

Investigator's Guide

Protecting Human Subjects in Research



Research Integrity Office
Revised: 08/09

The IRB Review Process at a Glance



Click CTRL and the task for more details

Complete required training

Request access to iRIS software program

Submit application to IRB for Initial Review

Respond to all IRB requests for clarification and/or revisions

Conduct study in accordance with GCP

Implement recruitment methods as approved by the IRB

Obtain and document Informed Consent

Report unanticipated/adverse events to the IRB, federal agencies, and sponsor

Notify the IRB of any changes in the study PRIOR to implementation

Submit study for IRB Continuing Review by the established deadline

Submit study for Final Closure

Table of Contents

The IRB Review Process at a Glance.....	1
Prerequisites for all personnel involved in human research.....	3
Introduction.....	4
Contact Information.....	4
What is subject to review?	5
TTUHSC IRBs	7
Who can be a Principal Investigator?.....	9
Training Requirements	10
Preparing for IRB Review	11
IRB Review & Approval	12
Other Requirements.....	16
Good Clinical Practice (GCP)	16
International Research.....	16
IRB Fees for Commercially Sponsored Research.....	16
IRB Relation to Other Committees.....	16
Amendments and Continuing Review	17
Study Closure & Suspension/Termination	19
Recruitment and Advertising	21
Informed Consent – A Process	23
Unanticipated Problems/Adverse Events.....	26
Vulnerable Populations	28
Investigational Drugs/Devices.....	29
Genetic Research.....	30
Packaging & Shipment of Infectious Materials	31
HIPAA	32
Recordkeeping & Confidentiality	33
Monitoring	34
Glossary	36
Appendices (Useful Tools).....	363
I. PI Responsibilities	44
II. Documentation of the Consent Process.....	47
III. Designation of Authorized Personnel.....	48
IV. Regulatory Files Checklist	49

Prerequisites for all personnel involved in human research

I. Education requirements: CITI Training

Principal Investigators, Co-Investigators, and research staff are required to receive training regarding the protection of human research subjects **prior to beginning any human research-related activities. Training must be renewed every three years.** The training course currently approved by TTUHSC is the internet based *Course in the Protection of Human Research Subjects* administered by the University of Miami through the *Collaborative IRB Training Initiative (CITI)*.

Registration

To begin the on-line course, go the following website: www.citiprogram.org and select "Register for the Course." After selecting Texas Tech University Health Sciences Center as your institution, you will be directed to select a Username and Password. On the CITI registration page you will need to select "*Biomedical Investigator Course Only*". You will then have access to the required modules which include the HIPAA for Researcher requirements.

Course Completion

Upon successful completion of the course, you will be able to download a course transcript. TTUHSC is also notified of your successful completion of the course. You will be required to achieve an overall score of at least **80%** to successfully complete the course.

II. iRIS Access

All submissions to a TTUHSC IRB must be submitted using the Internet Medical Research Information System (iRIS) software. In order to gain access to the system, all users must download, complete, and submit an iRIS Access Request form **after** completing the CITI training. You can request an iRIS account at the iRIS website: <https://www.sobmrmedris.ttuhs.edu:8867/Login.jsp>

III. Financial Disclosure

All research staff must have a current Annual Financial Disclosure statement on file with the Research Integrity Office in accordance with TTUHSC OP 73.09. (<http://www.ttuhs.edu/hsc/op/op73/op7309.pdf>) The Financial Disclosure statement is Appendix A to the Conflict of Interest Operating Policy and can be found at the following website: <http://www.ttuhs.edu/hsc/op/op73/op7309a.pdf>

QUESTIONS

For questions regarding any of these requirements, please contact Virginia Smith at (806) 743-2991 or by email at Virginia.Smith@ttuhsc.edu. You may also contact your local IRB Office:

- Amarillo – (806) 354-5419
- El Paso – (915) 545-0977
- Lubbock/Odessa – (806) 743-4753

Introduction

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

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

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

Contact Information

The *Investigator's Guide to Protecting Human Subjects in Research* was created by the Research Integrity Office. Additional resources, useful links, and current announcements are available at our website: www.ttuhscc.edu/research/RIO

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What is subject to review?

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

All research involving human subjects must be reviewed by the IRB if the research is sponsored by the institution, the research is conducted by or under the direction of any employee or agents of this institution (including students) in connection with his or her institutional responsibilities, the research is conducted by or under the direction of any employee or agent of this institution using any property or facility of this institution, or the research involves the use of this institution's non-public information to identify or contact human subjects.

What is considered human research?

This is a two-part question: 1) is this research? and 2) does it involve human subjects?

DEFINITION OF RESEARCH

Research is defined as any systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge [45 CFR 46.102(d)]. Quality assurance and public health projects do not meet the definition of research and are not reviewed by the IRB. Classroom projects that have the sole purpose to teach research methods to students are not reviewed by the IRB. Case studies of single patients do not fit the definition of a systematic investigation and therefore, do not require review by the IRB.

DEFINITION OF HUMAN SUBJECTS

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.

Intervention includes both physical procedures by which data are gathered and manipulations of the subject or the subject's environment that are performed for research purposes.

Interaction includes communication or interpersonal contact between investigator and subject.

Private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information that has been provided for specific purposes by an individual and which can reasonably expect will not be made public (e.g., medical record information.)

Since the definition of a human subject is a *living* individual, research involving autopsy materials or cadavers is not considered human subjects research and is not reviewed by the IRB. However, HIPAA privacy rules do apply to identifiable private information about decedents. Projects using identifiable information about decedents does require HIPAA Privacy Board review. Contact your local IRB Administrator if you are conducting this type of research.

Projects using commercially available, de-identified cell line do not meet the definition of interaction or private information. Therefore, the IRB does not review this type of research.

Consulting on Projects

TTUHSC IRB review is required ***unless*** the investigator has a strict consulting relationship in which:

- The investigator is hired on his/her own time (refer to TTUHSC OP 50.27);
- The investigator holds no rights in the work; *and*

- Neither the investigator nor TTUHSC obtains, receives, or possesses identifiable private information or receive coded data while at TTUHSC.

