive the consent process.

- The Secretary of Defense may waive the prohibition with respect to a specific research project to advance the development of a medical product necessary to the armed forces if the research project may directly benefit the subject and is carried out in accordance with all other applicable laws.

5.6.2 Exception from Informed Consent (EFIC)

- DoD regulations prohibit an exception from informed consent in planned emergency medicine research unless the PI obtains a waiver from the Secretary of Defense.
- The disclosure for research-related injury must follow the requirements of the DOD component. DoD-Affiliated Personnel as Research Subjects.

5.6.3 Limitations on Waivers of Informed Consent and Consent by LARs

- The Common Rule identifies conditions where an IRB may waive consent for DoD conducted and DoD -supported research involving humans as research participants. However, the requirement to obtain consent cannot be waived for any research using DoD funds and me eting the definition of research involving a human being as an experimental subject. This places limitations on research involving deception, adults with impaired decision -making capacity, or research being conducted under emergency conditions where the pa rticipant may not be able to provide consent.
- When the research meets the 10 USC 980 definition of research involving a human being as an experimental subject, informed consent must be obtained in advance from the participant or the participant's legally authorized representative (LAR) consistent with the Common Rule if the participant cannot consent. Informed consent may be provided by a LAR only if:
  - The research participant lacks decision-making capacity, and
  - The IRB has determined that the research is intended to be beneficial to the individual research participants.
- This statute applies only to certain intervention studies. It does not apply to retrospective research involving analysis of data or bio -specimens, observational studies, blood draws, or tissue collection, and does NOT apply to screening of records to identify possible research participants. The IRB may grant a waiver of consent for such activities.
- The Secretary of Defense may waive this consent requirement for a specific project in order to advance the development of a medical product necessary to the Armed Forces, but only if the research participant and the research is carried out in accordance with all other applicable laws and regulations.

5.7 Large Scale Genomic Data (LSGD)

Research Involving Large Scale Genomic Data (LSGD) Collected on DoD -Affiliated Personnel, DoD-conducted or DoD-supported research involving LSGD collected on DoD -affiliated personnel, or for which research the DoD provides assistance, is subject to additional requirements.

- LSGD is data derived from genome -wide association studies; single nucleotide polymorphisms arrays; genome sequencing; transcriptomic, metagenomic, epigenomic analyses; and gene expression data. Research involving LSGD may or may not also constitute human subjects research. Examples of research involving LSGD includes, but is not limited to, projects that involve generating the whole genome sequence data for

more than one gene from more than 1,000 individuals or analyzing 100 or more genetic variants in more than 1,000 individuals.

- The disclosure of DoD-affiliated personnel's genomic data may pose a risk to national security; accordingly, such research requires administrative, technical, and physical safeguards commensurate with risk, including the secondary use or sharing of deidentified data or specimens.
- All research involving LSGD collected from DoD-affiliated personnel will apply an HHS Certificate of Confidentiality pursuant to Title 42, U.S.C., and Public Law 114-255.
- Research involving LSGD collected from DoD-affiliated personnel is subject to DoD component security review to ensure the adequacy of the proposed administrative, technical, and physical safeguards, including the secondary use or sharing of deidentified data or specimens.

5.8 Certificate of Confidentiality

- A DoD institution conducting human subjects research or non-DoD institution conducting human subjects research with DoD support may request a CoC pursuant to Section 241 of Title 42, U.S.C. All studies involving LSGD collected on DoD-affiliated personnel (described above in section 7) will apply an HHS CoC.
- A CoC prohibits disclosing or providing, in any federal, State, or local civil, criminal, administrative, legislative, or other proceeding, or to any other person not connected with the research, the name of any individual or any such information, document, or biospecimen that contains identifiable information about the individual, created or compiled for purposes of research.
- Exceptions to the CoC must be listed in all informed consent documents, pursuant to this issuance and as stated in Section 241 of Title 42, U.S.C.
- See section 2.11.6 of this TTUHSC HRPP Manual.

5.9 DoD Personnel as Research Subjects

5.9.1 DoD-Affiliated Personnel

Service members and all reserve component and National Guard members in a federal duty status are considered for purposes of this issuance, to be adults. If a service member, reserve component, or National Guard member in federal duty status, a student at a Service Academy, or a trainee is under 18 years of age, the IRB must carefully consider the research recruitment process and the necessity of including such member as a research subject.

