TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER EL PASO

HUMAN RESEARCH PROTECTION PROGRAM MANUAL

Version 2.0

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CHAPTER 1 ORGANIZATION OF THE TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER EL PASO HUMAN RESEARCH PROTECTION PROGRAM

1.1 Introduction and Organizational Summary

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 El Paso (TTUHSC El Paso) has developed and implemented a Human Research Protection Program (HRPP). This program includes an integrated system of research administration and oversight functions, including education, compliance, and review by Institutional Review Boards (IRBs). These guidelines and activities are designed to promote excellence in all aspects of human research by guaranteeing ethical treatment of all who volunteer to serve as research subjects, and by ensuring compliance with relevant regulations and ethical standards at all levels. The HRPP also addresses the needs and concerns of investigators, study coordinators, and study sponsors.

This manual describes the policies and procedures of the TTUHSC El Paso HRPP. Its purpose is to communicate comprehensive information about the organization, structure, and function of the human research protection program to the scientific community at TTUHSC El Paso and affiliated institutions. This Manual incorporates in one core document TTUHSC El Paso's program to protect human subjects (also referred to as research participants), operating procedures of the Institutional Review Board (IRB), and references to TTUHSC El Paso Institution-Wide Operating Policies and Procedures. The document is organized around the elements and standards required by the Association for the Accreditation of Human Research Protection Programs. The Manual describes applicable regulations governing research involving human subjects, such as the Common Rule (45 CFR 46), Food and Drug Administration regulations relating to human subjects (21 CFR 50 and 21 CFR 56), and ethical standards as found in the Belmont Report.

All members of the TTUHSC El Paso 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 El Paso HRPP may be found at the TTUHSC El Paso Research website.

The HRPP is led by the Vice President for Research (VPR) who has been designated as the Institutional Official (IO) for purposes of executive responsibility for research programs at TTUHSC El Paso. Delegation of day-to-day responsibility of the TTUHSC El Paso HRPP is shared by personnel in the Office of Research Resources (ORR), TTUHSC El Paso IRB Chairs, and IRB members. Ultimately, however, success of the TTUHSC El Paso HRPP requires commitment from all parties involved in human research, including institutional administrators, faculty, staff, students and other trainees, sponsors and affiliates.

The VPR/IO, Managing Director, and Sr. Director of the ORR engage in an on-going review of the status of the HRPP via monthly meetings to discuss pertinent issues. An annual written summary of the activities of the TTUHSC El Paso IRBs is prepared by the Sr. Director and is provided to the VPR, usually near the beginning of the fiscal year. This annual summary is used to assess IRB composition and provides a basis for adjusting membership as needed. The institutional effectiveness process also provides ongoing quality assessment and quality improvement goals for issues related to the efficiency of the TTUHSC El Paso HRPP.

The funds to support the TTUHSC El Paso HRPP, including the salaries of full-time personnel, and the costs of maintenance and operations, are derived from the budget of the ORR. The budget is reviewed at least annually by the Managing Director of the ORR and the VPR; adjustments are made as necessary to cover any unexpected expenses. IRB review fees provide supplemental funding for the HRPP. Fees include initial and continuing review of industry-sponsored research and/or for provisions 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 ORR staff and associated research committee members, and for membership fees and certifications for professional organizations.

1.2 Statement of Ethical Principles

TTUHSC El Paso 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).

These 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; and
Justice: fairness in the distribution of research benefits and burdens.

International and multi-site clinical trials conducted at TTUHSC El Paso will be conducted in accordance with ICH-GCP [International Conference on Harmonisation-Good Clinical Practice] guidelines. These guidelines have their origins in the Declaration of Helsinki and were developed in the United States, Canada, the European Union, and other countries and organizations. Although compliance with all ICH-GCP guidelines is 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 El Paso are incorporated into relevant sections of this manual.

1.3 Components of the TTUHSC El Paso HRPP

In order to function effectively, the TTUHSC El Paso HRPP requires commitments and assistance from many areas within and outside of the institution. The major components of the TTUHSC El Paso HRPP include:

- **The Institutional Official.** The Vice President for Research (VPR) serves as the Institutional Official with overall responsibility for the TTUHSC El Paso HRPP. Specific duties and responsibilities of the VPR with regard to the Human Research Protection Program can be found under Institutional Authority.
- **Office of Research Resources**. The ORR is recognized by the Institutional Official as the point of contact with DHHS's Office of Human Research Protections (OHRP). ORR staff members exercise operational responsibility on a day-to-day basis for the HRPP. This includes IRB administration, compliance, and educational components of the TTUHSC El Paso HRPP.
- **Institutional Review Boards (IRBs)**. TTUHSC El Paso has two local IRBs. Both IRBs review research involving human subjects conducted under the oversight of Principal Investigators (PIs) at the El Paso campus. The IRBs have the authority to approve, require modifications to secure approval, or disapprove all human research overseen

and conducted by TTUHSC El Paso faculty and staff. The IRB, or chairperson working 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, and study feasibility, as described in more detail under Principal Investigator Sign-off.
- **General Counsel**. The TTU System Office of General Counsel is available to provide advice upon request of the VPR, IRB, or other individuals involved with the HRPP. The Office of General Counsel may provide legal guidance and interpretation of TTUHSC El Paso policies, and of State and Federal laws and regulations as they relate to the conduct of research involving human subjects.
- **Office of Sponsored Programs (OSP).** The TTUHSC El Paso OSP handles grant and clinical trial contract administration. Personnel in this office review sponsor contracts and funding agreements for compliance with Federal and State regulations, and with TTUHSC El Paso 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 El Paso IRB. Further details are found in TTUHSC EP OP 73.09.
- **Health Insurance Portability and Accountability Act (HIPAA) Privacy Officer**. This individual is responsible for HIPAA Privacy oversight at the TTUHSC El Paso campus. The HIPAA Privacy Officer reports to the Institutional Compliance Officer.
- **Investigators and Research staff**. Investigators and research staff have a responsibility to follow the HRPP requirements described throughout this Manual and to comply with all determinations of the IRB and the VPR.
- **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 actions and compliance as they relate to research, for fostering support for IRB members, and for providing adequate resources to conduct human research at TTUHSC El Paso.
- **All TTUHSC El Paso faculty, staff and students**. Everyone associated with TTUHSC El Paso 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 EP OP 73.14, Research Compliance and TTUHSC EP OP 73.07, Honesty in Research and Allegations of Scientific Misconduct.

1.3.1 Communication between components

TTUHSC El Paso uses several mechanisms to communicate information relevant to the HRPP. These may include a general announcements website, which posts all institutional policy changes/updates, as needed. In addition, issues specifically pertinent to human research (for example: updates to the HRPP manual, template form changes, relevant policy alterations) are communicated to investigators and staff via the iRIS Announcement feature on an as needed basis.

The Managing Director of the ORR serves as a central liaison between the HRPP and other research compliance committees, the IO, and various departments.

The IRB application form serves as a primary tool for assessment of the institutional requirements to be met to ensure protection of subjects involved in a human research project. IRB members and IRB administrative staff review each submission to verify that these institutional components are adequately described. Examples include appropriate signatory authorization, consent template language reflecting terminology required in the clinical study contract, training and financial disclosures of all study personnel, and the presence of approved conflict management plans when necessary. If the IRB or IRB administrative staff determines that any of the institutional requirements necessary to protect participants are lacking, then the principal investigator (PI) will be notified in writing. The PI will be required to address the issue(s) and to provide additional necessary documents and/or information needed to comply with institutional policies and procedures.

1.4 Scope

Only research that involves the use of human subjects requires review by the TTUHSC El Paso IRBs. Further, TTUHSC El Paso, or an affiliated entity with which TTUHSC El Paso 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 El Paso IRB. To determine whether an activity meets the definition of research involving human subjects, the following definitions should be considered.

1.4.1 Definitions

1.4.1.1 Research

A systematic or clinical 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. case report(s).

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).

Quality improvement (QI) projects 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 QI project is more narrow; QI projects are designed to implement and measure improvements 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, generally using Plan-Do-Study-Act cycles.

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 Chair or Sr. Director. 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 that is exempt from formal IRB review can be found in Section 2.10 Determination of Exempt Human Research.

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

1.4.1.2 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. Please note: Public use data available from outside sources, may include protected health information (limited data set), and require an electronic data use agreement (DUA) to be signed. For more information regarding institutional Data Use Agreement requirements, visit the Institutional Compliance website here.

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 El Paso investigators who intend to conduct research using themselves as research subjects (or intend to use their own tissues or specimens) are required to submit the project for review and approval by a TTUHSC El Paso IRB prior to engaging in the research activity.

1.4.1.3 Engagement

TTUHSC El Paso 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 El Paso in connection with responsibilities to TTUHSC El Paso.
- The research is conducted by or under the direction of any employee, student or agent of an entity with which TTUHSC El Paso has a written agreement to serve as the IRB of record or as a relying IRB, if the project falls under the auspices of the agreement.
- The research involves nonpublic information maintained by TTUHSC El Paso 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 El Paso IRB is designated as the IRB of record.

TTUHSC El Paso 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 El Paso

OR

- The research is sponsored by TTUHSC El Paso.

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 El Paso is engaged in the project should contact their local IRB administrative staff 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

All research involving human subjects conducted at or in affiliation with TTUHSC El Paso shall be conducted in accordance with federal regulations and TTUHSC EP 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, 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 El Paso IRBs, supplanting anything written in TTUHSC El Paso Policies and Procedures.

1.5.1 Federalwide Assurance

TTUHSC El Paso has an approved, signed Federalwide Assurance (FWA) (00020736) filed with the Department of Health and Human Services (DHHS). The FWA is TTUHSC El Paso'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 in 45 CFR 46, including all Subparts, provide the practical basis for the review and approval of all human research at TTUHSC El Paso, regardless of funding source.

1.5.2 Institutional Authority

The VPR is the TTUHSC El Paso Institutional Official with overall responsibility for the TTUHSC El Paso HRPP. Components of the HRPP have been described previously in this document. Additional references include TTUHSC EP OP 73.06, Research Involving Human Subjects, Federalwide Assurance 00020736, the ORR, and the TTUHSC El Paso Research Compliance Program along with the TTUHSC El Paso Research Compliance Manual.

The VPR/IO 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.
- Ensuring that adequate funds, 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 El Paso and other organizations, including those that establish reliance on TTUHSC El Paso 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 IO if they experience undue influence or if they have concerns about the function of the IRB.

The VPR/IO has access to the Internet Medical Research Informational Systems (iRIS) program, which contains all documents, correspondence, and deliberations regarding each project reviewed by one of the TTUHSC El Paso IRBs. This access permits review of all activities of the TTUHSC El Paso IRBs as well all documents submitted. However, the VPR is not permitted to be involved in the day-to-day operations of the IRBs.

Day-to-day operation of the TTUHSC El Paso IRBs is delegated to staff members in the TTUHSC El Paso ORR, specifically the administrative staff of the IRB, who are assigned to oversee the various components of the TTUHSC El Paso HRPP.

1.5.3 Limitation on Institutional Authority

All human research conducted by TTUHSC El Paso must be approved by an 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 El Paso HRPP Manual. Research that has been reviewed and approved by a TTUHSC El Paso IRB may be subject to further review and disapproval by other review bodies or officials (including the VPR); however, no person or group may override the IRB's disapproval determination and approve research that had been previously disapproved by the IRB.

1.5.4 IRB Authority

The TTUHSC El Paso 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 El Paso 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 El Paso IRB shall have signatory power for review and actions taken by each local IRB. Electronic documents found in iRIS--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.

1.5.5 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 EP 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 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 El Paso leadership (ex: President, Vice-Presidents, Provosts, Deans, Development Office, OSP officials) are prohibited from serving as members, alternate members or ex-officio members of the TTUHSC El Paso 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 IRB administrative staff who are involved in the HRPP have numerous interactions with investigators and others in the performance of their assigned roles. TTUHSC El Paso will investigate and resolve any reported attempt to inappropriately pressure an IRB member or other representative of the TTUHSC El Paso HRPP through undue influence. Undue influence includes interference with the normal functioning or decision-making of a TTUHSC El Paso 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 IRB administrative staff member should be reported and investigated as follows:

- An IRB Chair, IRB member, or IRB administrative staff member who experiences undue influence should report the occurrence to the Managing Director of ORR who will attempt to mediate or resolve the concern in consultation with the VPR, and/or Research Compliance Officer.
- Alternatively, the person(s) experiencing undue influence may report directly to the VPR, acting as the IO.
- 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.

1.8 Institutional Conflict of Interest

As it relates to research with human subjects, institutional conflict of interest refers to a situation in which licensing, technology transfer, patents or investments of--or gifts to--Texas Tech University Health Sciences Center El Paso OR the financial interests of TTUHSC El Paso 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 EP OP 10.05 Conflict of Interest and Commitment Policy and TTU System Regents' Rules Other potential sources of institutional conflict of interest (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 Resources, 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 TTUHS senior administrators. Any potential conflicts of interest will be referred to the Office of General Counsel as indicated in TTUHSC EP OP 10.05. The COICC will have primary responsibility for reviewing disclosures involving gifts to the institution. Potential institutional conflicts that involve research, including research with human subjects, will be forwarded by the Office of General Counsel or the COICC for review by the Conflict of Interest in Research Committee (COIRC) as described in TTUHSC EP 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 HSCEP OP 73.09.

1.9 Confidential Medical Committee

The IRB is a committee of TTUHSC El Paso established for the purpose of carrying out requirements governing research involving human subjects under federal law and TTUHSC El Paso policies and procedures. The IRB is a "medical committee" as defined under Texas Health & Safety Code Chapter Section 161, 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."

1.10 IRB Relation to Other Entities

1.10.1 Other TTUHSC El Paso Compliance Committees

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

- **Conflict of Interest in Research Committee** (COIRC)
- **Institutional Biosafety Committee** (IBC)
- **Radiation Safety Committee** (RSC)

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

1.10.2 Affiliated Entities

The TTUHSC El Paso 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 (reviewing IRB) for another institution or to rely on an IRB from another institution (relying IRB) when involved in collaborative research. Such agreements will require written contracts and amendment to the Office for Human Research Protections (OHRP) assurances as appropriate. Templates for contractual agreements between TTUHSC El Paso and other institutions can be obtained through the Managing Director of the TTUHSC El Paso ORR.

Institutions for which the TTUHSC El Paso 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 El Paso IRB serving as the IRB of record.