All three of these criteria must be met or the IRB must review the project.

Research Conducted at Another Site with its own IRB

For a TTUHSC investigator to participate in a research project at another site, the project must be reviewed by the TTUHSC IRB as well as by the other entity's IRB. For example, a TTUHSC investigator engaged in research at another academic medical center must secure approval from both entities' IRBs. Investigators who must submit a project to another IRB should include copies of the application and the review conducted by the TTUHSC IRB. One exception to this rule is research conducted jointly by TTUHSC and TTU researchers. These projects will generally be reviewed ONLY by a TTUHSC IRB.

Chart Reviews

A human subject is defined, in part, as a living individual about whom an investigator conducting research obtains identifiable private information. The IRB approves who may have access to this information for research purposes and how access to this information for research purposes is obtained. All medical or other chart/record review for research requires IRB review and approval. The Principal Investigator should provide the IRB a list of specific variables that will be collected from the medical record chart. The data collection form that will be used to compile information from the chart can be used to fulfill this requirement. Medical record data that are already in existence at the time the application is submitted to the IRB and is recorded in such a way that subjects can not be identified directly or through identifiers linked to the subjects may be classified as having exempt status. However, the TTUHSC IRB, not the investigator, will make the determination of exemption from formal IRB review.

Research Conducted in Foreign Countries

Research conducted by TTUHSC investigators in foreign countries **must** have prior approval by the TTUHSC IRB.

Resident and Student Research Projects

In accordance with federal regulations, TTUHSC requires that all human research be prospectively reviewed by the IRB. Accordingly, resident research projects, theses, research practica, and Master's or Doctoral theses involving human subjects must be submitted for IRB review. TTUHSC IRB policy requires that only faculty member must serve as the principal investigator on resident/student research projects.

Additional TTUHSC Approval

Approvals by the following committees may be required prior to submission to the IRB. Information about these committees is available on the TTUHSC Office of Research website: www.ttuhsr.edu/research .

- Office of Sponsored Programs (grants)
- Office of Research Director of Contracting (clinical trial agreements)
- TTUHSC Institutional Biosafety Committee (IBC)
- TTUHSC Radiation Safety Committee (RSC)
- TTUHSC Recombinant DNA Biosafety Committee (RDBC)
- TTUHSC Conflict of Interest Committee (COIC)

WHEN IN DOUBT - ASK YOUR IRB ADMINISTRATOR! Always contact the IRB administrator with questions PRIOR to beginning any phase of research.

TTUHSC IRBs

TTUHSC has three (3) registered Institutional Review Boards (IRBs) which review research conducted by investigators in the following geographic areas:

TTUHSC IRB 1 – 00000096 Lubbock, Midland, Odessa

TTUHSC IRB 2 – 00000097 Amarillo, Dallas, Abilene

TTUHSC IRB 3 – 00000098 El Paso

The purpose of the IRB is to ensure the protection of the rights, safety, and well-being of human subjects involved in research. The IRBs review all human research conducted at TTUHSC or affiliated entities. For a list of affiliated entities contact your local IRB office.

GUIDING 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* (<http://www.fda.gov/oc/ohrt/IRBS/belmont.html>). The ethical principles are:

Respect for Persons Recognition of the personal dignity and autonomy of individuals and special protection of those persons with diminished autonomy

Beneficence Obligation to protect persons from harm by maximizing anticipated benefits and minimizing possible risks of harm

Justice Fairness in the distribution of research benefits and burdens

FEDERAL-WIDE ASSURANCE

TTUHSC has filed an assurance of compliance called a Federal-Wide Assurance (FWA) with the Office of Human Research Protections (OHRP) in the Department of Health and Human Services (DHHS). An FWA is an agreement between TTUHSC and DHHS which states that TTUHSC is guided by the ethical principles of the Belmont Report and will comply with federal regulations for all research involving human subjects.

This Assurance applies to research conducted at TTUHSC or by its employees or agents regardless of the research site.

AFFILIATED ENTITIES

The TTUHSC IRB also reviews research for “affiliated entities”. These “affiliated entities” are separate facilities or institutions that have designated the TTUHSC IRB on their Federalwide Assurance with DHHS and have a contractual relationship with the TTUHSC IRB.

TTUHSC provides IRB review for human subjects research conducted at these entities under a DHHS IRB authorization agreement. Research reviewed for these entities receive the same level of IRB review as those conducted at TTUHSC. A list of Affiliated Entities can be found on the IRB Website. If the entity where you wish to conduct research is not listed, contact the IRB office (www.ttuhs.edu/research/RIO/irb/) for assistance.

FEDERAL REGULATIONS AND TTUHSC POLICY

All research involving human subjects, regardless of funding source, conducted at or in affiliation with TTUHSC shall be conducted in accordance with federal regulations, TTUHSC Operating Policy (including HSC OP 73.06, 10.16), TTUHSC IRB Policies and Procedures and VA policies and regulations where applicable.

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,

References to federal regulations are current through revision date October 1, 2003 (for 45 CFR 46) and April 1, 2003 (for 21 CFR 50, 56, 312, 812). All of these can be found on the IRB website (www.ttuhsoc.edu/research/RIO/irb/).

SCOPE OF THE IRB

IRB approval is **required** for any research involving human subjects that meet any of the following criteria.

If you answer yes to any of the following questions, your research project will need to be reviewed by the TTUHSC IRB.

- Are you an employee or student of TTUHSC?
- Is the research being conducted at TTUHSC or at an affiliated entity?
- Does the research use any property, equipment, and/or facilities of TTUHSC or an affiliated entity?
- Are you using TTUHSC patient, student, or employee data?

For additional requirements regarding industry-sponsored research refer to TTUHSC OP 73.08 (<http://www.ttuhsoc.edu/hsc/op/op73/op7308.pdf>).