- If the research involves DoD-affiliated personnel as subjects and if the research includes any risks to their fitness for duty (e.g., health, availability to perform the job, data breach), the informed consent document must inform DoD-affiliated personnel about these risks and that they should seek command or component guidance before participating.
- If the research involves DoD-affiliated personnel, the key investigator must receive command or component approval to execute the research.
- Military and civilian supervisors, officers, and others in the chain of command are prohibited from influencing their subordinates to participate in research.
- Military and civilian supervisors, officers, and others in the chain of command must not be present at any research subject recruitment sessions or during the consent process for DoD-affiliated personnel. Excluded supervisors or those in the chain of command may participate in separate human subject research recruitment sessions, if applicable.

- For greater than minimal risk research and where recruitment is conducted in a group setting, the IRB must appoint an ombudsman. The ombudsman
  - Must not have a conflict of interest with the research or be a part of the research team.
  - Must be present during the research recruitment, monitoring that the recruitment and informed consent explain that participation is voluntary and that the information provided about the research is consistent with the IRB-approved script and materials, including digitally provided materials.
  - Should be available to address DoD-affiliated personnel's concerns about participation.
- Service members must follow their command policies regarding the requirement to obtain command permission to participate in research involving human subjects while on-duty or off-duty.
- The IRB shall confirm the following additional protections are in place to minimize undue influence (as applicable):
  - Officers are not permitted to influence the decision of their subordinates.
  - Officers and senior non-commissioned officers may not be present at the time of recruitment.
  - Officers and senior non-commissioned officers have a separate opportunity to participate.
  - When recruitment involves a percentage of a unit, an independent ombudsman is present.

5.9.2 Limitations on Compensation

Compensation to DoD-affiliated personnel for participation in research while on duty is prohibited in accordance with Title 5, U.S.C., with reference to Subparts G and H, with some exceptions for purposes consistent with Section 30 of Title 24, U.S.C.

The IRB will confirm that there are limitations on dual compensation:

- Which prohibits an individual from receiving payment compensation for research during duty hours.
- U.S. military personnel may be compensated for research if the subject is involved in the research when not on duty.

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

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

5.9.3 Informed Consent Requirements

For the IRB to approve research involving DoD-affiliated personnel as human subjects, the consent documentation must include, if applicable, potential risks for the revocation of clearance, credentials, or other privileged access or duty.

5.10 Reporting

Reporting Requirements, the following must be promptly reported to the HRPO (within 30 days of the event):

- IRB-approved changes to research that involve changes to key investigators or institutions; decreased benefit or increased risk to subjects in greater than minimal risk

research as defined in Part 219 of Title 32; addition of vulnerable populations, or DoD-affiliated personnel as subjects.
- Transfer of research oversight to a different IRB.
- Notification by any federal body, state agency, the official governing body of a Native American or Alaskan native tribe, other entity, or foreign government that the non-DoD institution's DoD-supported research is under investigation.
- Any problems involving risks to subjects or others, suspension or termination of IRB approval, or any serious or continuing noncompliance pertaining to DoD's supported research.
- The results of the IRB's continuing review, if required.
- Change in status when a previously enrolled human subject becomes pregnant, or when the researcher learns that a previously enrolled human subject is pregnant, and the protocol was not reviewed and approved by the IRB in accordance with Subpart B of 45 CFR 46.
- Change in status when a previously enrolled human subject becomes a prisoner, and the protocol was not reviewed and approved by the IRB in accordance with Subpart C of 45 CFR 46.
- A DoD-supported study's closure.

5.11 Research Related Illness and Injury

When conducting DoD research, TTUHSC follows 32 CFR 219.116.

See TTUHSC HRPP Manual section 3.11 for institutional policy.

5.12 Recordkeeping

Consistent with Texas Tech University Health Sciences Center policy, research records must be maintained for at least three (3) years after the completion of the research. The DoD may require that research records be transferred to the DoD component rather than being retained by TTUHSC. Records that document compliance or noncompliance with DoD regulations must be made accessible for inspection and copying by authorized representatives of the DoD at reasonable times and in a reasonable manner as determined by the supporting DoD component.

5.13 References

32 CFR 219.102
32 CFR 219.116
45 CFR 46.104
45 CFR 46.116
45 CFR 46 Subparts B, C, D
DoD Directive 2310.01
DoD Instruction 3216.02

6 GLOSSARY

ADMINISTRATIVELY CLOSED STATUS Decision of the IRB based on PI non-responsiveness to IRB requests or no study activity at the local site for a period of three or more years. This can occur prior to initial IRB approval or any time following IRB approval. No further research activity is permitted for studies which are administratively closed. Any further activity on such studies will require the submission of a new application to the IRB.