TTUHSC EP currently has the following types of Agreements in place:
•TTUHSC EP IRB serves as IRB of record for a study
•TTUHSC EP IRB relying on another IRB for a study
•Reciprocal IRB agreement: TTUHSC EP either relying on or reviewing for partner IRBs

1.10.2.1 Cooperative Research Activities Involving Other Entities

When TTUHSC El Paso 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 El Paso) IRB review, delegation to an external IRB, or separate review by each institution's designated IRB. When single (TTUHSC El Paso) IRB review or delegation to an external IRB is involved, TTUHSC El Paso 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 El Paso ORR 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 El Paso researchers may establish agreements with TTUHSC El Paso 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.

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 El Paso will enter into agreements with designated reviewing IRBs as necessary in order to comply with regulatory requirements.

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

At present, TTUHSC El Paso will not permit the delegation of IRB review to an external IRB for multi-site industry-sponsored clinical trials for which TTUHSC El Paso faculty are serving as local site investigators.

At present, the TTUHSC El Paso IRB has limited resources to serve as the single/primary IRB of record when a TTUHSC El Paso investigator is the lead researcher of a multi-site study. If single IRB review is required for this type of trial where a TTUHSC El Paso faculty member is the lead researcher, the TTUHSC El Paso ORR will review the proposal for feasibility. If the TTUHSC El Paso IRB will not be able to serve as the single/primary IRB of record, the ORR will provide assistance as requested to develop a formal, written agreement with an external IRB to serve in this role.

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 agreement and/or for questions related to establishment of a new agreement.

1.11 Developing and Maintaining Human Research Protection Program Policies and Procedures

ORR staff, including IRB administrative staff, with input from the IO, 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 EP Operating Policies, and standards of regulatory, accreditation, and funding agencies that apply to research conducted under the auspices of the TTUHSC El Paso human research protection program.

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

The Managing Director of ORR and the IRB Sr. Director will maintain the **TTUHSC El Paso HRPP Program Manual**. When portions of the manual are revised, the Managing Director of ORR will maintain a historical archive of all previous versions. The entire manual will be reviewed at least once every odd-numbered year by the Managing Director of ORR and the Sr. Director. If no changes are required, the Managing Director of ORR will make and file note to that effect.

CHAPTER 2 INSTITUTIONAL REVIEW BOARD STRUCTURE AND FUNCTION

2.1 Organization of the IRBs

2.1.1 There are two registered TTUHSC El Paso IRBs.

- IRB #1-ID #IRB00009945
- IRB #2-ID #IRB00009946

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

2.2 IRB Scope

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

TTUHSC El Paso also has written affiliation agreements with other institutions. Each of those written agreements spells out the conditions under which TTUHSC El Paso 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 El Paso serves as the IRB of record.

2.2.1 Research conducted by students/residents with IRB approval from another institution

In certain cases, TTUHSC El Paso 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 El Paso IRB.

TTUHSC El Paso will not generally require a separate review of a study protocol in which a TTUHSC El Paso 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 El Paso or at an institution affiliated with a TTUHSC El Paso 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 El Paso 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 El Paso 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 the TTUHSC El Paso IRB and Office of Student Affairs, prior to participation in the project. TTUHSC El Paso reserves the right to limit, suspend or terminate the involvement of TTUHSC El Paso students or residents in studies approved by another institution's IRB.

2.2.2 Local Research Context

TTUHSC El Paso's responsibilities under its FWA apply whenever TTUHSC El Paso 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 El Paso 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 El Paso will request a local IRB to review the project in order to address local context issues.
- Copies of the non-TTUHSC El Paso IRB approval must be submitted to and acknowledged by the TTUHSC El Paso 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.

2.2.3 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.

2.2.3.1 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 included in the design of the research.
• A description of how community members will be included in the dissemination of results.

In addition, community members who serve as study personnel will be expected to abide by the **TTUHSC EP OP 10.28** on Volunteers if they do not have a TTUHSC EP faculty appointment. Verification of either status is required prior to obtaining an iRIS

account and/or being added to a research study. Community members serving in this dual role should be given contact information for the IRB or the Research Protection hotline number found on informed consent documents if they have questions about their rights as a study team member and/or as a subject.

2.2.4 International Research

The IRB reviews all research involving human subjects conducted under the auspices of TTUHSC El Paso, 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 the 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 El Paso IRB for review. When a formal IRB/Ethics Committee review is not possible, it is the responsibility of the PI 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 is also required, as described elsewhere (2.22) 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 the translated documents must also be submitted and approved prior to their use in the study as described elsewhere (2.14) 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 submitting PI 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, and at least one member who is unaffiliated with TTUHSC El Paso (i.e. not a family member or spouse of an employee). A single member may fulfill more than one of these characteristics.

2.3.1.1 Diversity

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

2.3.1.2 Unaffiliated Member

Consistent with OHRP IRB member registration guidelines, unaffiliated members may not be employees of TTUHSC El Paso or immediate family members of TTUHSC El Paso employees because TTUHSC El Paso 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 El Paso affiliate entities.

2.3.1.3 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 at all convened meetings.

2.3.1.4 Prisoner Advocate

Federal Regulations require that the IRB membership be modified if the IRB is to review research that involves prisoners. Therefore, if any TTUHSC El Paso IRB will review research that involves prisoners, at least one member of that IRB shall be a prisoner, or a prisoner advocate with appropriate background and experience to serve in that capacity. The prisoner advocate member must be present at any convened IRB meeting at which research that involves prisoners is reviewed. Research within the TTUHSC El Paso system may be reviewed by any IRB with a prisoner advocate.

2.3.1.5 Child or Minor Representative

An IRB considering a study that involves 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.

2.3.1.6 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 Administrative Staff 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 who act in the course and scope of their role and responsibility(ies) as an IRB member in good faith without malice and in the reasonable belief that the action or recommendation is warranted by the facts known by that person have civil immunity pursuant to the Texas Tort Claims Act and Sections 160.010 of the Texas Occupations Code and 161.033 of the Texas Health & Safety Code.

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. The courses are web-based and available through the Collaborative Institutional Training Initiative (CITI).

- Human Subjects Research Course- this is the institutionally approved basic course in the Protection of Human Research Subjects.
- Conflict of Interest Course-this is the institutional approved basic course for training in financial conflicts of interest.

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 iMedris system (iRIS) for processing IRB submissions.

- TTUHSC El Paso Human Research and Protection Policies and Procedures
- Interaction between the IRB Office and the Board;
- Terms and regulations (FDA, OHRP, NIH, TTUHSC El Paso, 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 El Paso 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 El Paso 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.
- 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 Human Subjects Research Course- completed at least once every 3 years
- CITI Conflict of Interest Course – completed at least once every 4 years.

All required education is monitored by the Education Coordinator 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 annually as part of the TTUHSC El Paso performance management program. The formal evaluation process includes a self-evaluation and further evaluation by both the direct supervisor and/or 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 Conflict 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 a 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

IRB members are required to complete TTUHSC El Paso conflict of interest training and a financial disclosure form prior to the initial appointment and annually thereafter. A financial conflict of interest (FCOI) is defined in TTUHSC EP Operating Policy **73.09, Financial Conflicts of Interest in Research**. TTUHSC El Paso'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 in research 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 participation 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.).

Conflicted IRB members shall leave the 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.

Further, the iMedRIS software system used by the TTUHSC El Paso IRBs does not permit any IRB member who is listed as study personnel on a particular project to access the IRB review comments or meeting discussions for that project.

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 Sr. Director 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 and the Board;
- Effective meeting skills;
- Terms and regulations (FDA, OHRP, NIH, TTUHSC El Paso, etc.);
- Meeting basics (quorum, voting procedures, acceptable templates, etc.);
- Vulnerable populations;
- Liability issues; and
- The use of the iRIS software system 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 Administrative Staff Roster;
- TTUHSC El Paso HRPP Manual

Required Education: All new IRB members are required to successfully complete two online courses prior to their appointment as a voting member of the IRB. The courses are offered through the University of Miami's Collaborative Institutional Training Initiative (CITI) Program. These include a) Human Subjects Research Course, and b) Conflicts of Interest Course.

All required education is monitored by the IRB Administrative Staff on an ongoing 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 VPR will be kept aware of the continuing education opportunities made available to IRB members during periodic meetings or emails from the Sr. Director or Administrative Staff. 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 El Paso training seminars focusing on relevant topics;
- Attending regional or national seminars or conferences that involve discussion of research ethics. A stipend may be available to IRB members to help defray costs of attending regional/national meeting, depending on availability of funds.

Required Education: The following are mandatory educational requirements that may be included for IRB continuing education:

- Completion of the "Collaborative Institutional Training Initiative (CITI) Human Subjects Research Course" administered by the University of Miami. This training is REQUIRED of all IRB members at least once every 3 years.
- Completion of the "Collaborative Institutional Training Initiative (CITI) "Conflict of Interest Course" administered by the University of Miami. This training is REQUIRED of all IRB members at least once every 4 years.

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

2.4.5 IRB Chairperson and Vice-Chairperson

2.4.5.1 Appointment

The VPR, in collaboration with the IRB Sr. Director and Managing Director of ORR, appoints the IRB Chairperson and vice-chairperson for a two-year term. 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. However, the IRB Chairperson may be removed or reappointed at any time upon written notice by the VPR or designee.

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

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 manages the matters brought before the IRB in accordance with applicable procedures and regulations. The chair of the meeting monitors the quorum during the meeting.

Chairpersons and vice-chairpersons will be presented in the Board roster.

The chairperson will ensure that the VPR and the Managing Director of ORR are notified of pertinent information to facilitate compliance with federal regulations and TTUHSC El Paso policy.

Pertinent information requiring prompt reporting to the VPR 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 VPR, in collaboration with the IRB Sr. Director and Managing Director of ORR, appoints the IRB members for a two-year term. 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 and/or incumbent members will be reappointed. However, any member may be removed or reappointed at any time upon written notice by the VPR or designee.

At the time of appointment/reappointment the IRB members will sign an agreement to serve and a confidentiality agreement, and shall disclose any known or potential conflicts of interest.

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 the 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 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 primary and secondary reviewers conduct an in-depth review of all materials and enter their comments into iRIS. The primary and secondary reviewers shall present an oral summary of the study and their recommendations regarding its disposition.

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, 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 administrative staff 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 VPR in collaboration with the IRB Sr. Director and Managing Director of ORR 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 VPR or designee.

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.

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 re-appointment to the IRB each IRB Chairperson, Vice Chairperson, and member will be asked to complete a self-evaluation tool regarding IRB membership and knowledge. Assessment of current training is also included. The IRB administrative staff 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;
- each action will include separate deliberation;
- the vote on each of these actions including: (a) members present for the vote (located in the IRB Voting section in iRIS for each submission), (b) the number of members voting for, (c) against, and (d) abstaining;
- 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:

- for initial and continuing reviews the approval period will be documented;
- for research involving pregnant women or and/or fetuses - documentation of IRB findings required under 45 CFR 46 Subpart B;
- for research involving prisoners – presence of appropriate prisoner representative - documentation of IRB findings required under 45 CFR 46Subpart C;
- for research involving children – documentation of IRB findings in accordance with 45 CFR 46 Subpart D and 21 CFR 50;
- consideration of additional safeguards for vulnerable subjects;
- determination of significant risk or non-significant risk device for FDA regulated research;
- alternate member replacement of regular/primary voting member;
- names of IRB members who abstained from a vote with the reason for abstention; and
- names of IRB members recused from a discussion/vote due to a conflict of interest.

TTUHSC El Paso IRB meeting minutes are created through the iRIS 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 administrative staff 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 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 adverse event reports. IRB 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;
- requests to modify or amend the approved research project;
- reports of unexpected events, including protocol deviations, unanticipated problems involving risks 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 El Paso Compliance Committees (e.g., IBC, Radiation Safety Committee, etc.);
- drug or device information (including Investigator's Brochures, as applicable)
- recruitment materials

2.6.2 Record Retention

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

Electronic files are maintained in iRIS 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, IRB administrative staff, compliance officer(s), IO 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 administrative staff may grant other TTUHSC El Paso/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 administrative staff, the Managing Director of ORR, or IO.

2.7 IRB Submission Process

2.7.1 Submission Mechanism

All information relative to human research projects must be submitted using the proprietary software program, Internet Medical Research Informational Systems (iRIS). Assigned privileges within iRIS 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 Board Submission Deadlines).

Information is communicated between the IRB and investigators via iRIS. All correspondence generated by IRB administrative staff and iRIS, 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 iRIS for IRB review:

- completed electronic IRB study application form;
- completed iRIS 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;

If a TTUHSC El Paso PI is one of the primary investigators for a multisite study, documentation regarding communication between all site IRBs (for example: unanticipated problems, amendments, etc.)

- Investigational New Drug (IND) or Investigational Device Exemption (IDE) number;
- Investigator's Brochure;
- Data Safety Monitoring Reports;
- proposed informed consent document using TTUHSC El Paso IRB-approved template which may include an Authorization to Use and Disclose PHI for Research (HIPAA authorization form);
- any proposed data collection forms;
- letters of approval or support from non-TTUHSC El Paso research sites;
- recruitment materials;
- surveys, questionnaires, or videotapes;
- non-English versions of any materials to be seen by subjects (as needed and after English versions are approved);
- certificate of confidentiality as needed (**http://grants.nih.gov/grants/policy/coc/**);
- documentation of review/approval by required TTUHSC El Paso compliance committees (example: Institutional Biosafety Committee, Conflict of Interest in Research Committee, etc.);
- CV of 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**.111.1; **21 CFR 56**.111.1). 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

Departmental Signatory Authority prior to submission for IRB review as noted **here**. The Departmental Signatory Authority must review the proposal and attest that it is consistent with TTUHSC El Paso'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 *may* 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 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:

- Are the Specific Aims and hypotheses clearly stated?
- Are the outcomes clearly stated and defined?
- Has a literature search supporting study rationale been conducted?
- Will testing the hypothesis provide important knowledge for the field?
- Is the study design appropriate?
- Will the proposed tests/measurements address the hypotheses?
- Are the validity/reliability of measures established?
- Are all of the proposed tests/measures required/related to at least one proposed outcome?
- Are the proposed statistical methods clearly stated/correlate with study design?
- Is the proposed sample size adequately justified?
- Is the PI 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. The VPR and/or IRB Chairperson will determine an appropriate consultant or committee member(s) to conduct the scientific review.