AUTHORITY OF THE IRB

- The IRB has the authority to approve, require modifications of, or disapprove all human research that falls within its jurisdiction. Research that has been reviewed and approved by the IRB may be subject to further review and disapproval by TTUHSC officials. However, as stated in 45 CFR 46.112, TTUHSC officials may not approve research if it has been disapproved by a TTUHSC IRB.
- The IRB monitors and conducts continuing review of approved research at intervals of at least once per year.
- The IRB has authority to inspect research facilities and obtain records and other relevant information relating to the use of human subjects in research.
- The IRB has authority to observe or have a third party observe the consent process.
- The IRB takes actions to comply with federal regulations or other applicable laws, including action to suspend or terminate approval of research.
- The IRB must report to appropriate TTUHSC and federal government officials and any funding agency:
 - any suspension or termination of research
 - any unanticipated problems involving risks to subjects
 - any serious or continuing noncompliance with IRB requirements.

IRB CALENDAR

Refer to the IRB website at www.ttuhsoc.edu/research/RIO/irb/ for information on submission deadlines and meeting dates.

Who can be a Principal Investigator?

The Principal Investigator has ultimate responsibility for conducting and overseeing the research (refer to the Appendix for a description of Principal Investigator responsibilities). Only employees with faculty status may be Principal Investigators in research involving human subjects for TTUHSC-sponsored research projects.

FACULTY

TTUHSC employees with a faculty appointment (full or part time) may be designated as the Principal Investigator in a human research study. TTUHSC employees who do **not** have faculty status (including staff, residents, students, assistants, fellows or other individuals receiving training at TTUHSC) cannot be designated as Principal Investigator for a research study involving human subjects. These individuals may participate in research as sub-investigators or study personnel.

“AFFILIATED FACULTY” or “CLINICAL FACULTY”

Affiliated faculty/clinical faculty are faculty members who are not employees of TTUHSC but hold clinical or adjunct appointments. Clinical or affiliated faculty may be designated as the Principal Investigator in a human research study reviewed by TTUHSC IRB.

INVESTIGATORS FROM AFFILIATED ENTITIES

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

- Affiliated entity has a Federalwide Assurance (FWA) approved by DHHS;
- Affiliated entity has designated the TTUHSC IRB on its FWA;
- Affiliated entity has a current IRB Agreement/Memorandum of Understanding with TTUHSC;
- PI submits application and protocol in accordance with federal regulations and TTUHSC policy with signature of authorized official from the affiliated entity. The signature of the authorized authority from the affiliate entity signifies that the affiliated entity (1) approves of the research; (2) has sufficient resources to conduct the research and (3) agrees that the PI has the appropriate education and experience to conduct the research.
- The PI Agrees to comply with the compliance requirements of TTUHSC.

Collaborators from institutions that are not affiliated with TTUHSC may not be Principal Investigators on TTUHSC IRB applications.

NOTICE OF ABSENCE/SEPARATION

If they are engaging in on-going human research, Principal Investigators are required to notify the IRB in writing at least two (2) months prior to any extended absences, faculty development leaves, or separations. (See TTUHSC OP 60.02) Principal Investigators shall submit information and/or an amendment to the IRB designating an alternate investigator responsible for any active research study during their absence. Notice and/or amendments shall be made in accordance with local IRB submission requirements. Principal Investigators who are terminating employment with TTUHSC shall submit information and/or an amendment to the IRB designating an alternate investigator responsible for any active research study or their research will be terminated.

Training Requirements

HUMAN RESEARCH PROTECTION TRAINING

Principal Investigators, Co-Investigators, and research personnel are required to receive training regarding the protection of human research subjects **prior** to beginning any human research-related activities. The course currently approved by TTUHSC is the web-based *Course in the Protection of Human Research Subjects* through the *Collaborative IRB Training Initiative* (CITI). Details regarding this course can be found on Page 3 of this manual.

Exceptions

In cases where co-investigators or other research personnel are not associated with TTUHSC, other forms of human research protection training may be approved. A description of the training and a copy of a completion certificate should be submitted to the IRB Office for consideration.

RENEWAL OF TRAINING FOR THE PROTECTION OF HUMAN RESEARCH SUBJECTS

Every 3 years all investigators and research staff are required to renew their training for the protection of human research subjects. The currently approved course is the **Basic Course in the Protection of Human Research Subjects** administered by the University of Miami through the *Collaborative IRB Training Initiative* (CITI) as described above (www.citiprogram.org). Initial and Continuing Reviews cannot be approved if training requirements are not up-to-date. See page 2 of this manual for additional information.

CONTACT INFORMATION

For training-related questions, contact Virginia Smith, Educational Coordinator, at (806) 743-2991 or by email at Virginia.Smith@ttuhsc.edu.

Preparing for IRB Review

The TTUHSC IRBs use the web-based iRIS program to review and track research study information. Principal Investigators and research personnel **must use** this software to submit study-related information to the IRB.

iRIS is located at www.ttuhs.edu/research/iris

In order to obtain access to iRIS, you must first “Request a New Account” by clicking on these words on the iRIS home page.

The most common problem that causes delays in the approval of initial applications is the absence of adequate detail for the IRB to evaluate the study’s purpose and/or procedures. In particular, investigators are encouraged to provide specific information on how potential subjects are initially identified and how consent is to be obtained. There is no such thing as too much detail when describing study procedures! The more complete the initial description, the less likely that time will be spent with correspondence back and forth between the Principal Investigator and the IRB. Staff in the IRB office are 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 IRB-approved format (required for all non-exempt studies);
- Authorization to Use and Disclose PHI for Research (HIPAA authorization) **or** Request to Use and Disclose PHI Without Authorization for Research;
- Investigator Agreement Form signed by the Principal Investigator and the Department Chair approval (or signature of authorized official designated in entity’s IRB Agreement). This form can be available at www.ttuhs.edu/research/RIO/irb/general.asp.
- Copies of letters of assurance or cooperation with research sites (as applicable);
- Data collection forms;
- Recruitment materials (if any will be used);
- Relevant grant applications;
- Surveys, questionnaires, or videotapes (if any will be used);
- Documentation of approval by other TTUHSC institutional committees as applicable;
- Curriculum Vitae of Principal Investigator as requested.

Materials for initial review shall be submitted by the established deadlines (see the IRB website for current deadlines at www.ttuhs.edu/research/RIO/irb).