APPROVED The IRB has reviewed the study and made a determination that the study has met all regulatory/institutional requirements.

ASSENT Agreement by an individual not competent to give legally valid informed consent (e.g., a child or persons with impaired decision-making capacity) to participate in research. Mere failure to object to the research may not be construed as assent.

AUDIT A systematic and independent examination of trial-related activities and documents to determine whether the evaluated research related activities were conducted, and the data were recorded, analyzed, and accurately reported according to the protocol, sponsor's standard operating procedures (SOPs), good clinical practice (GCP), and the applicable regulatory requirement(s).

AUTHORIZED OFFICIAL An officer of an entity with the authority to speak for and legally commit the entity to comply with requirements of the federal regulations regarding the involvement of human subjects in biomedical and behavioral research. The authorized official for TTUHSC is the Senior Vice-President of Research.

AUTONOMY Personal capacity to consider alternatives, make choices, and act without undue influence or interference of others.

BELMONT REPORT (Belmont Report) A statement of basic ethical principles governing research involving human subjects issued by the National Commission for the Protection of Human Subjects in 1978.

BENEFIT A valued or desired outcome; an advantage.

BENEFICENCE An ethical principle discussed in the Belmont Report that entails an obligation to protect persons from harm. The principle of beneficence can be expressed in two general rules: (1) do not harm; and (2) protect from harm by maximizing possible benefits and minimizing possible risks of harm.

BIOLOGIC Any therapeutic serum, toxin, anti-toxin or analogous microbial produce applicable to the prevention, treatment, or cure of diseases or injuries.

BIOSPECIMEN Samples of material, such as urine, blood, tissue, cells, DNA, RNA, and protein from humans, animals, or plants. A human biospecimen is any natural material from the human body, such as tissue, blood, and urine.Material may be fresh or frozen samples, formalin-fixed paraffin-embedded blocks, slides, blood spots, or in other formats. "Samples" are portions or aliquots of biospecimens.

CANCELLED Study status assigned to research project the investigator or study sponsor decided to stop prior to study completion as outlined in the approved protocol.

CASE REPORT FORM (CRF) A printed, optical, or electronic document designed to record all of the protocol-required information to be reported to the sponsor on each trial subject.

CHILDREN Persons who have not attained the legal age for consent to treatment or procedures involved in the research, as determined under the applicable law of the jurisdiction in which the research will be conducted [45 CFR 46.402(a)].

CLINICAL TRIAL A research study to answer specific questions about vaccines or new therapies or new ways of using known treatments. Clinical trials are used to determine whether new drugs or devices are safe and/or effective. Carefully conducted clinical trials are the fastest and safest way to find treatments that work in people.

CLOSED TO ACCRUAL Investigator or sponsor-initiated decision to stop subject enrollment. This may be permanent or temporary. *Note:* Study interventions will continue as needed for subjects currently enrolled and ongoing continuing review is also required.

CLOSURE Study approved by the IRB that may be closed by the investigator, the sponsor, the IRB, TTUHSC, or by an affiliated entity. No research activities may occur after the closure date.

COMPETENCE A legal term used to denote capacity to act on one's own behalf; the ability to understand information presented, to appreciate the consequences of acting (or not acting) on that information, and to make a choice. (See also: Incompetence, Incapacity.)

COMPLETED Study status assigned to projects that have been closed by the principal investigator after completion of all research related interventions and collection of subject data.

COMPLIANCE Adherence to all the trial-related requirements, good clinical practice (GCP) requirements, and the applicable regulatory and institutional requirements.

CONFIDENTIALITY The treatment of information that an individual has disclosed in a relationship of trust and with the expectation that it will not be divulged to others without permission in ways that are inconsistent with the understanding of the original disclosure; ref ers also to the agreement between the investigator and participant in how data will be managed and used ensuing that information is accessible only to those authorized to have access.

CONFLICT OF INTEREST IN RESEARCH COMMITTEE See TTUHSC OP 73.09 Financial Conflicts of Interest in Research The Conflict of Interest Committee is appointed by the SVPR to review and oversee the management of financial conflicts of interest in research.

CONSENT A person's voluntary agreement, based upon adequate knowledge and understanding of relevant information, to participate in research or to undergo a diagnostic, therapeutic, or preventive procedure. In giving informed consent, subjects may not waive or appear to waive any of their legal rights, or release or appear to release the investigator, the sponsor, the entity or agents thereof from liability for negligence (Also referred to as informed consent).