2.7.4 Principal Investigator (PI) Sign-off

Initial and continuing review submissions must be signed by the PI electronically in iRIS prior to the IRB receiving the submission. In signing the submissions, the PI is indicating

that s/he has reviewed the information in the submission. Prior to submitting an initial review, the signature of the PI indicates an understanding and 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
- 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.
- A review of HSCEP OP 73.02 - Ownership and Transfer of Externally Sponsored Projects and Research Records and section 3.19- Recordkeeping, of the HRPP manual has been completed, and it is understood that all research records, including data and specimens, are the property of TTUHSC El Paso and shall not be transferred to another entity without prior approval of the VPR.

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 or refer to the TTUHSC El Paso Research Compliance 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 El Paso's research mission.
- The PI 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.
- A review of HSCEP OP 73.02 - Ownership and Transfer of Externally Sponsored Projects and Research Records and the Human Research Protection Program

Manual 3.19.1- Recordkeeping has been completed, and it is understood that all research records, including data and specimens, are the property of TTUHSC El Paso and shall not be transferred to another entity without prior approval of the VPR.

The IRB may request documentation from the Department Signatory authority regarding review and approval of any of these requirements. In cases where the PI is the department chair and/or related to the PI, sign off by a designated alternate will be required.

2.7.6 Submission Screening

IRB administrative staff will prescreen all IRB submissions. If the submission is incomplete or otherwise not fully prepared for review, it will be returned to the PI for completion. When the submission is adequately prepared, it will be accepted and assigned to an IRB member or members for review.

2.7.7 Agenda

The IRB agenda consists of all IRB submissions that have been prescreened by IRB administrative staff, and acknowledged or assigned. IRB staff, in consultation with the IRB Chair as necessary, make assignments based on an 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.

New studies are assigned to either IRB #1 or #2 by IRB administrative staff. For existing studies, continuing reviews and amendments are assigned to the Board that completed the Initial Review.

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

2.7.8 Notifications to Investigators

All IRB decisions are communicated to the PI and designated research team members via the iRIS 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 IRB's determination.

For multisite research studies, the TTUHSC EP PI and research team members will be responsible for communicating all IRB decisions to and from other sites.

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 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. when 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.
    c. Note: In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research, as distinguished from risks and benefits of therapies 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.
    a. 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.
    a. 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.
    a. 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.
    a. This will be done in accordance with (FDA **21 CFR 56**.111(a) (6); DHHS **45 CFR 46**.111(a) (6)).
    b. When research is minimal risk, the IRB may determine that no formal data safety monitoring is required.
    c. 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.
    d. 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 frequently 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.
    a. 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.
    a. Subjects who are likely to be vulnerable to coercion or undue influence may include students, children, prisoners, pregnant women, handicapped or individuals with impaired decision-making capacity , persons with acute or severe physical or mental illness, persons who are economically or educationally disadvantaged, or persons who are vulnerable because they are institutionalized (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 administration 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 El Paso Research Compliance Officer;
- establishment of an independent data safety monitoring committee;
- establishment of specific stopping rules.

2.8.1.3 Determination of review cycle

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, the approval date is the date all approval requirements have been met and the PI 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-The expiration date for research required to be approved at a convened meeting is determined by the date of the convened meeting, not necessary 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 by either expedited review or 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 11/4/2018 will expire on 11/3/2019. Research activities are allowed to take place on 11/3/2019 (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 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 IRB (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 IRB/experienced IRB member may request clarifications, protocol modifications, revisions to the informed consent document, or other supporting documentation. In iRIS, these requests are entitled “Stipulations.” Stipulations must be satisfactorily addressed before approval is effective.

The IRB will classify modifications of submissions requiring review at a convened meeting 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 as 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 iRIS 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 El Paso officials cannot 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 El Paso 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 administrative 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 iRIS 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 IRB 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 IRB requires follow-up of participants for safety reasons, the IRB will consider whether participants should be informed.

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

IRB oversight continues, so the research is considered active for the purposes of continuing review. Investigators must continue to follow the IRB'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 iRIS 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 that had qualified for expedited initial/continuing review as well as those that 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 IRB 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 PI 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. All data analyses must 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 El Paso IRB requirements;

- to protect the safety, welfare, and rights of subjects; or
- other situations, as the IRB 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;
- whether current participants should be informed of the suspension;
- any 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 Managing Director of ORR and the VPR of a decision to suspend within 2 business days of the decision. The VPR, serving as the IO, will promptly (within 30 days) notify other TTUHSC El Paso officials or outside entities (HHS, FDA, NIH, affiliated institutions, etc.) as required to comply with our FWA.

IRB oversight continues, so the research is considered active for the purposes of continuing review. Investigators must continue to follow the IRB'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 detail can be found regarding corrective action plans in the Research Compliance Section, 2.21, of this manual and in the TTUHSC El Paso Research Compliance Manual.

2.8.6.2 Suspension by Institutional Official or IRB Chairperson

In urgent situations the VPR acting in the role as IO or IRB Chairperson acting on behalf of the IRB may determine that research activity must be suspended immediately. If this action occurs, the VPR/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 the 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 VPR 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 termination, a request by the PI for reconsideration shall be reviewed by a subcommittee, consisting of the IRB chair and two IRB members, who were jointly selected by the IRB Chair and Sr. Director. The subcommittee may also invite individuals with expertise in that area of research to assist the subcommittee in its review of the issues. The Sr. Director, Research Compliance Officer, and Managing Director of ORR will provide assistance to the subcommittee as needed, although they will not be considered to be 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, and suspension documentation, and may speak with the PI. The subcommittee shall submit findings and a recommendation to the full IRB 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, reject, or revise its 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 project is final, and may not be reversed by the VPR or any other officer/agency of TTUHSC El Paso or affiliated entities.

2.8.7 Terminate Research Activity

When the IRB terminates approval the PI is required to permanently cease all research activities, including data analysis, for the terminated study(ies). A research study may be terminated only by the full IRB at a convened meeting. This is true for studies that had qualified for expedited initial/continuing review, as well as for those that were originally approved by the full IRB 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 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 administrative staff will notify the Managing Director of ORR and the VPR of decision to terminate approval within 2 business days of the decision. The VPR, serving as the IO, will promptly (within 30 days) notify other TTUHSC El Paso 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 VPR acting in the role of IO or the IRB Chairperson acting on behalf of the IRB may determine that research activity must be terminated immediately. If this action occurs, the VPR/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 VPR 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 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 Sr. Director. The subcommittee may also invite individuals with expertise in that area of research to assist the subcommittee in its review of the issues. The Sr. Director, Research Compliance Officer, and Managing Director of ORR will provide assistance to the subcommittee as needed, although 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 recommendation to the full board 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 IRB shall consider the subcommittee's recommendation(s) and make a ruling to accept, reject, 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 El Paso (**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 VPR or any other officer/agency of TTUHSC El Paso or affiliated entities.

2.9 Determination of Exempt Human Research

Federal regulations 45 CFR 46.104(d) provide for eight specific categories of activities that may qualify as exempt from formal IRB review and oversight. Categories 7 and 8, related to broad consent for storage and secondary research of identifiable private information or biospecimens, will not be implemented at this time. Consent for future use of data/samples will continue to be addressed on an individual study-by-study basis. Exempt status will never apply to research involving prisoners. The exemption categories are summarized below:

2.9.1 Exempt Research Categories as outlined in 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 educators who provide instruction. This includes:

◊ Most research on regular and special education instructional strategies; or

◊ Research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management.

Category 2: Research that only includes interaction involving the use of 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 is met:

(i) Information obtained is recorded by the investigator in such a manner that the identity of human subjects cannot be readily ascertained, directly or through identifiers linked to the subjects. Children may only be included in research under this exemption when involving educational tests or observation of public behavior if the investigator(s) do not participate in the activities being observed and the information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot be readily ascertained directly, or through identifiers linked to the subjects; or

(ii) Any disclosure of the human subjects' responses outside of 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. Children may only be included in research under this exemption when involving educational tests or observation of public behavior if the investigator(s) do not participate in the activities being observed and the information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot be readily ascertained directly, or through identifiers linked to the subjects; or

(iii) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can be readily ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by 45 CFR 46.111(a)(7). Children may not be included in this section.

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

(A) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot be readily ascertained, directly or through identifiers linked to the subjects; or

(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 be readily ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by 45 CFR 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 (e.g., playing an online game, solving puzzles, etc.).

(iii) If the research involves deception, this exemption is not applicable unless the subject authorizes the deception through a prospective agreement to participate in research and the subject is informed that they will be unaware of or they will be misled regarding the nature or purposes of the research. Children may not be included in research under this exemption.

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 are met:

(i) The identifiable private information or identifiable biospecimens are publically 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 160 and 164, Subparts A and E (HIPAA), for the purposes of "health care operations" or "research" as those terms are defined under HIPAA or for "public health activities and purposes" under HIPAA; 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.

Category 5: Research and demonstration projects, which are conducted by or subject to the approval of Federal Department or Agency heads, and which 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.

Category 6: Taste and food quality evaluation and consumer acceptance studies:

(i) If wholesome foods without additives are consumed; or

(ii) If a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the

Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

2.9.2 Exempt Review Process

The determination of whether a TTUHSC El Paso study qualifies for status as exempt from IRB review must be made by an IRB representative. TTUHSC El Paso researchers or departmental representatives 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 and/or review the decision charts found at the OHRP website (see Human Subject Regulations Decision Charts). 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 administrative staff 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 criteria the IRB administrative staff 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 in accordance with TTUHSC EP HRPP processes.

2.10 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.

2.10.1 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, non-pregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8-week period and collection may not occur more frequently than 2 times per week; or
   b. from other adults and children considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8-week period and collection may not occur more frequently than 2 times per week.
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(d)(2)** and (d)(3). This listing refers only to research that is not exempt.)
8. Continuing review of research previously approved by the convened IRB as follows where:
   a. the research is permanently closed to the enrollment of new subjects;
   b. all subjects have completed all research-related interventions; and
   c. the research remains active only for long-term follow-up of subjects; or where no subjects have been enrolled and no additional risks have been identified; or where the remaining research activities are limited to data analysis.
   d. 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.

e. Minor modifications to currently approved research.

2.10.2 Deadlines

Submissions that 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.

2.10.3 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)**.

2.10.4 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 had required full IRB 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 IRB for reference at the next convened meeting. This documentation should cite the specific permissible category or categories justifying 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.

2.11 Review at Convened Meetings of the IRB

2.11.1 Deadlines

Materials for convened board meetings will be submitted to the IRB through iRIS by pre-established deadlines. Submission deadline dates and IRB meeting dates and times are found in iRIS and on the TTUHSC El Paso IRB's **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 agenda, the submission and all documents are immediately available for review by 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 iRIS 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 Sr. Director, more items have been submitted than can be effectively reviewed during the meeting, items will be prioritized. Submissions related to previously approved research will have priority over new projects (e.g., continuing reviews, amendments, etc.). Extra submissions will be assigned for review at the next convened meeting.

2.11.2 Conduct of the Meeting

TTUHSC El Paso IRB meetings are conducted using the iRIS 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 EP 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, as needed.

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

2.11.3 Duties of IRB Member Reviewers

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 iRIS system. Reviews are to be written in the “member comments” section of iRIS prior to the meeting. The primary reviewer is responsible for 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 available for use by the reviewer(s) 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 IRB 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 reviewers are responsible for making formal recommendation for IRB action (approval with risk level and review cycle, disapproval, request for more information) as appropriate to the submission. A majority vote of the voting members present is required to formalize IRB decisions.

2.11.4 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. 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 assembled members do not have the expertise to review the proposed research. Individuals who are not appointed to the IRB but attend IRB meetings by virtue of their institutional status may not be counted toward the quorum and do not have voting privileges.

2.11.5 Investigator Presence during Meetings

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

2.12 IRB Submission Categories

2.12.1 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 El Paso IRB may commence prior to IRB approval of the project. In no case will a TTUHSC El Paso IRB grant “retroactive” approval to a research project where data have been collected prior to IRB approval.

2.12.2 Continuing reviews

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

2.12.2.1 IRB Determination

2.12.2.1.1 Continuing Review Required

Studies that were originally approved by the full board at a convened meeting and have enrolled subjects who are actively being followed for purposes outlined in the study procedures will require continuing reviews in accordance with the IRB assigned review cycle. This includes studies overseen by external IRBs.

2.12.2.1.2 No Continuing Review Required

Unless the IRB determines otherwise, the following research projects will generally not require continuing review:
• non-funded 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 (b) 1 categories 1-7; 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 2.12.3, 2.12.4 and 2.12.5).

2.12.2.2 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;
- involvement of recombinant DNA or other types of gene transfer studies;
- 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 and those that received expedited review usually will be assigned a 12-month review cycle.

2.12.2.3 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 board 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 submitting continuing review materials in a timely manner.

2.12.2.4 Required Information

Information included on the “Continuing Review Form” in iRIS 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 any reason). 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: 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 unreported 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.

2.12.2.5 Submission Screening

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

2.12.2.6 Duties of IRB Members

All study materials are routinely available to all IRB members for review through the iRIS 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 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 iRIS 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 will be noted so this information will be provided to participants.

2.12.2.7 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(b) (4)).

Such sources include, but are not limited to, FDA inspection reports, subject complaints, research staff whistle-blowers, 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 for-cause audit by the Research Compliance Officer with findings to be reported back to the IRB. See **TTUHSC EP OP 73.14, Research Compliance, the TTUHSC El Paso Research Compliance Manual** and the **Research Compliance Section 2.21**.

- 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 IRB 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 IRB 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.

2.12.2.8 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, a research project approved for annual review on 11/4/2018 will expire on 11/3/2019; research activities are allowed to take place on the day of expiration).

2.12.2.9 Continuing review – Convened Meeting Review

This includes studies that were originally approved by the IRB at a convened meeting and have enrolled subjects who are actively being followed for purposes of providing study procedures. Studies which were originally approved by the full IRB, which have not yet enrolled subjects or which are not providing active study treatment/procedures, will also be reviewed by the full IRB if significant new risks or findings are reported by the PI at the time of the continuing review.

PI responses to IRB stipulations regarding continuing reviews conducted at a convened meeting may be reviewed by expedited procedure (if requirements **45 CFR 46**.111 are met).

2.12.2.10 Continuing review – Expedited Review

This includes studies that:
• the IRB reviewer explicitly stated rationale in the initial review that continuing review would be required to enhance the protection of research subjects; or
• a study that was originally approved by the full board in which enrollment of subjects has not yet taken place and no additional risks have been identified during the review period.