IRB Review & Approval

STUDY SCREENING AND PROCESSING

All IRB submissions will be screened by the IRB Office Staff. This service is designed to alert investigators to major omissions or other non-scientific problems with the application. Successful pre-screening does not guarantee IRB approval. Investigators must have their applications submitted well in advance of the deadline if they wish to take advantage of the pre-screening. If the application has not been submitted for screening and is incomplete or otherwise not fully prepared for review, it will be returned to the Principal Investigator with a request for correction. When the submission is adequately prepared for review, it will be placed on an agenda for IRB review.

Types of IRB Review

Full Board Review - conducted at a convened meeting of the IRB.

Expedited Review - the Chair or his/her designee is permitted to perform the review.

Exempt Status – the IRB Office staff reviews an abbreviated application form to determine exempt status. Studies determined by the IRB to be exempt do not require formal IRB review. However, the IRB (not the Principal Investigator) makes the determination about whether a project is exempt.

FULL BOARD REVIEW

Research that requires full board review includes:

- Research that involves greater than minimal risk;
- Non-exempt research that involves children or other vulnerable populations;
- Research that involves investigational drugs or devices;
- Research that involves invasive procedures;
- Research that involves deception;
- Surveys involving sensitive questions or information about sexual practice or illegal behavior or likely to be stressful for the subject as determined by the IRB.

Types of IRB Actions:

The Principal Investigator will receive written notification of one of the following IRB actions:

- Approval
- Clarification or revision needed (this may or may not result in further full board review, depending on the nature of the changes required).
- Tabled
- Disapproval

Approval

The IRB may approve an application only when the requirements for approval stated in 45 CFR 46.111 are satisfied. These requirements are summarized as follows:

- Risks to subjects are minimized.
- Risks to subjects are reasonable in relation to anticipated benefits.
- Selection of subjects is equitable.
- Informed consent will be sought from each prospective subject or authorized representative.
- Informed consent will be appropriately documented as required by federal regulation.
- Plans for data monitoring are included when appropriate.
- Adequate provisions are in place to protect the privacy of subjects and the confidentiality

- of data.
- Additional safeguards have been included when necessary to protect the rights and welfare of vulnerable subjects.

No research activity may be conducted until the Principal Investigator receives written IRB approval.

Clarification or Revisions

The IRB may request clarifications, protocol modifications, and/or revisions to the informed consent document, or other supporting documentation. This request shall be made in writing to the Principal Investigator in a timely manner. Replies are due within 30 days of the date of the written notice to the Principal Investigator unless otherwise specified. If no response has been received after 30 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. Your response will be reviewed either by the full Board or through an expedited process, as circumstance indicates.

Tabling of the study

The IRB may recommend that the study be tabled under the following circumstances.

- ***Extensive changes required***
The IRB may review the study and determine that extensive changes are necessary before the study can be effectively reviewed.

The Principal Investigator will be notified of the decision and of the corrective action(s) needed before further review can take place. The investigator will have 30 days from the date of notice to respond to the written request for changes. If no response has been received from the Principal Investigator after 30 days, the study may be administratively closed and removed from the IRB agenda. Further review of the study will require a new IRB application.

- ***IRB members or consultants not available for review***
It is possible that a study submitted for review may be delayed under circumstances that include, but are not limited to, loss of quorum, unavailability of a qualified IRB member to conduct a thorough review; or the need for outside consultation to assist the IRB.

All studies which are tabled at a full Board meeting will require subsequent full Board review.

Disapproval

The IRB may vote to disapprove a study and determine that there will be no further consideration of the study.

The IRB shall provide the Principal Investigator with written notification of the reasons for its decision. The Principal Investigator may request reconsideration of the IRB's decision in writing within ten (10) days of the date of notice (see Section 4.1 of the TTUHSC IRB Policies and Procedures). TTUHSC officials **cannot** approve research if it has been not been approved by the IRB.

EXPEDITED REVIEW

Certain applications may be reviewed on an expedited basis if they meet specified criteria. Federal regulations limit the use of expedited review procedures to specific research categories published in the Federal Register. These are research activities that

- present no more than minimal risk to human subjects, and
- involve only procedures that are listed in one or more of the research that may be found at <http://www.hhs.gov/ohrp/humansubjects/guidance/expedited98.htm>

Studies that meet both of these qualifications may be reviewed by the IRB using the expedited review procedures found in 45CFR 46.110 and 21 CFR56.110. A list of the expedited categories is available at www.ttuhs.edu/research/RIO/irb.

The IRB staff assures that all the required elements have been submitted. The application is then forwarded to a designated board member for review and decision. The research may be approved, additional information may be requested, or the submission may be forwarded for full board review.

EXEMPT STATUS

The IRB makes the determination of *exempt status*. The Principal Investigator does not have the authority to make this determination. To be exempt, an application must fit into one of six specific categories of activities summarized below (Federal regulations 45 CFR 46.101(b)). Exempt status does **not** apply to research involving prisoners.

- 1) Research conducted in established or commonly accepted educational settings, involving normal educational practices
- 2) Research involving the use of educational tests, surveys or questionnaires, provided that human subjects cannot be identified and that responses by the subjects will not place them at risk of liability or be damaging to financial standing or reputation. An example of a study that might be exempt is one conducting a survey on all graduate students by stopping them in the hallway but not asking for their names or any other identifying information.
- 3) Research involving the use of educational tests or observation of public behavior that is not exempt under the previous category if (1) the human subjects are elected or appointed public officials or candidates for public office or (2) the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.
- 4) Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the PI in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects. An example of this category is a retrospective chart review where no identifiers are taken. Remember that this is research and that the exemption must be granted by the IRB office prior to the research taking place.
- 5) Research and demonstration projects which are conducted by or subject to the approval of Federal Department or Agency heads in order to review public service programs; procedures for obtaining benefits under those programs; possible changes to those programs or possible changes in methods or levels of payment for benefits under those programs.
- 6) Taste and food quality evaluation and consumer acceptance studies.

If the research application meets the criteria for exemption, approval will be provided to the Principal Investigator in writing and shall include the citation of the specific category justifying the exemption. If the research application does not meet the criteria for exemption, the IRB Office will provide written notice to the Principal Investigator specifying the additional information needed and stating the appropriate category for review (e.g., expedited or full Board).