CONTINUING NON-COMPLIANCE A pattern of repeated non-compliance which continues:

- after initial discovery and after IRB approval of corrective action plan and suggests that non-compliance will continue if there is no intervention, OR
- increases the risk of serious non-compliance, OR

- if continued, could significantly increase risks to, or jeopardize the safety, welfare, and/or rights of subjects or others, OR
- if continued, could decrease potential benefits (the scientific integrity of the research).

CONTINUING REVIEW Periodic review of a research study by an IRB to evaluate whether risks to participants are reasonable in relation to potential benefits and to verify that the study continues to meet regulatory and institutional requirements. Continuing review shall be conducted at intervals appropriate to the degree of risk but not less than once per year , except as described in 46.109(f). [45 CFR 46.109(e); 21 CFR 56.109(f)]

CONTRACT An agreement; as used here, an agreement that a specific research activity will be performed at the request, and under the direction, of an entity providing funds. Research performed under the contract is more closely controlled by the entity than resear ch performed under a grant.

DATA SAFETY MONITORING BOARD A committee of scientists, physicians, statisticians, and others that collects and analyzes data during the course of a clinical trial to monitor for adverse effects and other trends (such as an indication that one treatment is significantly better than another, particularly when one arm of the trial involves a placebo control) that would warrant modification or termination of the trial or notification of subjects about new information that might affect their willingness to continue in the trial.

DECISIONALLY IMPAIRED Persons who may be compromised in any way (temporarily or permanently) in their ability to make decisions in their best interests.

DECLINED Study status assigned to projects submitted to the IRB for review and assessed to be not acceptable for IRB review. The most common reason is the project does not meet the definition of human research as designed and therefore does not require IRB review.

DE-IDENTIFIED no information is linked to the specimen that would allow the investigator to identify the donor **and** no attempts will be made by the investigator to identify the donor using genetic analysis technology, detailed demographic/clinical parameter matching or other means.

DEVICE (MEDICAL) A diagnostic or therapeutic article that does not achieve any of its principal intended purpose through chemical action within or on the body. Such devices include diagnostic test kits, crutches, electrodes, pacemakers, arterial grafts, intraocular lenses, and orthopedic pins or other orthopedic equipment.

DHHS A federal agency: U.S. Department of Health and Human Services; the Office of Human Research Protection (OHRP) and the Food and Drug Administration (FDA) are agencies of DHHS.

DISAPPROVED The IRB has reviewed the study and determined that it is not approved and may not receive further review. This only applies to studies that have not previously been approved. See section on disapproval for request to reconsider requirements and timeframes.

DRAFT Status of a research project that has not been submitted to the IRB.

DRUG Any chemical compound that may be used on or administered to humans as an aid in the diagnosis, treatment, cure, mitigation, or prevention of disease or other abnormal conditions.

EMERGENCY As defined under the current TTUHSC emergency management plan under TTUHSC OP 76.01

ENGAGEMENT IN A RESEARCH PROJECT Includes *any one or more* of the following conditions:

- The research is conducted by or under the direction of any employee, student or agent of TTUHSC in connection with responsibilities to TTUHSC.
- The research is conducted by or under the direction of any employee, student or agent of an entity with which TTUHSC has a written agreement to serve as the IRB of record, if the project falls under the auspices of the agreement.
- The research involves non-public information maintained by TTUHSC or an affiliated entity.
- The research is conducted in accordance with an assurance filed with the DHHS Office of Human Research Protection in which a TTUHSC IRB is designated as the IRB of record.

ENROLLMENT The action of enrolling one or more subjects. NOTE: The subject will have met the inclusion/exclusion criteria to participate in the trial and will have signed an informed consent form.

ENTITY An organization, institution or being that has its own existence for legal or tax purposes, is legally separate from TTUHSC, and possess OHRP-approved Assurances and IRB Agreements with TTUHSC.

EXEMPT Status assigned to research project that involves human subjects for six specific categories of activities that may qualify as exempt from formal IRB review and oversight.Exempt status will never apply to research involving prisoners. Determination may be made by person(s) designated by the Research Integrity Office.

EXISTING Data or specimens already have been collected and stored at the time the research is proposed to the IRB for a determination of whether the research is exempt. Material collected after the date of the initial submission to IRB is not “existing” for purposes of this policy.