2.12.2.11 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.

2.12.2.12 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 30 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.

2.12.2.13 Exempt studies – No Continuing Review Submission Required

These studies are not approved by the IRB and do not require continuing review. NOTE: Regardless of exempt/ no continuing review status, all projects submitted to the IRB require ongoing reporting of changes to the project (amendments), any unanticipated events and study closures.

2.12.3 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 to prevent 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 iRIS.

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.

2.12.3.1 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 that were initially approved by the expedited procedure and those acknowledged as exempt from formal IRB review. Examples of minor amendments include editorial changes or corrections to study documents, submission of missing documents, letters of support, changes to advertisements, etc.

The IRB Chairperson, a member designee, and/or administrative staff will review minor modifications. No reviewer may disapprove a requested modification via an expedited review procedure.

Amendments that involve only changes 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 the principal investigator), correction of typographical errors in study documents, data safety or monitoring committee reports with recommendation 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 approved or acknowledged, will be immediately available on the IRB agenda for review by all IRB members at any time.

2.12.3.2 Greater-than-minor amendments

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 a 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 iRIS. The IRB will use the same criteria as initially used to approve the research (**45 CFR 46**.111 and/or **21 CFR 56**.111) for review/approval of the amendment. If the IRB determines that the amendment includes information that might alter participants’ willingness to continue participation, the PI 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, responses to major amendments may be reviewed by expedited procedure (if requirements **45 CFR 46**.110 are met) or by full board review. If no response has been received from the PI 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.

2.12.3.3 Notification to the PI

The decisions by the IRB will be promptly conveyed to the PI in writing by the IRB administrative staff. All correspondence is sent electronically through the iRIS system.

2.12.4 Unanticipated Events

Unanticipated events include protocol deviations, unanticipated problems involving risk to subjects or others (UPIRSOs), unanticipated adverse device effects (UADE), local adverse events, and serious local adverse events. The mechanism for reporting these events to the IRB is the Internal Unanticipated Event Form found in iRIS. 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.

2.12.4.1 Protocol Deviations

2.12.4.1.1 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 have already occurred for a single subject; they are not intended to change 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/incorrect compensation 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.

2.12.4.2.2 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.

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

IRB administrative staff prescreens protocol deviation submissions for completeness. If adequate, the submission is assigned to the IRB Chair and Research Compliance Officer/designee for initial review.

The IRB Chair and compliance officer's/designee's review may include acknowledgment, 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 2.21].

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

2.112.4.2.1 Definition

Unanticipated problems involving risk to subjects or others 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.

2.12.4.2.2 Reporting to IRB

Any report of an UPIRSO will be submitted for IRB review using the Unanticipated Events Form found in iRIS. 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 regarding unexpected risks that 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) that require prompt reporting to the sponsor by the PI.
- UPIRSOs 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.

Questions about whether or not to report any particular occurrence may be directed to the respective IRB administrative staff 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.

2.12.4.2.3 Assessment/Review

IRB administrative 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.

2.12.4.2.4 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;
- for-cause 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).

2.12.4.2.5 Reporting to Regulatory Agencies

If the IRB determines that the increased risk is significant, the IRB Chair or IRB administrative staff will notify the IO's office. The IO will notify OHRP and/or FDA within 30 days, in compliance with the TTUHSC El Paso Federal-wide Assurance.

2.12.4.3 Unanticipated Adverse Device Effects (UADEs)

2.12.4.3.1 Definition

Unanticipated adverse device effects include: any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects).

See **Guidance for Clinical Investigators, Sponsors, and IRBs**.

2.12.4.3.2 Reporting to IRB

Any report of an UADE that is submitted to the IRB by the study sponsor or the Principal Investigator should use the Unanticipated Events Form found in iRIS. 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 UADE;
- 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 UADE which require reporting to the IRB:
- The device was not programmed by as outlined by the protocol by the technical support personnel (field clinical engineer).
- The subject's device would not electronically submit the data from their home (remote transmission) as outlined in the protocol.
- UADEs should be reported to the IRB as soon as possible, but in any event, no later than ten (10) business days after the sponsor or principal investigator becomes aware of the event.

2.12.4.3.3 Assessment/Review

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

The Research Compliance Officer/designee will also receive notification of the UADE 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 UADE involves more than minimal risks to participants or others, the submission will be referred to the convened meeting for review.

2.12.4.3.4 Convened IRB Actions for UADE

The following are examples of actions that are authorized by the IRB for UADEs 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;
- for-cause 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).

2.12.4.3.5 Reporting to Regulatory Agencies

If the IRB determines that the increased risk is significant, the IRB Chair or Administrative staff will notify the IO's office. The IO will notify OHRP and/or FDA within 30 days, in compliance with the TTUHSC El Paso Federal-wide Assurance.

2.12.4.4 Adverse Events

2.12.4.4.1 Definition

An AE is any untoward medical occurrence in a subject administered a pharmaceutical product which does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding for example), symptom, or disease temporally associated with the use of a medicinal product, whether or not related to the use of the medicinal product.

AE's may include:

- Abnormal laboratory finding
- An intercurrent illness, injury, or any other concomitant impairment of the subject's health, deemed to have clinical significance
- A worsening of an existing symptom or condition or post-treatment event that occurred as a result of protocol-mandated procedures (i.e. exacerbation of a pre-existing illness following the start of the study or an increase in frequency or intensity of a preexisting episodic event or condition.

2.12.4.4.2 Reporting to IRB

Any report of an AE 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 an AE
- 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.

2.12.4.4.3 Assessment/Review

IRB administrative staff prescreens AE submissions for completeness, which includes an initial assessment of whether the information meets the criteria of an AE. 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. If the reviewer determines that the AE involves more than minimal risk to participants or others, the submission will be referred to the convened meeting for review.

2.12.4.5 Serious Adverse Events (SAEs)

2.12.4.5.1 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.

2.12.4.5.2 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.

2.12.4.5.3 Exceptions for Reporting to IRB

For non-FDA regulated 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 SAEs as they occur. These requests will be reviewed on an 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.

2.12.4.5.4 Assessment/Review

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.

IRB administrative staff prescreens SAE submissions for completeness, which includes an initial assessment of whether the information meets the criteria of a 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. 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.

2.12.4.5.5 Convened IRB Action for SAE

The following are examples of actions that are authorized by the IRB for SAEs 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;
- for-cause 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).

2.12.4.5.6 Reporting to Regulatory Agencies

If the increased risk is significant, the IRB will notify the IO. The IO will notify OHRP and/or FDA within 30 days, in compliance with the TTUHSC El Paso Federal-wide Assurance.

2.12.4.6 External Adverse Event

2.12.4.6.1 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 El Paso IRB. In order to require reporting to the TTUHSC El Paso IRB, the adverse event must exhibit all of the following characteristics:
Non-local event reported in an externally sponsored multisite research project
Unexpected
Serious
AND
have implications for the conduct of the study (e.g. requires a significant and usually safety-related change in the protocol).

2.12.4.6.2 Reporting to the IRB

Events that meet the definition must be submitted to the IRB using the Amendment form in iRIS. 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 PI may submit such events using the External Adverse Event form in iRIS. IRB administrative staff will acknowledge the submission. These reports will be available for IRB members to review, but will generally not be individually deliberated at a convened meeting of the IRB.

2.12.4.7 Sponsor Monitoring Reports

2.12.4.7.1 Definition

A report submitted by a sponsor to the PI and/or research team after each monitoring visit. Each report summarizes what the monitor reviewed during the visit, what findings were noted, and what actions were recommended or taken to ensure compliance.

2.12.4.7.2 Reporting

For sponsored studies, Sponsor Monitoring Reports must be submitted through iRIS upon receipt, using the Sponsor Monitoring Report form. Failure to do so will be viewed as non-compliance. The Research Compliance Officer reviews all Sponsor Monitoring Reports upon receipt to ensure that each research team remains compliant with institutional and federal regulations.

2.12.5 Study Closures

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

1.1.2

2.12.5.1 Study Status - Completed

Studies that have been completed (including de-identification of data) and are closed at the local research site will be designated as “Completed” in iRIS. The PI shall submit the “Study Closure Report” 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 must be de-identified and stored separately from any information that may identify the participants. Additionally, any and all other identifiable information (master list, videos, tapes, etc.) must be destroyed that the study protocol or IRB application targeted for destruction at the completion of the study. If there are any associated samples, these may also be destroyed at study closure unless the study documents and/or grant indicated any extended sample storage. Study materials must be stored by the PI’s department for a minimum of 3 years, 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.

2.12.5.2 Study Status - Cancelled

If, after IRB approval, a study is permanently closed by the PI or sponsor for any reason prior to its completion, it will be designated as “Cancelled” in iRIS. 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 “Cancelled,” all data must be de-identified and stored separately from any information that may identify the participants. Additionally, any and all other identifiable information (master list, videos, tapes, etc.) must be destroyed that the study protocol or IRB application targeted for destruction at the completion of the study. If there are any associated samples, these may also be destroyed at study closure unless the study documents and/or grant indicated any extended sample storage. 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.

2.12.5.3 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 iRIS. No new subject enrollment may take place while studies have this designation. Submission of continuing reviews, amendment, unanticipated events that may 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 PI 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.

2.12.5.4. 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 that are administratively closed. Any further activity on such studies will require the submission of a new application to the IRB.

2.13 Informed Consent

2.13.1 Documents

2.13.1.1 Template Consent Forms

Consent form templates are available for download in iRIS. Investigators must use these templates as a guide to create study specific consent forms unless the IRB grants exceptions or a waiver. The consent templates contain key information, the eight required elements, and additional elements of informed consent as required by the DHHS and the FDA, and additional IRB requirements for TTUHSC El Paso research involving human subjects. 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 this information is included.

2.13.1.2 English Document

All research studies requiring documentation of consent shall utilize one of the TTUHSC El Paso Informed Consent templates found in iRIS. 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.

2.13.1.3 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 administrative 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.

2.13.1.4 Approval and Expiration Dates

IRB-approved Informed Consent documents will have the TTUHSC El Paso seal and approval and expiration dates, as applicable, 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 studies, or the date of approval of a change to the informed consent document.

Expiration Date - The expiration date shall be the date of the expiration of the current IRB approval period. In the case of expedited reviews, an expiration date will only be assigned if the IRB determined the need to enhance the protection of research subjects. The expiration date will be calculated based on the approval period recommended by the IRB Chair (or designee) using the date of the initial IRB application or continuing review application was approved. In the case of full IRB reviews, the expiration date will be based upon the date that the IRB voted to approve the study at a convened meeting. If minor modifications are required prior to final approval, the actual approval period will be shortened. Note that approved informed consent documents may be used to document the informed consent process on the expiration date of the study. 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 PI to conduct the informed consent discussion in an unhurried manner and to assure 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 between 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) of the study team members to conduct the consent discussion;
- 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.

2.13.2 Alteration or Waiver of Informed Consent

2.13.2.1 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 witness unaffiliated with the research study must be present during the reading and will be required to sign and date the consent form as a 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.

2.13.2.2 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 must be a third party 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 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 the required elements of informed consent to the subject orally. The oral presentation must be in a language understandable to the subject. The investigator answers any questions from the prospective subject. There must be a witness to the oral presentation who is not the person obtaining informed consent, and who must be fluent in the language of the oral presentation (the interpreter may serve as the 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 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.
6) 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.

2.13.2.3 Waiver of the Informed Consent Process

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

- The research involves no more than minimal risk to the subjects;
- The research could not practicably be carried out without the requested waiver or alteration;
- If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format;
- The waiver or alteration will not adversely affect the rights and welfare of the subjects; and
- Whenever appropriate, the subjects or legally authorized representatives will be provided with additional pertinent information after participation.

An investigator who requests a waiver of informed consent for a project will include a justification of the five 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.

2.13.2.4 Waiver of Documentation of Informed Consent

In accordance with 45 CFR 46.117(c)(1), the IRB may waive the requirement for the PI to obtain a signed consent form for some or all subjects if it finds that, i) 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; ii) 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; or iii) the subjects or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not the norm, that the research presents no more than minimal risk of harm to subjects and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained.

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 in the IRB approval letter. Expedited review of requests to waive documentation of informed consent process is permitted.

2.13.2.5 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 2.18.4 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.

2.13.2.6 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 Section 3, Texas Probate 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.

2.13.3 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 provide 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 medical course or laboratory results obtained through non-invasive chart review, and addresses 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 establishing survival status.

2.13.4 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.

2.13.4.1 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 insure 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.

2.13.4.2 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 (e.g., in emergency situations).

If the subject lacks the mental capacity to offer 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.

2.13.5 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 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. Detailed instructions for obtaining the Certificate of Confidentiality can be found at NIH Grants and Funding: Intramural Research Projects.

2.14 Vulnerable Populations

2.14.1 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.

2.14.2 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.

2.14.2.1 Neonates of Uncertain Viability

No research may take place until the following conditions have been met.
The IRB finds 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's 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.

2.14.2.2 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.

2.14.2.3 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.

2.14.2.4 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.

2.14.2.5 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; the research will be conducted in accord with sound ethical principles; and informed consent will be obtained in accord with the informed consent provisions.

2.14.3 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. Additionally, a majority of board members must have no association with the prison involved. No federally funded or FDA regulated research may be conducted with prisoners unless the conditions set forth in 45 CFR 46.305 and 46.306 have been met and are reflected in the IRB minutes. Research involving prisoners may not be exempted nor may federally funded or FDA regulated initial reviews involving prisoners be expedited; there must be full board review.

2.14.3.1 Definition of Prisoners

Prisoners are any individuals involuntarily confined or detained in a penal institution. The definition includes persons who are detained pending arraignment, trial, or sentencing, and persons who become prisoners after research has begun. Persons on parole or who are not detained while awaiting sentencing, or otherwise are not involuntarily confined to a penal institution, are not considered prisoners

2.14.3.2 Types of Research Permitted

The following categories are listed in 45 CFR 46, Subpart C [section 306(a)(2)].

1. Study of the possible causes, effects, and processes of incarceration, and of criminal behavior; or
2. Study of prisons as institutional structures or of prisoners as incarcerated persons.

Because categories 1 and 2 likely do not directly benefit the subject, studies in these categories can carry no more than minimal risk. In research involving prisoners, minimal risk is 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)].

3. Research on conditions particularly affecting prisoners as a class (e.g. vaccines on illnesses that are more prevalent in prisons than elsewhere; research on psychological/social problems); or
4. Research on practices, accepted or innovative, that may have the intent and expectation of improving the health or well-being of the subject and require control groups who will not benefit from the research.