Minimum Submission Requirements for Survey/Questionnaire studies

TTUHSC IRB Application

Study protocol (the research plan)

Any scripts to be used to explain study to respondents

Copies of any surveys/questionnaires to be given. Instructions should indicate that:

- This is a research project
- No identifying information will be collected
- The respondent can skip any questions that they don't wish to answer
- By completing the survey/questionnaire the respondent is giving consent to participate

- Any questions about the research can be directed to the principal investigator (with phone number or email address provided)

Minimum Submission Requirements for Retrospective Chart reviews

TTUHSC IRB Application

Study protocol (the research plan)

Data collection sheet (to ensure that no identifying information is being collected. Note that the HIPAA rules indicate that dates associated with treatment are considered identifying information)

HIPAA “Waiver” form (found in iRIS—officially known as a Principal Investigator’s Request to Use and Disclose PHI Without Authorization)

For retrospective chart reviews, all data have to be in existence on the date the application is submitted to the IRB. The study is “retrospective” from that date. Both the IRB Application and the study protocol should indicate the dates that the information was recorded on the medical record. Both the start AND END dates should precede the date that the application was submitted to the IRB.

Other Requirements

Good Clinical Practice (GCP)

Principal Investigators, regardless of their affiliation, shall follow the Good Clinical Practice Guidelines as published by the FDA (found at www.fda.gov/cder/guidance/959fnl.pdf) in designing and conducting clinical trials.

International Research

The IRB reviews all research involving human subjects conducted under the auspices of TTUHSC, regardless of the research location, including research conducted in foreign countries. When reviewing an international proposal, the IRB must be aware of the local research context. The IRB reviews translations of all relevant research documents (including informed consent, recruitment materials, and questionnaires, etc.) for accuracy. 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.

IRB Fees for Commercially Sponsored Research

All industry-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 Research Integrity Office and established during contract negotiations with sponsors and in IRB Agreements with affiliated entities. (see: TTUHSC Operating Policy OP 73.08.) The current IRB fees are \$1500 for an initial review and \$500 for continuing reviews. There is no fee for amendments to protocols.

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

Waiving IRB Fees

There may be extenuating circumstances where charging IRB fees would be unwarranted. Principal Investigators may submit a written letter requesting waiver of IRB processing fees to the EVPR by either campus or regular mail (not email). The Principal Investigator will be notified of the EVPR's decision.

IRB Relation to Other Committees

The TTUHSC IRB functions independently of, but in coordination with other committees, including:

- TTUHSC Institutional Biohazards Committee (IBC) (806) 743-2960
- TTUHSC Radiation Safety Committee (RSC) (806) 743-2597
- TTUHSC Conflict of Interest Committee (806) 743-4566
- Texas Tech University IRB (806) 742-3884 x-232

If required, approval from these other committees shall be obtained prior to approval by the IRB.

Amendments and Continuing Review

An approved project is limited in its conduct to the recruitment activities and study procedures that were described in the initial application submission and approved by the IRB. If Principal Investigators wish to change the recruitment activities or study procedures from what was initially described, they should submit an Amendment to the IRB for review.

AMENDMENTS TO PREVIOUSLY APPROVED STUDIES

For previously approved projects, 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. In the event that any procedures are performed in variance with the protocol, the IRB must be notified of the deviation. Exempt studies do not require approval of amendments unless the investigator determines that the changes would no longer qualify the study as exempt. If there is any doubt, the investigator should contact the IRB Administrator.

Minor modifications

A minor modification is defined as a change that would not materially affect an assessment of the risks and benefits of the study and/or substantially change the specific aims or design of the study. Minor modifications proposed for previously approved studies may be reviewed in an expedited manner. Modifications to the protocol require submission of an updated copy of the protocol highlighting the changes.

Major modifications

A major modification is defined as any change which materially affects an assessment of the risks and benefits of the study or substantially changes the specific aims or design of the study. Major modifications to an exempt or expedited study may require full board review and approval before the changes can be implemented; for a study that has previously required full board review, full board review is always necessary. Modifications to the protocol require submission of an updated copy of the protocol highlighting the changes.

Change of Study Personnel

Principal Investigator shall notify IRB of any changes in research personnel by amendment. The IRB must review and approve changes of research personnel prior to initiation of these changes. Any additional research personnel must complete required training prior to beginning any research-related activities. If a PI is leaving TTUHSC or will be absent from campus for an extended period of time, an alternate PI should be named and approved prior to the absence.

CONTINUING REVIEW OF APPROVED STUDIES

Continuing review of all non-exempt research, whether funded externally or not, will take place on at least an annual basis. The initial approval letter will indicate the review interval.

The Principal Investigator shall submit required documentation no less than 10 days prior to the Full Board meeting preceding the study expiration date. Although reminders will be sent out, the Principal Investigator is responsible for being aware of upcoming expiration dates in order to submit continuing review materials in a timely manner.

Information required for continuing review includes:

- Number of subjects enrolled, screened, and withdrawn (with reasons for withdrawal);
- 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 risks to the subjects;
- A summary of any unreported 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).

- Unreported amendments or modifications to the research since the last review;
- An updated complete protocol (if changes have been made);
- 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;
- Updated Financial Disclosure (HSC OP 73.09a) statements may also be submitted at the time of annual review.

The approved continuing review template is found in the iRIS software 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.

Continuing review requiring full Board approval

Documentation received prior to the submission deadline will be reviewed at the next regularly scheduled IRB meeting. The IRB review will include:

- An assessment of risks, benefits, and safeguards for human subjects;
- A determination that the currently approved or proposed informed consent document is accurate and complete; and
- A review of any significant new findings that may relate to the subjects' willingness to continue participation.

Continuing review NOT requiring full Board approval

The following types of studies may not require full Board review:

- Studies whose initial review received expedited review.
- Studies in which enrollment has not yet taken place and no new risks have been identified;
- Research closed to accrual of new subjects and in which participants are no longer receiving study-intervention. A research study for which no new subjects will be enrolled must be periodically (at least annually) reviewed until such time that there is no need to re-contact enrolled subjects or access their protected health information.