EXTERNAL ADVERSE EVENT Adverse events experienced by subjects enrolled by investigators at other sites participating in the same clinical trial as investigators at TTUHSC/Affiliates (also known as IND Safety Reports).

EQUITABLE Fair or just; used in the context of selection of subjects to indicate that the benefits and burdens of research are fairly distributed.

EXPEDITED REVIEW Review of proposed research by the IRB chair or a designated voting member or group of voting members rather than by the entire IRB. Federal rules permit expedited review for certain kinds of research involving no more than minimal risk and for minor changes in approved research.

EXPERIMENTAL Term often used to denote a therapy (drug, device, procedure) that is unproven or not yet scientifically validated with respect to safety and efficacy. A procedure may be considered "experimental" without necessarily being part of a formal study (research) to evaluate its usefulness.

FDA Food and Drug Administration; an agency of the federal government established by Congress in 1912 and presently part of the Department of Health and Human Services.

FEDERALWIDE ASSURANCE (FWA) An agreement between a federally funded entity and OHRP that stipulates methods by which the entity will protect research participants assuring that any engagement in human research is guided by a statement of principles such as the Belmont Report or the World Medical Association Declaration of Helsinki.

FETUS The product of conception from implantation until delivery [45 CFR 46.202 (c)].

FOLLOW-UP Status assigned when either: **A)** study involving interventions/treatment/ procedures have been completed and procedures for all locally enrolled subjects are the same as for patients managed off study or **B)** identifiable research data continue to be maintained pending further analysis.

FULL BOARD REVIEW Review of proposed research at a convened meeting at which a majority of the voting membership of the IRB is present, including at least one member whose primary concerns are in non-scientific areas. For the research to be approved, it must receive the approval of a majority of those voting members present at the meeting.

GRANT Financial support provided for research study designed and proposed by the principal investigator(s). The granting agency exercises no direct control over the conduct of approved research supported by a grant.

GUARDIAN An individual who is authorized under applicable state or local law to give permission on behalf of another to general medical care [45 CFR 46.402(e)]

HIPAA Health Insurance Portability and Accountability Act of 1996

HUMAN SUBJECTS Individuals whose physiologic or behavioral characteristics and responses are the object of study in a research project. Under the federal regulations, human subjects are defined as: living individual(s) about whom an investigator conducting research obtains: (1) data through intervention or interaction with the individual; or (2) identifiable private information (45 CFR 46.102[e (5)]. This term is used interchangeably with Participants.

IDE (INVESTIGATIONAL DEVICE EXEMPTION) An investigational device exemption (IDE) allows a device which has not yet been approved by the FDA to be used in a clinical study in order to collect safety and effectiveness data. Regulations regarding IDE's can be found at 21 CFR 812

IDENTIFIABLE BIOSPECIMEN A biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information

IDENTIFIABLE PRIVATE INFORMATION Private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information

IDENTIFIER a piece of information that identifies a specific person or that could be used to identify a specific person. For purposes of human research, names, codes linked to names, social security numbers, patient ID numbers and other such commonly -used data elements are considered identifiers. However, the Health Insurance Portability and Accountability Act (HIPAA) definition is broader, including a specific list of data elements

IND (INVESTIGATIONAL NEW DRUG) A drug permitted by FDA to be tested in humans but not yet determined to be safe and effective for a particular use in the general population and not yet licensed for marketing.

IND SAFETY REPORT Adverse events experienced by subjects enrolled by investigators at other sites participating in the same clinical trial as investigators at TTUHSC/Affiliates (also known as External Adverse Event Reports).

INFORMED CONSENT A person's voluntary agreement, based upon adequate knowledge and understanding of relevant information, to participate in research or to undergo a diagnostic, therapeutic, or preventive procedure. In giving informed consent, subjects may not waive or appear to waive any of their legal rights, orrelease or appear to release the investigator, the sponsor, the entity or agents thereof from liability for negligence (also referred to as consent).

INSTITUTIONAL REVIEW BOARD (IRB) A specially constituted review body established or designated by an entity to protect the welfare of human subjects recruited to participate in biomedical or behavioral research. At TTUHSC, the IRB is deemed to be a medical committee.

INTERACTION Includes communication or interpersonal contact between two persons (i .e.: investigator and subject).

INTERNAL SERIOUS ADVERSE EVENT Any serious adverse events experienced by a single subject enrolled in TTUHSC or TTUHSC IRB affiliate research project.