For categories 3 and 4, if the research is federally funded or FDA regulated, the IRB administrator will write the requisite letter to the Secretary of DHHS as required by OHRP.

2.14.3.3 Approval Criteria for Prisoner Research

Research involving prisoners may not be reviewed and acknowledged as exempt from formal IRB review, even if the research would be categorized in that manner if the subjects were not prisoners. Expedited review of research involving prisoners may be considered by the IRB.

Before research with prisoners can be approved by the IRB, 45 CFR 46 subpart C specifies that the following additional requirements must be met. Each specific requirement must be addressed with discussion reflected under the specific condition in the IRB minutes. Each condition must be reviewed separately, and, in the case of projects reviewed at a convened meeting of the IRB, must be voted on separately, and each vote must be recorded under the appropriate condition in the IRB minutes.

The research being reviewed falls into either category 1, 2, 3, or 4 listed above and meets the following criteria:

- Any possible advantages to prisoners participating in the proposed research do not outweigh the risks associated with the research. Discussion of this point should take into account the limited choices available in a prison environment.
- The risks to the prisoners are no greater than they would be to non-prisoners involved in the same research.
- All prisoners who meet study eligibility criteria must be considered for participation without arbitrary intervention by authorities or other prisoners. Unless the IRB members are provided written justification for other procedures, all subjects in control groups must be chosen randomly from the pool of eligible subjects.
- Information about the study must be presented to the subjects clearly and in a form that is understandable.
- Adequate assurance is given to the prisoner that participation or lack of participation in the study will not affect chances of parole. Additionally, there must be adequate assurance that parole boards will not consider the individual's participation or lack of participation in the study when making a decision.
- The IRB members must consider if there may be a need for follow-up care of participants after their part in the study has concluded and whether provision

for this follow-up has been made, taking into account the varying length of the participant's sentences and whether the participant has been informed of this fact.

- IRB members must consider that, for prisoners, "minimal risk" refers to 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.
- Epidemiological research conducted using prisoners must meet the following criteria:
  - The sole purposes are one for the following: a) to describe the prevalence or incidence of a disease by identifying all cases, or b) to study potential risk factor associations for a disease
  - The research presents no more than minimal risk and no more than inconvenience to prisoner-subjects, and
  - Prisoners are not a particular focus of the research.

2.14.3.4 Special Considerations for Participants who Become Prisoners

If a previously enrolled participant becomes a prisoner while participating in a clinical trial, the following actions are to be taken by the investigator/study team.

Confirm that the participant meets the definition of a prisoner.

Terminate enrollment of the participant and notify the IRB within 30 days of the withdrawal and the reason for the withdrawing the participant from the study.

If the prisoner's health or safety would be adversely impacted by removal from the study the investigator should consider continuing the study intervention under an alternate mechanism such as compassionate use, off-label use, etc. The IRB should be made aware of accommodations made by the study team to provide ongoing medical care for the prisoner after being removed from the study.

The following will only apply if a prisoner advocate/representative is a member of the board. Alternatively, the IRB will consider re-reviewing the project at a convened meeting under the requirements of Subpart C. The investigator will need to submit a request to the IRB to conduct this review, and will need to halt enrollment of new participants until the Subpart C review has been completed and approved. Previously enrolled, non-prisoner participants may continue to be treated as per the study protocol if the investigator and IRB agree that it is in the best interests of the health and safety of the previously enrolled non-prisoner participants.

If the IRB reviews the project under Subpart C, and some of the requirements of Subpart C cannot be met, but it is in the best interests of the participant to remain in the study, the IRB might permit the participant to remain in the study. If the project is subject to oversight by OHRP, OHRP will be notified of the decision along with the justification.

2.14.4 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 IRB 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 IRB adopts all FDA 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.

2.14.4.1 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 research that involves 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).

2.14.4.2 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.

2.14.4.3 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.

2.14.4.4 Age of majority and Reconsenting as an Adult

Informed consent should be viewed as an ongoing process throughout the duration of a research project. When a child who was enrolled in research with parental or guardian permission subsequently reaches the legal age of consent to the procedures involved in ongoing research, the subject's participation in the research is no longer regulated by the requirements of 45 CFR part 46.408 regarding parental or guardian permission and subject assent.

Unless the Institutional Review Board (IRB) determines that the requirements for obtaining informed consent can be waived, the investigators should seek and obtain the legally effective informed consent, as described in 45 CFR 46.116, for the now-adult subject for any ongoing interactions or interventions with the subjects. This is because the prior parental permission and child assent are not equivalent to legally effective informed consent for the now-adult subject. However, the IRB could approve a waiver of informed consent under 45 CFR 46.116(f), if the IRB finds and documents that the required conditions are met.

Similarly, if the research does not involve any ongoing interactions or interventions with the subjects, but continues to meet the regulatory definition of "human subjects research" (for example, it involves the continued analysis of specimens or data for which the subject's identity is readily identifiable to the investigator(s)), then it would be necessary for the investigator(s) to seek and obtain the legally effective informed consent of the now-adult subjects. The IRB may consider, if appropriate, a waiver under 45 CFR 46.116(f) of the requirements for obtaining informed consent in order for the subjects to continue their participation in the research.

2.14.5 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. PIs and/or those in a supervisory role should refrain from recruiting from their subordinates.

TTUHSC El Paso 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 El Paso, and will be taxed accordingly. Further information regarding payment of employees as research participants can be found in TTUHSC EP OP 72.19 Payment to Research Participants.

2.14.6 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 alternatives to participation are available.

Any IRB concerns regarding the use of students should promptly be forwarded to the Research Compliance Officer or to the VPR.

2.14.7 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 answered satisfactorily 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-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.

2.14.8 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.

2.15 Health Insurance Portability and Accountability Act (HIPAA)

The HIPAA Authorization form or a request for a Waiver of Authorization shall be included in initial applications for any project that utilizes protected health information. Once the HIPAA documentation has been reviewed for compliance with TTUHSC El Paso policy, it does not

need to be re-submitted for the duration of the study, unless there are changes required on the HIPAA form.

Further information regarding HIPAA compliance, including approved forms, can be found at: http://www.elpaso.ttuhsc.edu/hipaa/.

2.15.1 HIPAA Authorization

Each TTUHSC El Paso 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 the IRB administrative staff. Requests to alter HIPAA documents shall be submitted to the TTUHSC El Paso HIPAA Privacy Officer.

PI's who are members of unaffiliated organizations that have designated TTUHSC El Paso as their Privacy Board may use the TTUHSC El Paso HIPAA authorization form that is found in iRIS. All references to TTUHSC El Paso 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 addition to the TTUHSC El Paso HIPAA Authorization Form, should they so wish.

2.15.2 HIPAA Waiver Request to Privacy Board

PIs 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 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 iRIS 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 El Paso IRBs will act as Privacy Boards as defined by 45 CFR 164.512(i). IRB administrative staff shall verify Privacy Board Agreements with affiliated Entities are in place prior to a Privacy Board Review. The Sr. Director is a member of the Privacy Board and may acknowledge HIPAA waiver requests.

2.16 Recruitment Methods

2.16.1 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, they 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 distribution 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.

2.16.2 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 as 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 El Paso 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 be not 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.

2.16.2.1 Additional approval

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

2.17 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.

2.17.1 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.

2.17.2 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 El Paso payment system, but the compensation will be subject to appropriate withholding taxes. 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 EP OP 72.19 Payment to Research Participants and TTUHSC EP 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.

2.17.3 Alterations in Payments

Any alterations in previously approved amount(s) or timing of human research subject payment or revision 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.

2.17.4 Documentation

The PI must keep documentation of payment(s) made to each subject in study files and retain them for three years after the study is completed. All records shall be made accessible for inspection and copying by authorized TTUHSC El Paso representatives. This includes but is not limited to TTUHSC El Paso Accounting and Research Compliance administrators, TTUHSC El Paso auditors, the VPR, and federal regulatory officials. Additional details can be found in TTUHSC EP OP 72.19 Payment to Research Participants.

2.17.5 Finder's Fees

Due to the conflict of interest created by offering such incentives, TTUHSC El Paso 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 El Paso also prohibits any payments to study personnel designed to accelerate the recruitment rate and that are tied to the rate or timing of enrollment (bonus payments). 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.

2.18 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 a FDA investigational device exemption (IDE), detailed in 21 CFR 812.

2.18.1 Investigational Article Accountability

The PI 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 a qualified pharmacist or individual health care provider. However, the PI is still ultimately responsible and should maintain internal controls to ensure guideline compliance.

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

The PI, 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 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.

2.18.2 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. This FDA number or letter waiving the requirement for an FDA number shall be included in the submission to the IRB.

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 IRB.

2.18.3 Expanded Access

The use of an investigational drug when the primary purpose is to diagnose, monitor, or treat a patient's disease or condition and the use is not primarily intended to obtain information about the safety or effectiveness of a drug, detailed in (22 CFR 312).

There are three categories of expanded access:
• Expanded access for individual patients, including for emergency use (21 CFR 312.310)
• Expanded access for intermediate-size patient populations (generally smaller than those typical of a treatment IND or treatment protocol — a treatment protocol is submitted as a protocol to an existing IND by the sponsor of the existing IND)9 (21 CFR 312.315)
• Expanded access for widespread treatment use through a treatment IND or treatment protocol (designed for use in larger patient populations) (21 CFR 312.320)

2.18.4 IDE Application

IDE regulations specify that there are two different types of device studies, "significant" risk (SR) and "non-significant" 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.

2.18.4.1 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 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 assessment and the rationale for making the determination [21 CFR 812.150(b)(10)].

2.18.4.2 Non-significant 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. The determination of NSR is made by the sponsor.

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

2.18.4.3 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.

2.18.5 Emergency Use of Investigational Drug/Device

Emergency use is defined as the use of an investigational drug or biological product or investigational medical device 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 El Paso IRB if the physician responsible for the investigational drug/device is full time faculty at TTUHSC El Paso. 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 the 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.

The term '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 El Paso.
- 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,
    1. the patient is (was) in a life-threatening situation;
    2. there is (was) no standard acceptable treatment available;
    3. there is (was) not sufficient time to obtain IRB approval;
- a description of the anticipated consent process including the method of documentation.
- Documentation that the appropriate hospital administrator has been notified.

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 time-frame 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 adverse events or unanticipated problems

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

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 El Paso IRB should receive a copy of the report to the FDA and sponsor as well as any follow-up information received.

2.18.6 Planned Emergency Research

TTUHSC El Paso does not intend to conduct planned emergency research. However, in very limited circumstances, the TTUHSC El Paso 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 El Paso HRPP representatives prior to protocol development or when receiving a proposed protocol from an external sponsor.

2.18.7 Humanitarian Device Exemption (HDE)

A humanitarian device exemption requires IRB review and approval of a humanitarian use device (HUD). An HUD is a medical device intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in fewer than 4,000 individuals in the United States per year.

The IRB is responsible for initial as well as continuing review of the HUD. Initial review should be performed at a convened IRB meeting (21 CFR 56.108). For continuing review, the IRB may use the expedited review procedures (21 CFR 56.110). The IRB does not need to review and approve individual uses of an HUD, but rather the IRB may

approve use of the device as it sees fit. That is, the IRB may approve use of the HUD without any further restrictions, under a protocol, or on a case-by-case basis.

The IRB is responsible for ensuring that HDE approval has been granted before approving the device for use. A consent document provided by a sponsor may be used. Because the use of an HUD is for diagnosis or treatment purposes only, the HIPAA regulations for research are not applicable. Therefore, a HIPAA Research Authorization and/or Waiver of Authorization are not required. Modifications and/or unanticipated event reporting is as described in those sections.

The following materials should be submitted for review:

- A study application which includes how the physician proposes to use the device, a description of any screening procedures, the HUD procedure, any patient follow-up visits, tests and/or procedures.
- a copy of the HDE approval order;
- a description of the device;
- the product labeling;
- the patient information packet that may accompany the HUD;
- a consent form for the use of the HUD; template available in iRIS and on the IRB website.

2.19 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.

2.19.1 Prospective Collection and Use of Human Specimens for Research Purposes

IRB approval 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 and approval 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. IRB will typically require written consent/authorization from each research participant.

2.19.2 Use of EXISTING Human Specimens for Research Purposes

2.19.2.1 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 and conditions. Exception: permission is required for use of human embryonic stem cells, regardless of source.

2.19.2.2 Fee-for-service analyses of human cells or cell lines

TTUHSC El Paso 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 outside of TTUHSC El Paso solely on a commercial (non-collaborative) basis.

2.19.2.3 Identifiable commercially available human cells or cell lines

IRB review and approval **is 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; the IRB, not the investigator, will make this determination.

2.19.2.4 Identifiable human cells or cell lines obtained from collaborators outside of TTUHSC El Paso

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

2.19.2.5 Secondary use of identifiable previously-collected excess (i.e., otherwise to be discarded) clinical specimens from within TTUHSC El Paso 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 El Paso 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.

2.19.3 Special Categories of biological specimens

2.19.3.1 Human embryonic stem cells (hESC)

TTUHSC El Paso permission is required for research on existing human embryonic stem cell (hESC) lines, and IRB approval is required for the derivation of new hESC lines. In addition, there are other special ethical, legal, financial, and institutional issues related to the research use of hESCs. Investigators are asked to contact the IRB prior to any use of hESC cells or any derivation of new hESC lines at TTUHSC El Paso or its affiliated hospitals.

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

2.19.3.2 Fetal Tissue Specimens

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

2.19.3.3 Transfer of samples to research collaborators outside of TTUHSC El Paso

IRB must review any plan to transfer human specimens that were collected for research purposes (generally as part of a TTUHSC El Paso 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 TTUHSC El Paso OSP. Note**:** Transfer of **non-identifiable** human specimens from an IRB-approved TTUHSC El Paso Tissue Repository to another investigator, if approved by IRB as one of the procedures of the tissue bank, does NOT require separate IRB review and approval. This is because IRB already will have reviewed and approved the procedures of the Tissue Repository, which describes such transfers.

2.20 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 chromosomal 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 of 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 subjects 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 inherited).
- A clear statement that the sample/data, any cell lines, profits from data etc., are the property of TTUHSC El Paso 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 non-medical 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. This information must be clearly stated in the informed consent document.

2.20.1 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.

2.20.2 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.