NO GRACE PERIOD

If a Principal Investigator has failed to provide continuing review information to the IRB or the IRB has not reviewed and approved the research study by the continuing review date specified by the IRB, **all research activity**, including enrollment, data collection and analysis, **shall stop** unless the IRB informs the Principal Investigator in writing 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.**

Study Closure & Suspension/Termination

STUDY CLOSURE

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

If no subjects have been enrolled in a study for a period of three or more years, the IRB may request that a project be closed, unless there are extenuating circumstances for keeping the project open.

Studies which have been completed as approved by the IRB, including data analysis, and finalized at the local research site will be designated as “completed” in iRIS. The Principal Investigator shall submit a final report to the IRB which will include the number of subjects, any major problems, and a summary of the findings. A manuscript may be substituted for the summary of the findings.

Once the IRB has sent a written acknowledgment of the completed study and its closure, no further data can be collected about any of the subjects in that particular study and no further actions are necessary by the Principal Investigator.

Studies which have been permanently closed by the Principal Investigator or Sponsor will be designated as “closed” in iRIS. Once the IRB has acknowledged in writing the closure of a study, no further data shall be collected about any of the subjects in that particular study and no further actions are necessary on the part of the Principal Investigator.

Studies which are temporarily closed to accrual by the Principal Investigator, Sponsor, or IRB will remain in “Active” status. Therefore, reviews of the research by the IRB are required.

Studies may be closed administratively by the IRB due to non-responsiveness to requests for information from the investigator. No further research activity is permitted for studies which are closed administratively. Any further activity on such studies will require the submission of a new application to the IRB.

SUSPENSION/TERMINATION OF APPROVAL

The IRB and/or the EVPR have authority to suspend/ terminate research. The term “Suspension/Termination” applies when the IRB withdraws its approval from a study for any of the following reasons:

- unanticipated problems involving risks to subjects or others;
- serious or continuing noncompliance with regulations governing human subjects research (45 CFR Part 46);
- research is not being conducted in accordance with the requirements or determinations of the IRB.

Notification of suspension/ termination requires immediate cessation of all research activities by the Principal Investigator and mandatory reporting to federal regulatory agencies by TTUHSC.

The Principal Investigator shall be immediately notified by the chair of the IRB in writing of suspension/termination of IRB approval along with the reasons for the suspension/termination. The EVPR shall promptly report suspension/termination of research to the appropriate federal agencies in compliance with federal regulations and TTUHSC policy (See Section 2.6)

Studies which have been suspended require submission of a written Correction Plan by the Principal Investigator and approval by the IRB before any research can resume. Suspended studies shall require ongoing continuing review by the IRB.

APPEAL OF SUSPENSION/TERMINATION

Request to IRB

The Principal Investigator shall be immediately notified of the decision in writing, which shall include a statement of the reasons for the suspension/termination.

The Principal Investigator may appeal the decision of the IRB or EVPR by submitting a written request to the IRB or EVPR, as applicable, and provide a rationale for the appeal and any other supporting documentation. The Principal Investigator must submit an appeal within five (5) business days of the date of suspension.

Review by Subcommittee and Recommendation to Board

Within 14 days of receipt of the appeal, the Principal Investigator's request for reconsideration shall be reviewed by a subcommittee consisting of the IRB Chair and two IRB members selected by the IRB and Senior Director of RIO. The subcommittee may also invite individuals with expertise in that area of research to assist the subcommittee in its review of the issues (See 21 CFR 56). Individuals assisting the IRB shall maintain confidentiality of the IRB proceedings.

This subcommittee shall review the Principal Investigator's documentation, the research, the suspension documentation, and may speak with the PI. The subcommittee shall submit findings and recommendation(s) to the full Board at its next regularly scheduled meeting if possible. At the discretion and invitation of the subcommittee, the Principal Investigator may address the IRB in person at its next regularly scheduled meeting.

Decision by Board

The Full Board 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 suspension be upheld and the IRB accepts this recommendation, this decision falls under disapproval of research involving human subjects, and there is no further appeal within TTUHSC. (45 CFR 46.112).

A decision by the full IRB to disapprove, suspend/terminate a research project is final and may not be reversed by the EVPR or any other officer/agency of TTUHSC or affiliated entities.

FACULTY GRIEVANCE POLICIES NOT APPLICABLE

TTUHSC Schools have faculty grievance policies to address grievances of faculty members through and with their supervisors. A school faculty grievance procedure is not available to appeal an IRB decision with respect to research.

Recruitment and Advertising

All research studies are approved to recruit only the number of subjects indicated on the IRB approval letter. If the Principal Investigator finds that actual recruitment is approaching that limit, an Amendment should be submitted requesting an increase in the number of subjects to be enrolled in the study.

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. All advertisements must indicate in small letters on the bottom that they have been reviewed by the TTUHSC IRB.

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.

PAYMENTS TO SUBJECTS

The IRB must determine that the risks to subjects are reasonable in relation to anticipated benefits and that the consent document contains an adequate description of the study procedures as well as the risks and benefits. 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.

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.

Method of Payments

The Informed Consent must clearly establish how the subject is to be paid, i.e. cash, check, etc. A subject must sign a receipt for any cash payment, and this procedure must also be described as part of the Informed 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 report to the IRS). If the subjects are receiving cash and are not being paid by check, a rationale must be provided to the IRB.

Disclosure of Payments

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

Alterations in Payments

Any alterations in human research subject payment or revising of the payment schedule must be reported to 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.

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.

Documentation of Payments

The Principal Investigator must keep documentation of payment(s) made to each subject in study files. All records shall be made accessible for inspection and copying by authorized TTUHSC representatives, including TTUHSC Compliance personnel, IRB Office, TTUHSC RIO, the EVPR, as well as federal regulatory officials.

Informed Consent – A Process

The informed consent **process** is different from the informed consent document. It involves meeting with a potential subject, finding out whether he or she is capable of giving consent, and discussing the purpose, risks, and benefits of participation. The informed consent document itself formalizes the agreement to participate and serves to document the process. The appendix includes an additional form that can be used to document the process of obtaining informed consent.