INTERVENTION Includes both physical procedures by which information or biospecimens are gathered (e.g., venipuncture) and manipulations of the subject or the subject's env ironment that are performed for research purposes.

INVESTIGATIONAL NEW DRUG OR DEVICE (IND) A drug or device permitted by FDA to be tested in humans but not yet determined to be safe and effective for a particular use in the general population and not yet licensed for marketing.

INVESTIGATIONAL PRODUCT A device or pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorization when used or assembled (formulated or packaged) in a way different from the ap proved form, or when used for an unapproved indication, or when used to gain further information about an approved use.

INVESTIGATOR'S BROCHURE A compilation of the clinical and non-clinical data on the investigational product(s) which is relevant to the study of the investigational product(s) in human subjects.

IRB (INSTITUTIONAL REVIEW BOARD) A specially constituted review body established or designated by an entity to protect the welfare of human subjects recruited to participate in biomedical or behavioral research. At TTUHSC, the IRB is deemed to be a medical committee.

IRB RECORDS IRB records include but are not limited to: all minutes of IRB meetings, a copy of all proposals reviewed including all amendments, investigator brochures, and any supplemental information including recruitment and informational materials, consent forms, information submitted for continuing review, all correspondence, and IRB membership with a resume for each member.

JUSTICE An ethical principle discussed in the Belmont Report requiring fairness in distribution of burdens and benefits; often expressed in terms of treating persons of similar circumstances or characteristics similarly.

MINIMAL RISK The probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in the participant's daily life or during the performance of routine physical or psychological examinations

or tests [45 CFR 46.102(j); 21 CFR 50.3(k)]. In research involving prisoners, minimal risk is also defined as the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons. [45 CFR 46.303(d)].

MINOR NON-COMPLIANCE Noncompliance that is neither serious nor continuing.

MONITORING Overseeing the progress of a study and ensuring that it is conducted, recorded, and reported in accordance with the protocol and applicable regulatory requirements.

NON-COMPLIANCE A situation, event or process in research involving human subjects that is inconsistent with:

- the ethical principles of human subjects research as described in the Belmont Report, OR
- Federal, state, and/or local regulations applying to human subjects research under the jurisdiction of the TTUHSC IRB, OR
- TTUHSC policies and procedures governing human subjects research, OR
- the research activities as approved by the TTUHSC IRBs.

NONAFFILIATED MEMBER Member of an Institutional Review Board who has no ties to the parent entity, its staff, or faculty. This individual is usually from the local community (e.g., minister, business person, attorney, teacher, and homemaker).

OFFICE FOR HUMAN RESEARCH PROTECTIONS (OHRP) The office within the U.S. Department of Health and Human Services, responsible for implementing DHHS regulations [45 CFR 46] governing research involving human subjects.

OPEN Status of an IRB approved research project that is currently enrolling subjects.

PARTICIPANT Individuals whose physiologic or behavioral characteristics and responses are the object of study in a research project. Under the federal regulations, human subjects are defined as: living individual(s) about whom an investigator conducting research obtains: (1) data through intervention or interaction with the individual; or (2) identifiable private information (45 CFR 46.102[e]). This term is used interchangeably with Human Subjects.

PENDING –SUBMITTED FOR INITIAL REVIEW Status of a research project that has been submitted to the IRB for review. This status label remains until a final decision regarding the project is made by the IRB. Decisions by the IRB may include a request for additional information, approval, declined,or disapproved.

PERMISSION Parent(s) or guardian's written agreement to the participation of their child or ward in research.

PREGNANCY 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].

PRINCIPAL INVESTIGATOR (PI) The scientist or scholar under whose immediate direction the study procedures are carried out. The Principal Investigator has ultimate responsibility for the design and conduct of a research project.

PRISONER Prisoners are any individuals involuntarily confined or detained in a penal institution. It includes persons who are detained pending arraignment, trial, or sentencing, and persons who become prisoners after research has begun.

PRIVACY The ability of an individual or group to seclude themselves or information about themselves and thereby reveal themselves selectively. For example, based on their privacy interests people want to control: a) the time and place where they give information, b) the nature of the information they give, c) the nature of the experiences that are given to them, and d) who receives and can use the information. Another example, persons might not want to be seen entering a place that might stigmatize them, such as a pregnancy counseling center that is clearly identified as such by signs on the front of the building.

PRIVACY BOARD IRB or another review body which reviews requests to use or disclose Private Health Information (PHI) for research purposes without authorization under HIPAA.