2.20.3 Genetic Information Nondiscrimination Act (GINA)

The following information should be included in TTUHSC El Paso 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 following OHRP Guidance document: http://www.hhs.gov/ohrp/policy/gina.pdf.

2.21 Research Compliance

TTUHSC El Paso IRBs are authorized to monitor research involving human subjects approved by the IRB pursuant to the responsibilities and assurances made by TTUHSC El Paso under federal regulations (FWA 00020736) and TTUHSC El Paso Policy (TTUHSC EP OP 73.06

Research Involving Human Subjects and TTUHSC EP OP 73.14 Research Compliance). The Office of Research Resources shall be responsible for compliance activities on behalf of the IRB and VPR, including audits and monitoring of IRB approved research as described on the TTUHSC El Paso Research Compliance Manual.

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.

As an educational component, the Research Compliance Unit provides continuous educational training sessions on a variety of research related topics. In addition, research staff are highly encouraged to conduct routine self-monitoring of their studies. A self-monitoring tool has been created for this purpose. Please review information provided on the Research Compliance website.

2.21.1 Definitions

2.21.1.1 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 El Paso IRB, or
- TTUHSC El Paso policies and procedures governing human subjects research, or
- the research activities as approved by the TTUHSC El Paso IRB's.

Non-compliance is also defined as a:

- violation of any regulation that governs human subject research or of any institutional policy for human subjects research;
- violation of any conditions imposed by the IRB on the approval of the study or conduct of the research; or
- deviation or departure from an IRB-approved protocol.

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.

2.21.1.2 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.

2.21.1.3 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).

2.21.2 Reporting Non-compliance

The Office of Research Resources encourages the reporting of non-compliance by the PI, members of 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 potential non-compliance is reported by someone other than the PI, efforts 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. For more detailed information regarding allegations of research non-compliance, please refer to the **TTUHSC El Paso Research Compliance Manual.**

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

2.21.3 Regulatory Compliance Audits

The Research Compliance Officer conducts regulatory compliance audits on research approved by the TTUHSC El Paso IRB. These audits are conducted based upon allegations reported to the ORR or the IRB, 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. Audits will also be conducted on research that is determined to be exempt.

The PI is generally notified of the audit at least two weeks in advance and is provided with a scheduled date and time. The date may be adjusted to work with the PI’s schedule, but the audit may not be postponed for more than 30 days.

Each audit may have a targeted educational component that teaches research faculty and staff how to correct their mistakes and prevent the same mistakes in the future. An audit report is generated from each audit investigation and may be submitted to the IRB and/or Compliance representatives. For non-exempt research, an audit report is then

generated by the IRB and submitted to the PI/research personnel, the Department Chair, and Compliance Representatives on behalf of the IRB.

For more detailed information regarding allegations of research non-compliance, please refer to the **TTUHSC El Paso Research Compliance Manual.**

2.21.4 IRB Review of Audit reports

For routine non-exempt 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. The IRB then distributes the report to the PI/research personnel, Department Chair, IRB, and compliance representatives, through iRIS. Audit reports from exempt protocols will be reviewed by the Research Compliance Officer/designee, and distributed to Compliance Representatives, the PI/research personnel and Department Chair.

Findings involving serious or continued non-compliance *may* be submitted to an IRB subcommittee. The subcommittee can determine whether or not they are in agreement with the findings and what corrective actions they recommend. From there, the subcommittee will submit more difficult findings to the full-board for review and to determine what corrective actions will be appropriate for the items in question. A copy of the audit report may be placed on the next agenda for full board review. For regular non-compliance the IRB Chair, Sr. Director and/or Research Compliance Officer may determine what corrective actions are necessary without the need of full-board review.

The Research Compliance Officer will work with the PI, if requested, to implement any recommendations that were included in the audit report. Failure by the PI 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 of non-exempt research, 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 findings and recommendations will be reviewed. The IRB will make a final determination as to whether the findings meet the definition of serious and/or continuing non-compliance. The IRB will determine what corrective actions will be required or if there are any additional aspects of the corrective action plan that need to be implemented.

Following the IRB’s review of the audit findings and any additional determinations that they have made, the PI/research personnel will be notified (via iRIS) of the outcome of the review. If the IRB offers a plan of correction, the specific changes to be implemented will be communicated, and the changes will need to be implemented within 30 days.

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 VPR and Managing Director of the ORR will be notified of any IRB determinations of serious or continuing non-compliance and any decision to suspend or terminate a research project. The VPR will be responsible for notifying DHHS and/or the FDA (if necessary) or any other oversight or sponsoring agency. The Department Chairperson of the PI will also be notified of these decisions by the IRB.

CHAPTER 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 TTUHSC El Paso policies and procedures.

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

The Office of Research Resources (ORR) provides administrative support to the TTUHSC El Paso 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 El Paso HRPP can find more information at the TTUHSC El Paso Human Research Protection Program website. Contact information for IRB administrative staff, current IRB rosters, IRB deadlines and meeting dates, as well as links to other helpful information can be found at the site.

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. These 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

3.4.1 Education Requirements

All PIs, all Co-Investigators, and research staff are required to receive training regarding the protection of human research subjects and financial conflict of interests ***prior to*** beginning any human research-related activities. This training will be verified prior to iRIS access being granted. Initial approval of IRB submissions will be withheld until all

study personnel have been verified as having completed/updated training and financial disclosure reports.

3.4.1.1 Human Subject Protection Training and Financial Conflict of Interest Training

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 administered by the University of Miami through the Collaborative IRB Training Initiative (CITI). The web-based courses currently required by TTUHSC El Paso are the following:

- Human Subjects Research Course: Research Investigators, Research Personnel, and IRB members
- Clinical Research Coordinator Course: All Research Coordinators and key research personnel who are responsible for performing similar duties.
- Good Clinical Practice: All Research Investigators and research personnel involved with drug and/or device studies.
- Conflict of Interest course: All Research Investigators research personnel, and voting members of the TTUHSC El Paso research compliance committees.
- Informed Consent Training: Research Investigators and research personnel involved with research studies that will involve obtaining informed consent. This training is available online through ACME and may be requested at: http://elpaso.ttuhsc.edu/research/compliance/Training.aspx.
- Responsible Conduct of Research (RCR): Required for certain pharmaceutical sponsors and certain categories of researchers receiving funding from the National Institutes of Health (NIH), National Science Foundation (NSF) and the U.S. Department of Agriculture (USDA).

3.4.1.2 New CITI Account Instructions

Registration
To set up a new CITI account, go the CITI website and select "Register". After selecting "Texas Tech University Health Sciences Center El Paso" as your organization affiliation (Step 1), continue through the multiple step process to establish your Username and Password (Steps 2-6). On the CITI curriculum page (Step 7) select the **Human Subjects Research Course, Clinical Research Coordinator Course, Good Clinical Practice Course**, and the **Conflict of Interest Course.** This will provide you access to the required modules. TTUHSC El Paso personnel must use their TTUHSC El Paso email address for registration. More information on CITI Training can be found at the CITI Program Support Center or on the TTUHSC El Paso Research Website.

Course Completion
Upon successful completion of the course, you will be able to download a course transcript (for your records). TTUHSC El Paso is also notified of your successful completion of the courses. You will be required to achieve an overall score of at least 80% to successfully complete the courses.

3.4.1.3 CITI Renewal Training

All investigators and research staff are required to renew their Human Subjects Research Training, Clinical Research Coordinator Training, and Good Clinical Practice Training at least once every 3 years; the Conflict of Interest training is every

4 years. Initial approval of IRB submissions will be withheld until all study personnel have been verified as having completed/updated training and financial disclosure reports. Additionally, approval of continuing reviews may be denied if training of any study personnel has lapsed. Renewal training is identical to the initial CITI course. Lapsed training will also be reported as a finding requiring correction on any routine or for-cause audits conducted.

3.4.2 Research Financial Disclosure

All research staff must have a current Annual Research Financial Disclosure statement on file with the ORR in accordance with TTUHSC EP OP 73.09 Financial Conflicts of Interest in Research. The link to the Financial Disclosure form is available at http://elpaso.ttuhsc.edu/research/financial-disclosure.aspx.

3.4.3 Investigator Conflicts of Interest

All TTUHSC El Paso investigators and study personnel are bound to the policies set forth in TTUHSC EP OP 52.06 Standards of Conduct and Ethics, TTUHSC EP OP 10.05 Conflicts of Interest and Commitment and TTUHSC EP OP 73.09 Financial Conflicts of Interest in Research. Unaffiliated investigators may also be bound to these policies if their own institutions do not have internal conflict of interest policies. Failure of any PI and associated research personnel to comply with these policies may result in suspension of submission privileges. In accordance with the TTUHSC EP 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 more frequently as circumstances change.

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 EP OP 73.09 Financial Conflicts of Interest in Research. The IRB will not continue the review of a submission until the COIRC has met and made its recommendations, and the investigator has adequately addressed these. The IRB must also approve the CMP prior to enrollment of any human subjects. Affiliated entities should submit documentation to the IRB specifying how the identified conflict of interest will be managed.

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 EP OP 10.05 Conflicts of Interest and Commitment and TTU System Regents' Rules, Chapter 10.

3.4.4 iRIS Access

All submissions to a TTUHSC El Paso IRB must be submitted using the Internet Medical Research Information System (iRIS) software. In order to gain access to the system, all users must **first** complete the CITI training, submit a financial disclosure form, and complete all other required training. The iRIS access request is web-based and can be found at the following website: https://ttuep.imedris.net.

INSTRUCTIONS: Click on the “Request New Account” link underneath the login area, and complete the request, including phone numbers, and TTUHSC El Paso email address. Enter ‘N/A’ or “NONE’ in fields that do not apply (i.e. Outside collaborators do not have an eRaider). Please add a note detailing the reason for needing access to iRIS

(i.e. to participate on a human research project or to participate on an animal research project or to participate on a specific committee, etc).

3.5 Who can be a TTUHSC El Paso PI?

Faculty status is required for all PIs. Exceptions may be granted on a case-by-case basis by the VPR. Details may be found in TTUHSC EP OP 73.08 Requirements for PI Status.

3.6 Who can be a PI from an affiliated entity?

Employees of entities affiliated with TTUHSC El Paso may not be designated as a PI in a research study.

Collaborators from institutions may be listed in other roles, and must comply with all TTUHSC El Paso policies and procedures.

3.7 Non-Salaried Appointments

Personnel with a Non-Salaried faculty appointment may not be PIs on TTUHSC El Paso IRB applications, but may be listed as coinvestigators. If listed as participants in a project, non-salaried faculty must comply with all TTUHSC El Paso policies and procedures.

3.8 Non-TTUHSC EP Research Personnel

Non-TTUHSC EP personnel who will be conducting research activities on campus will first need to submit an application to be processed as a research volunteer. This is done through the ORR and includes completion of safety training courses, HIPAA training, a criminal background check, orientation, and an immunization review. Additional information can be found at: http://elpaso.ttuhsc.edu/research/orr/volunteer.aspx. Successful completion of the prerequisites will allow the personnel to obtain an iRIS account once research training has been completed. However, research volunteers may not provide treatment or patient care services, write orders or notes in patient charts, obtain consent, or have TTUHSC El Paso computer privileges.

Non-TTUHSC EP personnel who will be collaborating on a research project and will not be physically present on campus will not be processed as a research volunteer and do not obtain an iRIS account. Typically, personnel in this position are considered to be consultants or may only be involved in the analysis of deidentified data, and/or they may have their own institutional IRB approval to collaborate on the project.

Non-TTUHSC EP personnel who will be collaborating on a research project and will not be physically present on campus, but will be involved in the analysis of identifiable information (limited dataset), are not processed as a research volunteer and do not obtain an iRIS account. However, they will be required to obtain a data use agreement.

3.9 PI Responsibility for Research Activities

The PI 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 authorized research personnel in accordance with TTUHSC El Paso IRB Policies and Procedures. Ensuring that prompt and proper payment of subjects 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 PI.

3.9.1 Notice of Absence

PIs 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. (See TTUHSC EP OP 60.02 Faculty Development Leaves of Absence) The 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.

3.10 Preparing the IRB Submission

The TTUHSC El Paso IRBs use the web-based iRIS program to review and track research study information. PIs and research personnel **must use** this software to submit study-related information to the IRB. The iRIS site is located at https://ttuep.imedris.net. In order to obtain access to iRIS, you must first "Request a New Account" by clicking on the button on the iRIS home page. After your account is activated, you will return to this website to enter 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 never 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 PI and the IRB. IRB administrative staff is available to respond to questions by email or phone.

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 El Paso IRB-approved format (required for all non-exempt studies);
- Authorization to Use and Disclose PHI for Research (HIPAA authorization), included with the biomedical consent template and/or HIPAA waiver request, included with the study application
- 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 EP institutional committees as applicable;
- Curriculum Vitae of PI (uploaded onto the iRIS account).

Materials for initial review shall be submitted by the established deadlines (see the IRB website for current deadlines at http://elpaso.ttuhsc.edu/research/committees/irb/submission-deadlines.aspx.

3.10.1 Relation to Other Committees

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

- Conflict of Interest Research Committee (COIRC)
- Institutional Biosafety Committee (IBC)
- Radiation Safety Committee (RSC)

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

3.11 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 VPR and Managing Director of ORR 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 $1000.
Currently, there is no fee for reviews of amendments to a 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. However, in reliance agreements where the TTUHSC El Paso IRB is designated as the Reviewing IRB, IRB fees may apply.

3.11.1 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 VPR, who has discretion and makes the final decision about whether or not fees will be waived.

3.11.2 Indirect Cost Rate for Industry Sponsored Clinical Trials

For corporate and industry sponsored clinical trials, TTUHSC El Paso's minimum rate is 31% of total indirect 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.

3.12 Compensation for Research Related Injury

Federal regulations [45 CFR 46.116(a)(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 El Paso 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 El Paso to conduct greater than minimal risk research make provisions for the coverage of all costs of necessary treatment for any injury, illness, 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 El Paso requirements can be found in TTUHSC EP OP 73.17, Research Related Injury in Privately Sponsored Research Studies.

3.13 Clinical Trial Registration

The sponsor and/or principal investigator of any applicable clinical trial must register the study on a publicly accessible trial registration site prior to enrolling the first subject, or within 21 days after enrollment depending on the specific agency's requirement. **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, the NIH, and ICMJE all have similar requirements for registration of applicable clinical trials. If an IRB-approved study is a clinical trial that has not been registered by the study sponsor, it may be the PI's responsibility to register the trial. The Protocol Registration System website provides specific information regarding how to register a new trial. The individuals in the Research Compliance Unit of ORR serve as the TTUHSC El Paso administrators 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 El Paso biomedical informed consent template.