Informed consent is an ongoing process that starts well before any documents are signed and continues until the subject's participation is complete. If consent is to be informed, the subject must genuinely understand the study. Hence, investigators should strive to convey information to subjects, not merely disclose it to them. Subjects should be able to demonstrate their understanding of the study procedures, risks, and benefits in which they are agreeing to participate.

Potential subjects may wish to discuss the decision with family, close friends, or trusted advisers. They should not feel rushed or coerced. They often need time, especially if the information is disturbing or particularly complex, to digest the information and come to terms with it.

DOCUMENTATION OF INFORMED CONSENT

The IRB may approve procedures for documentation of the informed consent process that involve either a written consent form signed and dated by the subject; or in limited circumstances, the IRB may waive the requirement for the Principal Investigator to obtain a signed and dated consent form (see below). The informed consent form must be written and presented in a manner that is not coercive or threatening.

The consent form shall be written in non-scientific language that is easily understood by all subjects or below the 7th Grade Level. The information must be comprehensible and should be presented in the most simple and straightforward manner possible. If the investigator has difficulty composing the appropriate language, please contact the IRB administrator. HIPAA language in the consent form is unnecessary and will not replace the requirement for the HIPAA form. A copy of the consent form is to be given to the subject.

TTUHSC research studies must utilize the TTUHSC Informed Consent template found on the iRIS system. It includes the required basic as well as optional elements of consent as described in 45 CFR 46.116.

Informed Consent Documents from Unaffiliated Principal Investigators

Principal Investigator's who are self employed or employed by another entity without a TTUHSC faculty appointment cannot use TTUHSC consent forms. Consent forms must conform to basic and optional required elements [45 CFR 46.116] and must be approved by the TTUHSC IRB prior to use.

Written Consent Form Signed by Subject or Authorized Representative

In most circumstances, the IRB will require that the informed consent process is documented by the use of a written consent form approved by the IRB and signed by the subject or the subject's authorized representative. This form may be read to the subject or the subject's authorized representative during a face-to-face presentation. However, the Principal Investigator shall allow the subject or the authorized 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. The requirement that the copy be signed may be waived by the IRB on a case-by-case basis following a written request by the investigator.

No Stamped Signatures

The Principal Investigator (or authorized designee listed in the Application) also signs the consent document contemporaneously with the subject or Authorized representative. Stamped signatures for the Principal Investigator are not acceptable.

Subjects who do not speak English

These subjects will be presented with an informed consent document written in a language understandable to them. A TTUHSC Spanish language consent template is available as a template in iRIS.

Oral Presentation

In cases **where the subject is unable to read** the required consent form, the approved consent form shall be read to the subject in its entirety in a language understood by the subject or the subject's authorized representative. A third party witness unaffiliated with the research study will be present during the reading and will be required to sign and date the consent form as a witness to the consent procedure.

Waiver of Documentation of Informed Consent

The IRB may waive the requirement for the Principal Investigator to obtain a signed consent form for some or all subjects if the IRB finds:

- that the only record linking the subject and the research is the consent document; and
- the principal risk is the potential harm resulting from a breach of confidentiality;
- OR
- that the research presents no more than minimal risk of harm to subjects; and
- does not involve procedures for which written consent is normally required outside of the research context

In cases in which the documentation of consent requirement is waived, the IRB may require the Principal Investigator to provide subjects with a written statement regarding the research.

WAIVER OF INFORMED CONSENT

Waiver for Minimal Risk Studies

The IRB may approve a consent procedure which does not include, or which alters some or all of the elements of informed consent or waive the requirement to obtain informed consent entirely provided the IRB finds and documents in the meeting minutes that:

- the research involves no more than minimal risk to the subjects; and
- the waiver or alteration will not adversely affect the rights and welfare of the subjects; and
- the research could not practicably be carried out without the waiver or alteration; and
- whenever appropriate, the subjects will be provided with additional pertinent information after participation.

A waiver of informed consent shall not be granted to research involving fetuses, pregnant women, human in vitro fertilization, prisoners, or cognitively impaired/disabled subjects.

This policy is not intended to limit the authority of a physician to provide emergency medical care, to the extent that the physician is permitted to do so under applicable Federal and State law.

ASSENT

Only legally competent adults can give legally effective informed consent. Minors and those individuals who are not competent to provide consent should be given the opportunity to *assent* to participate in the research project. Assent is a knowledgeable agreement to participate in the project. Adequate provisions should be made for soliciting the independent, non-coerced assent from minors or cognitively impaired persons who are capable of a knowledgeable agreement. In general, the IRB requires that children age seven (7) and older, and most cognitively impaired adults, be given the opportunity to assent. In cases where assent is obtained from a minor or cognitively impaired subject, permission must also be obtained from an authorized representative. Failure to object to participation in a research study is not assent.

In determining whether subjects are capable of assenting, the investigators and the IRB shall take into account the age, maturity, and psychological state of the subject 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.

APPROVAL AND EXPIRATION DATES ON INFORMED CONSENT DOCUMENTS

IRB approved informed consent documents will have the IRB approval and expiration dates stamped on the consent documents. Investigators shall only use copies of the consent document with the current approval date and stamp affixed in obtaining consent.

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 modification 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, the expiration date will be calculated based on the approval period recommended by the IRB Chair (or designee) using the date the initial IRB application or continuing review application was approved.

Tissue Bank Consent Documents

Tissue Bank Informed consent documents must contain language indicating whether or not the subject/donor will financially benefit from any product developed from their tissue. They must also have the current approval and expiration dates stamped on the consent documents. A sample consent may be found in iRIS.

Unanticipated Problems/Adverse Events

Unanticipated Problems

An *unanticipated problem* is an occurrence during the conduct of a study which meets the following three requirements. It is:

- (a) unexpected;
- (b) related to research participation; and
- (c) placed the subject or others at greater risk than previously identified.

The following are some examples of unanticipated problems in a research study:

- Stolen or lost sensitive, identifiable data.
- Gross pharmaceutical dosing error that resulted in no known harm to the subject.
- Donor sera were not appropriately screened.