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

PROSPECTIVE STUDIES Studies designed to observe outcomes or events that occur subsequent to the identification of the group of subjects to be studied. Prospective studies need not involve manipulation or intervention but may be purely observational or involve only the collection of data.

PROTOCOL The formal design or plan of an experiment or research activity; specifically, the plan submitted to an IRB for review and to an agency for research support. The protocol includes a description of the research design or methodology to be employed, the eligibility requirements for prospective subjects and controls, the treatment regimen(s), and the proposed methods of analysis that will be performed on the collected data.

PROJECT All components of a human research submission to the IRB. Used interchangeably with the term STUDY.

PROTOCOL DEVIATION Protocol deviations are unplanned or unforeseen changes in the implementation of an IRB-approved protocol. They generally refer to a modification of procedures that has already occurred for a single subject; they are not intended to modify the protocol.

QUORUM A majority of the voting members appointed to the IRB membership. A quorum must include at least one member whose primary concerns are in non-scientific areas. A quorum must be established, recorded, and maintained for the deliberation and vote on all matters requiring a vote.

RECRUITMENT Active efforts by study personnel to identify subjects who may be suitable for enrollment. Subjects are selected on the basis of the approved protocol inclusion and exclusion criteria.

REPRESENTATIVE A person who makes decisions on behalf of another person. In human subjects research, an individual or judicial or other body may be authorized to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research.

REQUEST FOR ADDITIONAL INFORMATION A request made by the IRB for changes or clarifications to studies it has reviewed.

RESEARCH A systematic or clinical investigation, including research development, testing and evaluation, designed to contribut e to generalizable knowledge. (45 CFR 46.102[l]; 21 CFR 56.102[c]).

RESEARCH INTEGRITY OFFICE (RIO) Office responsible for the oversight and direction of the human research protection program at TTUHSC, which includes administrative oversight of the IRB, the TTUHSC Research Compliance Program, and TTUHSC Educational requirements for human research.

RESPECT FOR PERSONS An ethical principle discussed in the Belmont Report requiring that individual autonomy be respected and that persons with diminished autonomy be protected.

RETROSPECTIVE STUDIES Research conducted by reviewing records which are already in existence at the time the research is submitted for IRB review.

REVIEW (OF RESEARCH) The oversight of research on a periodic basis by the IRB. In addition to the at least annual reviews mandated by the federal regulations, reviews may, if deemed appropriate, also be conducted on a continuous or periodic basis.

RISK The probability of harm or injury (physical, psychological, social, or economic) occurring as a result of participation in a research study. Both the probability and magnitude of possible harm may vary from minimal to significant. Federal regulations define only "minimal risk".

SECONDARY USE a purpose other than that for which data or a specimen originally was collected.

SERIOUS ADVERSE EVENT (SAE) Any adverse event temporally associated with the subject's participation in research that meets any of the following criteria:

1) results in death;
2) is life threatening (Places the subject at immediate risk of death from the event as it occurred);
3) requires inpatient hospitalization (for a person not already hospitalized) or prolongation of hospitalization (for a subject already hospitalized);
4) results in persistent or significant disability or incapacity;
5) results in congenital anomaly and/or birth defects;
6) an event that jeopardizes the subject's health and may require medical or surgical treatment to prevent one of the preceding outcomes.

SERIOUS NON-COMPLIANCE Non-compliance which could significantly:

1) Increase risks to, or
2) jeopardize the safety, welfare, and/or rights of subjects or others, or
3) decrease potential benefits (the scientific integrity of the research).

SOURCE DATA/DOCUMENTS All information in original records of clinical findings, observations, or other activities in a study necessary for the reconstruction of that study. Source data are contained in source documents which may include, but are not limited to hospital records, laboratory notes, subject evaluation checklists, x -rays, subjects' files, or pharmacy records . These documents may be either paper or electronic format.

SPECIMEN Any biological material obtained from or derived from patients or human research subjects. This includes, but is not limited to: fixed, frozen or fresh pathology or autopsy specimens; blood; urine; saliva; CSF; semen; breast milk; and any purified DNA, RNA, proteins, cell lines or clones.

SPONSOR A person or other entity that initiates a clinical investigation, but that does not actually conduct the investigation, i.e., the test article is administered or dispensed to, or used involving, a subject under the immediate direction of another individual. A person other than an individual (e.g., a corporation or agency) that uses one or more of its own employees to conduct an investigation that it has initiated is considered to be a sponsor (not a sponsor-investigator) and the employees are considered to be investigators.