A new mandate called the 2018 Revised Common Rule has also recently been released with revisions related to reporting clinical trials. As of January 21, 2019, all non-exempt clinical research that has been approved on or after this date will need to have a blank version of an approved informed consent form uploaded onto either **ClinicalTrials.gov** or **Regulations.gov** no later than 60 days after the last study visit by any subject. Older studies that have adopted the 2018 Revised Common Rule must also meet this requirement.

For more information on ClinicalTrials.gov and Regulations.gov requirements, please refer to the **TTUHSC El Paso Research Compliance Manual**.

3.14 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 representative. Authorized study personnel shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient 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 representative 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 El Paso or its agents from liability for negligence. Investigators must strive to write consent documents in language that would be understandable to a reader with a 7th grade education.

All TTUHSC El Paso research studies shall utilize one of the TTUHSC El Paso Informed Consent templates found in iRIS. 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 PI shall maintain all original consent documents. Original paper documents, once scanned into the electronic health record, can be used in place of the original paper source document. The FDA will allow electronic storage if the electronic copies are certified. As defined by the FDA, a certified copy is a copy of original information that has been verified, as indicated by a dated signature, as an exact copy, having all of the same attributes and information as the original. After scanning into the electronic medical record, the paper document may be destroyed as long as it meets the FDA requirements. As with all research activities, the principal investigator (PI) is responsible for maintaining adequate records. The PI should therefore ensure that this guidance is followed when implementing electronic storage of research study documents.

3.14.1 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.

3.14.2 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/oral presentation of the informed consent can be conducted as described elsewhere in this manual.

For studies with an approved informed consent document written in a foreign language, any other documents that will be provided or used with subjects will also need to be translated, as stated above.

3.14.3 Approval and Expiration Dates

IRB-approved Informed Consent documents will have the TTUHSC El Paso seal and approval and expiration dates 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 studies, or the date of approval of a change to the informed consent document.

Expiration Date - The expiration date shall be the date of the expiration of the current IRB approval period. In the case of expedited reviews that do not require continuing review, an expiration date will not be indicated. In the case of full board reviews, the expiration date will be based upon the date that the IRB, at a convened meeting, voted to approve the study. If minor modifications are required prior to final approval, the actual approval period will be shortened. Note that approved informed consent documents may be used to document the informed consent process on the expiration date of the study.

3.15 Recruitment and Advertising

All research studies are approved to recruit only the number of subjects indicated on the IRB approval letter. If the PI finds that actual recruitment is approaching that limit, an Amendment should be submitted requesting an increase in the number of subjects to be enrolled in the study. Over-enrollment should be reported to the IRB as an Unanticipated Event (see Section 2.12.4)

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. When recruiting the following methods may be used:

- Direct Person-to-Person Solicitation
- Letter of Solicitation
- Telephone Solicitation
- Newspaper Solicitation
- Posted notices of Solicitation
- Other

Recruitment that involves Direct Person-to-Person Solicitation must abide by the following criteria:

- The recruiter must be approved by the IRB to work on the protocol
- The recruiter must be delegated responsibility to recruit by the principal investigator
- The recruiter must have a direct or prior relationship with the individual being recruited
- The individual being recruited must be approached in private and in person by the recruiter
- The recruiter may not delegate recruitment to anyone outside of individuals approved to work on the protocol

Recruitment that involves telephone solicitation refers to potential subjects who contact researchers based on posted notices or contacting those who have previously signed a consent to contact for future research form.

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.

3.15.1 Finder's Fees

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

3.16 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.

3.16.1 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.

3.16.2 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 EL Paso musty comply with TTUHSC EP OP 72.19 Payment to Research Participants and TTUHSC EP OP 72.12 Payment to Nonresident Aliens.

3.16.3 Disclosure of Payments

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

3.16.4 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.

3.17 Investigational Drugs/Devices

3.17.1 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 a 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 PI 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 the sponsor 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 IND. The TTUHSC El Paso IRB will not approve a project until a valid IND is in effect.*

3.17.2 Emergency Use

An emergency exists when (a) a patient/subject meets the 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 El Paso.

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.

3.17.3 IVD Studies

FDA has issued guidance for studies involving the use of an in vitro diagnostic device (IVD) to analyze a sample whose donor is not individually identifiable. FDA will exercise

enforcement discretion (choose not to enforce a regulation) with respect to its current regulations governing the requirement for informed consent when such human specimens are used for FDA regulated IVD investigations. If specific conditions are met, FDA does not intend to object to the use, without informed consent, of leftover human specimens -- remnants of specimens collected for routine clinical care or analysis that would otherwise have been discarded – for IVD investigations.
http://www.fda.gov/RegulatoryInformation/Guidances/ucm078384.htm

3.17.4 Storage, Handling, and Dispensing of Investigational Agents

The PI 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 and/or individual health care provider. However, the PI is still ultimately responsible and should maintain internal controls to ensure guideline compliance.

The PI must designate a single, centralized location as custodian to receive and manage the investigational articles (i.e., the shipping address).

Regardless of where the investigational agent is retained, the PI, 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 PI 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 PI will ensure a copy of the current protocol is provided prior to dispensation of any investigational agent. Further, the PI 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.

3.18 Packaging and Shipment of Infectious Materials

The PI is responsible for overseeing training and ensuring that all specimens packaged and shipped from TTUHSC El Paso complies with TTUHSC EP OP 75.13 Shipment of Hazardous or Infectious Materials. A PI will also be required to have an approved Institutional Biosafety Committee License.

3.19 Recordkeeping and Confidentiality

3.19.1 Recordkeeping

Every PI is required by TTUHSC El Paso 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 PI's records. It is highly recommended to utilize the iRIS subject management module to register and track all study subjects.

All records of human subject research are subject to inspection by federal authorities, TTUHSC El Paso officials, including but not limited to ORR and Compliance Officers, VPR and the IRB. Research records (including data/specimens) are the property of TTUHSC El Paso and shall not be transferred to another entity without prior approval of the VPR. 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, by the PI's department. 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.

3.19.2 Confidentiality

An issue of primary importance is the protection of subject confidentiality. The PI 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 PI 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. PIs 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 using FDA-regulated articles must be kept in accordance with current FDA regulations or life of the data, whichever is longer.

3.19.3 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.

3.20 Useful Tools for Investigators

3.20.1 PI Responsibilities

The PI 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, 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 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
- 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 a 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

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, ensuring 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

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

The TTUHSC El Paso HRPP offers training on principles of ICH-GCP through the CITI Program Good Clinical Practice course (CITI Program). 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 El Paso.

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 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 researcher 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 until there are no pending or contemplated marketing applications in an ICH region or at least two years have elapsed since the formal discontinuation of clinical development of the investigational product.

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 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 or suspends 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:

The objectives of the trial cannot be met by means of a trial in subjects who can give informed consent personally.

The foreseeable risks to the subjects are low.

The negative impact on the subject's well-being is minimized and low.

The trial is not prohibited by law.

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.

3.20.3 Regulatory Files Binder Items

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

Binder Cover
This cover helps identify a binder without having to open the binder. The binder cover should include the PI name, protocol title, protocol number, IRB number.

Table of Contents
To organize the binder so that documents can be found quickly.

Study Team Contact Information (optional)
This includes a 24-hour contact person/number. This is meant to provide contact information for all the study team members and the sponsor or CRO. This is normally required for sponsored studies.

Delegation of Authority Log
This document helps identify the study team members and their roles, responsibilities, signature and initials, and the dates that they worked on the study.

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 the study. If required by the sponsor, ensure that the protocol title page has been signed and dated by the PI.

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 PI 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 and Licenses
Copies of the current CVs for all personnel listed on the FDA Form 1572. Copies of medical licenses should also be included in this section.

Training Records
Maintain a training log in order to document that all the personnel involved with the clinical trial are adequately trained and informed about the protocol, investigational product (IP), and their trial-related functions.

Financial Disclosure Forms
To document for the sponsor and TTUHSC EP, potential conflicts of interest or lack thereof. If the sponsor or TTUHSC EP determines that a COI exists, a management plan must accompany the disclosure forms.

IRB Membership Rosters (optional)
To document IRB compliance with applicable regulatory requirements. This is normally required for sponsored studies.

IRB Correspondence
All correspondence between the PI and the IRB regarding the 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 iRIS, and a separate file may not be required.

IRB-Approved Informed Consent Form
Maintain 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 iRIS or in the EHR, for example). Paper copies of consent documents, which are stored securely and available electronically, may be shredded.

Ancillary Approvals and Hospital Approvals (if applicable)
Retain all approvals to conduct the study at locations outside of TTUHSC EP. Maintain all approvals and additional reviews from ancillary committees such as RDBC and IBC.

Laboratory Certification (if applicable)
Obtain a copy of the most recent certificate issued showing the expiration date. CAP and CLIA should be retained to certify that the lab has valid credentials.

Range of Normal Values for the Reference Laboratory (if applicable)
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 (if applicable)
Includes sponsor investigational drug shipping inventory, drug dispensing log, and return shipment documentation.

Handling Investigational Product (IP) (if applicable)
Instructions for handling the investigational product and the trial related materials. This section is useful in order to document instructions needed to ensure proper storage, packaging, dispensing and disposition of the IP.

Record of Retained Body Fluids/Tissue Sample (if applicable)
To document that the investigator received instructions on how to obtain samples. To document samples obtained.

Monitoring Log (if applicable)
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.

External Safety Letters (IND Letters) (if applicable)
To document receipt of, and investigator's review of, external adverse events.

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

Blank Case Report Forms (if applicable)
Maintain all blank versions of case report forms provided by the sponsor or created by study personnel.

Written Requirements (optional)
To document receipt and review of sponsor requirements and/or updates. This is typically a requirement for sponsored studies.

Deviation and Note-to-Files
All copies of deviation outcome letters from the IRB and note-to-files should be maintained along with a protocol deviation log.

Subject Compensation (if applicable)
Evidence for subject compensation should be maintained along with receipts and subject compensation logs.

Final Study Report (if applicable)
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.

Research Team Minutes
To document pertinent discussions of trial related activity and oversight by the principal investigator.

CHAPTER 4 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 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.

ADVERSE EVENT (AE) Any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject's participation in the research, whether or not related to the subject's participation in the research. Also see: Internal Adverse Event; External adverse event; Unanticipated Adverse Event; Unanticipated Problem; Serious Adverse Event.

ALCOA This refers to the attributes that should be demonstrated in all source documents.

- Attributable
  - It should be clear who has documented the data.
- Legible
  - Readable and signature lines identifiable.
- Contemporaneous
  - The information should be documented in the correct time frame along with the flow of events. If a clinical observation cannot be entered when made, chronology should be recorded. Acceptable amount of delay should be defined and justified.
- Original
  - Original, if not original should be exact copy; the first record made by the appropriate person. The investigator should have the original source document.
- Accurate
  - Accurate, consistent and real representation of facts.

APPROVED The IRB has reviewed the study and made a determination that the study has met all requirements. Subjects may be enrolled in the study.

APPROVED DRUGS In the U.S., the Food and Drug Administration (FDA) must approve a substance as a drug before it can be marketed. The approval process involves several steps including pre-clinical laboratory and animal studies, clinical trials for safety and efficacy, filing of a New Drug Application by the manufacturer of the drug, FDA review of the application, and FDA approval/rejection of application.

ARM Any of the treatment groups in a randomized trial. Most randomized trials have two "arms," but some have three "arms," or even more.

ASSENT Agreement by an individual not competent to give legally valid informed consent (e.g., a child or decisionally impaired person) 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 trial-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.

AUTONOMY Personal capacity to consider alternatives, make choices, and act without undue influence or interference of others.

BASELINE 1. Information gathered at the beginning of a study from which variations found in the study are measured. 2. A known value or quantity with which an unknown is compared when measured or assessed. 3. The initial time point in a clinical trial, just before a participant starts to receive the experimental treatment which is being tested. At this reference point, measurable values such as CD4 count are recorded. Safety and efficacy of a drug are often determined by monitoring changes from the baseline values.

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.

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.

BENEFIT A valued or desired outcome; an advantage.

BIOLOGIC Any therapeutic serum, toxin, anti-toxin or analogous microbial produce applicable to the prevention, treatment, or cure of diseases or injuries.

BLINDING (OR MASKING) A clinical trial design strategy in which one or more parties involved in the trial, such as the investigator or participants, do not know which participants have been assigned which interventions.

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 46.401(a)].

CLINICAL RESEARCH ASSOCIATE (CRA) Person employed by the study sponsor or CRO to monitor a clinical study at all participating sites. See also, monitor.

CLINICAL RESEARCH COORDINATOR (CRC) Site administrator for the clinical study. Duties are delegated by the investigator. Also called research, study or healthcare coordinator, and data manager, research nurse or protocol nurse.

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.

CLINICALTRIALS.GOV IDENTIFIER (NCT NUMBER) A unique identification code is given to each clinical study registered on ClinicalTrials.gov. Because the format is "NCT" followed by an 8-digit number (for example, NCT00000419), this identifier is also known as the NCT Number.

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 El Paso, or by an affiliated entity. No research activities may occur after the closure date.

COLLABORATIVE RESEARCH is defined as research conducted in cooperation with an institution or faculty that is not affiliated with TTUHSC EP. When two or more institutions are engaged in research, multiple IRBs are responsible for providing oversight. As such, separate applications may be necessary; however, to avoid duplicate review an IRB Reliance Agreement may be arranged to establish one IRB as the designated IRB of Record.

COMMON RULE 1991 agreement to cover all federal-sponsored research by a common set of regulations.

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 PI 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; refers 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 A conflict of interest refers to a situation in which an Employee's financial, professional, or other personal considerations may directly or indirectly affect, or have the appearance of affecting, the Employee's judgment in exercising any duty or responsibility, including the conduct or reporting of research, owed to the Institution.

CONFLICT OF INTEREST IN RESEARCH COMMITTEE See TTUHSC EP OP 73.09 Financial Conflicts of Interest in Research The Conflict of Interest Committee is appointed by the VPR 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. [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 research performed under a grant.

CONTRACT RESEARCH ORGANIZATION (CRO) A person or an organization (commercial, academic or other) contracted by the sponsor to perform one or more of a sponsor's study-related duties and functions.