STUDY All components of a human research submission to the IRB. Used interchangeably with the term PROJECT.

STUDY CLOSURE Study approved by the IRB that may be closed by the investigator, the sponsor, the IRB, TTUHSC, or by an affiliated entity. No research activities involving interaction with participants or use of their identifiable information may occur after the closure date.

STUDY PERSONNEL Includes any individual directly involved in conducting research and who is interacting and/or intervening with human subjects or handles the identifiable private information of a human subject.

STUDY STATUS Label assigned to a study signifying subject enrollment, treatment and/or activity. Labels include: Draft, Pending -Submitted for Initial Review, Open, Exempt, Closed to Accrual, Follow-up, Cancelled, Completed, Declined, Disapproved, Suspended, Terminated, and Withdrawn. The **+** designation after a status is to denote the project is to be compliant with the 2018 version of 45 CFR 46 (Common Rule).

SUSPENDED Study status assigned to research projects that have been previously approved and the IRB has made a determination that approval is suspended. The PI will be instructed regarding the extent of the suspension. Instructions may include ceasing subject enrollment, ceasing data collection and or cessation of all research activities pending final IRB determination in writing.

SUSPENSION/TERMINATION IRB approval is suspended/terminated and all research activity halted as the result of unanticipated problems involving risks to subjects or others; serious or continuing non-compliance with 45 CFR 46; or the requirements or determinations of the IRB. Requires prompt reporting to federal regulatory authorities and TTUHSC pursuant to federal Assurance and 45 CFR 46.113.

SURVEY Studies designed to obtain information from a large number of respondents through written questionnaires, telephone interviews, door-to-door canvassing, or similar procedures.

TABLED Study status assigned when the IRB has reviewed the research project and determined that extensive changes are necessary. The study will be re-reviewed at a convened meeting of the IRB once changes have been made.

TERMINATED Study status assigned to projects that have been permanently closed as a result of 1) the need to protect the safety, welfare, and rights of subjects, 2) serious or continued non-compliance and/or 3) other situations, as the Board deems appropriate.

UNANTICIPATED ADVERSE DEVICE EFFECTS Adverse effects that occur with unlicensed devices approved by the FDA for research. These are reported directly to the IRB.

UNANTICIPATED PROBLEMS INVOLVING RISK TO SUBJECTS OR OTHERS (UPIRSO) Events that meet all of the following criteria: unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; **AND** (b) the characteristics of the subject population being studied (note: the unfounded classification of a serious adverse event as "anticipated" constitutes non-compliance); definitely related or probably related to participation in the research; **AND** suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

UNANTICIPATED PROBLEM Any incident, experience, or outcome that meets all of the following criteria: 1) events are not expected given: a) the nature of the research procedures and b) the characteristics of the subject population being studied; **AND** 2) related or possibly related to a subject's participation in the research; **AND** 3) suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) related to the research than was previously known or recognized.

UNEXPECTED ADVERSE EVENT Any adverse event occurring in one or more subjects in a research protocol, the nature, frequency, or severity of which is not consistent with either: 1) the known of foreseeable risk of adverse events associated with the procedures involved in the research that are described in (a) the protocol-related documents, such as the IRB-approved research protocol, any applicable investigator brochure, and the current IRB-approved informed consent document, and (b) other relevant sources of information, such as product labeling and package inserts; **OR** 2) the expected natural progression of any underlying disease, disorder, or condition of the subject(s) experiencing the adverse event and the subject's predisposing risk factor profile for the adverse event.

VOLUNTARY Free of coercion, duress, or undue inducement. Used in the research context to refer to a subject's decision to participate (or to continue to participate) in a research activity

WITHDRAWN (STUDY STATUS) Study status assigned to a research project that was submitted for IRB review and for various reasons the PI decides to withdraw the submission from further consideration by the IRB.

WITHDRAWN (STUDY SUBJECT) Any subject who elects to discontinue participation in a project or any subject required to be removed from a project after signing the informed consent (this may be due to ineligibility, principal investigator recommendation, invalid informed consent, etc.).

WITNESS, IMPARTIAL A person, who is independent of the trial, who cannot be unfairly influenced by people involved with the trial, who attends the informed consent process if the subject or the subject's legally acceptable representative cannot read, and who reads the informed consent form and any other written information supplied to the subject.

WRITTEN OR IN WRITING Refers to writing on a tangible medium (e.g., paper) or in an electronic format.