CONTROL GROUP A comparison group of study subjects who are not treated with the investigational agent. The subjects in this group may receive no therapy, a different therapy, or a placebo.

CORRECTIVE AND PREVENTIVE ACTION (CAPA) An effective CAPA program will include incident identification, investigation of incident causality, development of an action plan based on root cause analysis, action plan verification and validation, action plan implementation, effectiveness checks and closure.

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. Also referred to as a data monitoring committee (DMC).

DATA USE AGREEMENT (DUA) is an agreement between Texas Tech University Health Sciences Center El Paso and an outside party (e.g., contractor, private industry, academic institution, federal or state agency), when the outside party requests the use of non-public data that is subject to some restrictions on its use. Specifically, DUAs address important issues such as limitations on use of the data, obligations to safeguard the data, and privacy rights that are associated with transfers of confidential or protected data.

DECISIONALLY IMPAIRED Persons who may be compromised in any way (temporarily or permanently) in the ability to make decisions in their best interest.

DECLARATION OF HELSINKI A series of guidelines adopted by the 18th World Medical Assembly in Helsinki, Finland in 1964. The Declaration addresses ethical issues for physicians conducting biomedical research involving human subjects. Recommendations include the procedures required to ensure subject safety in clinical trials, including informed consent and Ethics Committee reviews.

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.

DEMOGRAPHIC DATA Refers to the characteristics of study participants, including sex, age, family medical history, and other characteristics relevant to the study in which they are enrolled.

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 may include diagnostic test kits, crutches, electrodes, pacemakers, arterial grafts, intraocular lenses, and orthopedic pins or other orthopedic equipment.

DEPARTMENT OF HEALTH AND HUMAN SERVICES (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.

DOCUMENTATION All records, in any form (including, but not limited to, written, electronic, magnetic, and optical records; and scans, x-rays, and electrocardiograms) that describe or record the methods, conduct, and/or results of a trial, the factors affecting a trial, and the actions taken.

DOUBLE-BLIND The design of a study in which neither the investigator nor the subject knows which medication (or placebo) the subject is receiving.

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.

DRUG OR DEVICE ACCOUNTABILITY RECORDS (DAR) Required documentation for material accountability, quantity used and left over, and date of disposal.

EFFICACY A product's ability to produce beneficial effects on the duration or course of a disease. Efficacy is measured by evaluating the clinical and statistical results of clinical tests.

ENDPOINT Overall outcome that the protocol is designed to evaluate. Common endpoints are severe toxicity, disease progression, or death.

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 El Paso in connection with responsibilities to TTUHSC El Paso.
- The research is conducted by or under the direction of any employee, student or agent of an entity with which TTUHSC El Paso 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 El Paso 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 El Paso IRB is designated as the IRB of record.

ENROLLING The act of signing up participants into a study. Generally this process involves evaluating a participant with respect to the eligibility criteria of the study and going through the informed consent process.

ENTITY An organization, institution or being that has its own existence for legal or tax purposes, is legally separate from TTUHSC El Paso, and possess OHRP-approved Assurances and IRB Agreements with TTUHSC El Paso.

EQUITABLE Fair or just; used in the context of selection of subjects to indicate that the benefits and burdens of research are fairly distributed.

EXCLUSION CRITERIA Refers to the characteristics that would prevent a subject from participating in a clinical trial, as outlined in the study protocol.

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 Office of Research Resources.

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.

EXPANDED ACCESS The use of an investigational drug when the primary purpose is to diagnose, monitor, or treat a patient’s disease or condition and the use is not primarily intended to obtain information about the safety or effectiveness of a drug.

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.

EXTERNAL ADVERSE EVENT Adverse events experienced by subjects enrolled by investigators at other sites participating in the same clinical trial as investigators at TTUHSC El Paso /Affiliates (also known as IND Safety Reports).

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.

FDA FORM 1572 A list of commitments and requirements by the FDA for each investigator performing drug/biologics studies. Also referred to as a statement of the investigator.

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].

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. *NOTE:* Continuing reviews are required.

FOOD DRUG AND COSMETIC ACT (FD & C Act) States only drugs, biologics and devices proven safe and effective can be marketed.

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.

GOOD CLINICAL PRACTICE (GCP) is an international quality standard that is provided by ICH, an international body that defines standards, which governments can transpose into regulations for clinical trials involving human subjects.

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(3)]

HEALTH INSURANCE PORTABILITYAND ACCOUNTABILITY ACT (HIPAA) a 1996 Federal law that restricts access to individuals' private medical information

HUMANITARIAN DEVICE EXEMPTION (HDE) A premarket approval application submitted pursuant to this subpart seeking a humanitarian device exemption from the effectiveness requirements of sections 514 and 515 of the act as authorized by section 520(m)(2) of the act.

HUMANITARIAN USE DEVICE (HUD) As defined in 21 CFR 814.3(n), a HUD is a "medical device intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in fewer than 4,000 individuals in the United States per year.

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: (1) obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or (2) obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens (45 CFR 46.102[e]). This term is used interchangeably with Participants.

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

IMPARTIAL WITNESS A person who is independent of the trial, who cannot be unfairly influenced by people involved in 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. The impartial witness should be present during the consent discussion and personally sign and date the consent form as an indication that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the subject or the subject's LAR, and that informed consent was freely given by the subject (or the subject's LAR).

INCLUSION CRITERIA A list of criteria that must be met by all study subjects.

IND SAFETY REPORT Adverse events experienced by subjects enrolled by investigators at other sites participating in the same clinical trial as investigators at TTUHSC El Paso /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, or release 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 El Paso, the IRB is deemed to be a medical committee.

INTERNAL ADVERSE EVENT Any adverse events experienced by a single subject enrolled in TTUHSC El Paso or TTUHSC El Paso IRB affiliate research project.

INTERNATIONAL COUNCIL ON HARMONISATION OF TECHNICAL REQUIREMENTS FOR REGISTRATION OF PHARMACEUTICALS FOR HUMAN USE (ICH) A project that brings together the regulatory authorities of Europe, Japan and the United States and experts from the pharmaceutical industry in the three regions to discuss scientific and technical aspects of pharmaceutical product registration.
The purpose of ICH is to reduce or eliminate the need to duplicate the testing carried out during the research and development of new medicines by recommending ways to achieve greater harmonisation in the interpretation and application of technical guidelines and requirements for product registration. Harmonisation would lead to a more economical use of human, non-human animal and material resources, and the elimination of unnecessary delay in the global development and availability of new medicines while maintaining safeguards on quality, safety, and efficacy, and regulatory obligations to protect public health.
ICH guidelines have been adopted as law in several countries, but are only used as guidance for the U.S. Food and Drug Administration.

INTERNET MEDICAL RESEARCH INFORMATION SYSTEM (IRIS) Internet Medical Research Information System—the software through which all IRB applications, reviews and approvals are submitted and through which information is communicated between investigators and the IRB.

INVESTIGATIONAL DEVICE EXEMPTION (IDE) 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

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 approved 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.

IN VITRO DIAGNOSTIC DEVICE (IVD) an instrument, apparatus, implement, machine, contrivance, implant, in vitro agent, or other similar or related article, including any component, part, or accessory which is intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, conditions, or infections.

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.

LEGALLY AUTHORIZED REPRESENTATIVE An individual or juridical or other body authorized under applicable law to consent, on behalf of a prospective subject, to the subject's participation in the clinical trial.

LIMITED DATA SET is described as health information that excludes certain, listed direct identifiers, but that may include city; state; ZIP Code; elements of date; and other numbers, characteristics, or codes not listed as direct identifiers.

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(i); 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)].

MONITOR Person employed by the sponsor or CRO who reviews study records to determine that a study is being conducted in accordance with the protocol. A monitor's duties may include, but are not limited to, helping to plan and initiate a study, and assessing the conduct of studies. Monitors work with the clinical research coordinator to check all data and documentation from the study. See also CRA.

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.

NATIONAL INSTITUTES OF HEALTH (NIH) Agency within DHHS that provides funding for research, conducts studies and funds multi-site national studies.

NATIONAL RESEARCH ACT Act created by the National Commission for Protection of Human Subjects of Biomedical and Behavioral Research in 1974 and mandated review of studies by institutional review boards and subject protection by informed consent.

NEW DRUG APPLICATION (NDA) The compilation of all non-clinical, clinical, pharmacological, pharmacokinetic and stability information required about a drug by the FDA in order to approve the drug for marketing in the U.S.

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 El Paso IRB, or TTUHSC El Paso policies and procedures governing human subjects research, or the research activities as approved by the TTUHSC El Paso IRB's.

NONAFFILIATED MEMBER Member of an IRB 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, homemaker, or others).

NOTE-TO-FILE (MEMO TO FILE) A memo created to identify a discrepancy or problem in the conduct of the clinical research study. This memo can be written to identify the root cause of a problem, to identify the corrective action taken to prevent recurrence of the problem, and to document that the corrective action has resolved the problem.

NUREMBERG CODE As a result of the medical experimentation conducted by Nazis during World War II, the U.S. Military Tribunal in Nuremberg in 1947 set forth a code of medical ethics for researchers conducting clinical trials. The code is designed to protect the safety and integrity of study participants.

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.

OFFICE OF RESEARCH RESOURCES (ORR) Office responsible for the oversight and direction of the human research protection program at TTUHSC El Paso, which includes administrative oversight of the IRB, the TTUHSC El Paso Research Compliance Program, and TTUHSC El Paso educational requirements for human research.

OFF LABEL The unauthorized use of a drug for a purpose other than that approved of by the FDA.

OPEN Status of an IRB approved research project that is currently enrolling subjects.

OPEN LABEL Describes a clinical trial in which blinding is not used. This means that all parties involved in the trial know which participants have been assigned which interventions.

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[f]). 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, or may be approved, declined, or disapproved.

PERMISSION Parent(s) or guardian's written agreement to the participation of their child or ward in research.

PHASE Food and Drug Administration (FDA) descriptions of the clinical trial of a drug based on the study's characteristics, such as the objective and number of participants. There are five phases [1]:

- Phase 0: Exploratory study involving very limited human exposure to the drug, with no therapeutic or diagnostic goals (for example, screening studies, microdose studies)
- Phase 1: Studies that are usually conducted with healthy volunteers and that emphasize safety. The goal is to find out what the drug's most frequent and serious adverse events are and, often, how the drug is metabolized and excreted.
- Phase 2: Studies that gather preliminary data on effectiveness (whether the drug works in people who have a certain disease or condition). For example, participants receiving the drug may be compared to similar participants receiving a different treatment, usually an inactive substance, called a placebo, or a different drug. Safety continues to be evaluated, and short-term adverse events are studied.
- Phase 3: Studies that gather more information about safety and effectiveness by studying different populations and different dosages and by using the drug in combination with other drugs.
- Phase 4: Studies occurring after FDA has approved a drug for marketing. These including postmarket requirement and commitment studies that are required of or agreed to by the study sponsor. These studies gather additional information about a drug's safety, efficacy, or optimal use.

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 PI 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.

PROJECT All components of a human research submission to the IRB. Used interchangeably with the term STUDY.

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.

PROTOCOL AMENDMENT Changes or clarifications made in writing to the original protocol.

PROTOCOL DEVIATION Less serious non-compliance - 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 VIOLATION Serious non-compliance - a divergence from the protocol that materially (a) reduces the quality or completeness of the data, (b) makes the Informed Consent Form inaccurate, or (c) impacts a subject's safety, rights, or welfare. Examples of protocol violations may include the following [3]:

- Inadequate or delinquent informed consent
- Inclusion/exclusion criteria not met
- Unreported serious adverse events
- Improper breaking of the blind
- Use of prohibited medication
- Incorrect or missing tests
- Mishandled samples
- Multiple visits missed or outside permissible windows
- Materially inadequate record keeping
- Intentional deviation from protocol, Good Clinical Practice, or regulations by study personnel
- Subject repeated non-compliance with study requirements

QUALITY ASSURANCE Systems and procedures designed to ensure that a study is being performed in compliance with Good Clinical Practice (GCP) guidelines and that the data being generated is accurate.

QUALITY IMPROVEMENT Systematic data guided activities designed to bring about immediate improvements in a particular setting for a distinct population.

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.

RANDOMIZATION Study participants are usually assigned to groups in such a way that each participant has an equal chance of being assigned to each treatment (or control) group. Since randomization ensures that no specific criteria are used to assign any patients to a particular group, all the groups will be equally comparable.

RECRUITMENT Act of enrolling subjects with the proper inclusion criteria.

RELIANCE AGREEMENT A formal, written document that provides a mechanism for an institution or individual engaged in research to delegate institutional review board (IRB) review to an independent IRB or an IRB of another institution. Institutions may use other descriptive terms, e.g. authorization agreement, reciprocity agreement, memorandum of understanding, etc.

RELYING IRB The IRB of the institution where the research will take place and which will rely on an external IRB which will serve as the IRB for a multi-center study.

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 contribute to generalizable knowledge. (45 CFR 46.102[d]; 21 CFR 56.102[c]).

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.

REVIEWING IRB The IRB that is responsible for the review, approval and regulatory oversight of a multi-center research study and serving more than one site. Sometimes referred to as the IRB of Record.

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

SINGLE-BLIND STUDY A study in which one party, either the investigator or participant, is unaware of what medication the participant is taking; also called single-masked study.

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.

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.

SPONSOR MONITORING REPORT a report submitted by a sponsor to the PI and/or research team after each monitoring visit. Each report summarizes what the monitor reviewed during the visit, what findings were noted, and what actions were recommended or taken to ensure compliance.

STANDARD TREATMENT The currently accepted treatment or intervention considered to be effective in the treatment of a specific disease or condition.

STANDARDS OF CARE Treatment regimen or medical management based on state of the art participant care.

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 El Paso, 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 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.

SUB-INVESTIGATOR Helps design and conduct investigation at a study site.

SUBJECT IDENTIFICATION CODE A unique identifier assigned by the investigator to each trial subject to protect the subject's identity and used in lieu of the subject's name when the investigator reports adverse events and/or other trial-related data.

SURVEY Studies designed to obtain information from a large number of respondents through written questionnaires, telephone interviews, door-to-door canvassing, or similar procedures.

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 El Paso pursuant to federal Assurance and 45 CFR 46.113.

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 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.

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.

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

VULNERABLE SUBJECTS Group/individual that cannot give informed consent because of limited autonomy (e.g., children, mentally ill and prisoners). Also refers to subjects who may be unduly influenced to participate (e.g., students, subordinates and patients).

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.