Note that none of these examples represented any detectable harm or adverse effect to any particular subject, but each requires substantive changes in the protocol and/or informed consent or other corrective actions to protect the safety, welfare, and rights of the body of research subjects.

If an *unanticipated problem* is identified, it must be reported to the IRB within 2 days of the PI becoming aware of it. The IRB will notify the Institutional Official who will notify appropriate agency heads and OHRP. The IRB will work with the PI in determining what other actions must be taken.

Any report of an *unanticipated problem* that is submitted to the IRB must contain the following information:

- (1) a detailed description of what happened;
- (2) an explanation of the basis for determining that the incident represents an unanticipated problem;
- (3) a description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the unanticipated problem.

The IRB may conduct an expedited review of the event if there is no change in the risk/benefit ratio, the research proposal, or the consent form; otherwise, full Board review is required. The Chair or designee, at the time of expedited review, may refer any adverse event to the full Board for review.

External Adverse Events (Previously known as IND Safety Reports)

External adverse events are adverse events which occur at another site in a multi-site study. The FDA and sponsor require that these events be sent to each site taking part in the study.

If an *External Adverse Event* is identified as:

- Unexpected;
- Related or possibly related;

AND

- Serious Adverse Event

it must be submitted to 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 a sponsor requires IRB submission of External AEs that do not meet the criteria above, the PI may submit them via iRIS and the submission will be acknowledged by the IRB. These External Adverse Events will not be deliberated by the IRB.

If the External Adverse Event does meet the criteria listed above, it is presumed that there will be changes to the risk status, consent, and/or protocol and should be filed as an AMENDMENT within 7 days of the investigator receiving the information and must include the sponsor's rationale for the change(s).

Internal Adverse Events

PIs shall submit a written report to the IRB in writing via iRIS all unanticipated (i.e. not consistent with the current investigator's brochure or with other current risk information) *adverse events* or problems (both serious and non-serious):

- that involve research at TTUHSC or an affiliated entity
- **known to be** related or **may possibly be related** to the research activities
- within two (2) business **days** after the PI becomes aware of the event.
- The PI is responsible for the accurate documentation, investigation and follow-up of all possible study-related adverse events and other unanticipated problems.
- Reports of all unanticipated adverse events must be retained in both the PI files and the IRB office files for reference if needed.

The IRB may conduct an expedited review of the event if there is no change in the risk/benefit ratio, the research proposal, or the consent form; otherwise, full Board review is required. The Chair or designee, at the time of expedited review, may refer any adverse event to the full Board for review.

Serious Adverse Events (SAEs)

- death
- life-threatening experience
- hospitalization (for a person not already hospitalized);
- prolongation of hospitalization (for a subject already hospitalized);
- persistent or significant disability or incapacity; congenital anomaly and/or birth defects; or
- an event that jeopardizes the subject and may require medical or surgical treatment to prevent one of the preceding outcomes,

ALL Serious Adverse Events--whether or not the event is related to the research activities--must be submitted to the IRB as soon as possible, but no later than two (2) business days after the PI becomes aware of the event.

Data Safety Monitoring Board Reports

The Principal Investigator shall submit any independent data safety monitoring board reports to the IRB within five (5) business days from the date the information is received by the Principal Investigator.

IRB REVIEW

The IRB is charged with the responsibility of reviewing reported unanticipated problems involving risks to subjects and adverse events. The IRB and/or EVPR has the authority to suspend/ terminate approval of research that has been associated with unexpected serious harm to participants or others or for failure to conduct research in accordance with the IRB approved protocol.

Vulnerable Populations

CHILDREN AND MINORS

When children or minors are research subjects, investigators must obtain both the consent of the parent or authorized representative and the assent of the child if he/she is 7 years or older. Mere failure to object is not assent. The IRB has the authority to waive the assent requirement. Special regulations applying to children may be found in 45 CFR 46.402 Subpart (D).

PREGNANT WOMEN AND FETUSES

Special DHHS regulations applying to pregnant women and fetuses may be found in 45 CFR 46 Subpart B. These studies are not eligible for exempt status. No research may be conducted with pregnant women or fetuses unless the conditions specified in 45 CFR 46.402 are met.

PRISONERS

Special DHHS regulations applying to prisoners may be found in 45 CFR 46 Subpart C. This includes situations in which the subject becomes a prisoner after the research has commenced. No 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.

EMPLOYEES

No investigator may give an indication that an employee is required or shall consent 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.

STUDENTS

Prior to enrollment in a course where students may be requested to participate as research subjects, students shall be informed of the possibility. The course syllabus shall clearly describe proposed participation in research activities for course credit and include an alternative means of earning the course credit. 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 concerns regarding the use of students will promptly be forwarded to the EVPR.

Investigational Drugs/Devices

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 Principal Investigator must secure an IND or IDE number from the FDA or correspondence from the FDA waiving this requirement. This FDA number or letter waiving the requirement for an FDA number shall be included in the submission to the IRB.

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.

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.

STORAGE, HANDLING, AND DISPENSING OF INVESTIGATIONAL AGENTS

All inpatient and outpatient research studies involving either FDA approved or investigational agents (including radioactive agents used therapeutically or diagnostically) will receive automatic review by an IRB member who is a pharmacist or if not available, the IRB may request review by a pharmacist who is not an IRB member. Such review will include an assessment of source, purity, quality, and method of preparation and delivery.

Investigational agents to be given to inpatients shall be dispensed through affiliated entities' pharmacy whenever possible. The Principal Investigator is required to send the following materials to the pharmacy prior to initiation of the study:

- IRB approval letter
- Full protocol
- Investigator's Brochure (if available)
- IND/IDE documentation.

Investigational agents dispensed on an outpatient basis shall follow the above procedures when possible. If affiliated entities' pharmacies are not used, the Principal Investigator shall be responsible for proper storage and documentation pursuant to State and Federal regulations and Institutional policies.

Affiliated entities external to TTUHSC are responsible for proper storage, handling, and dispensing of investigational agents used in research at those facilities.

Genetic Research

Genetic information must be carefully maintained in order to protect against stigmatization, discrimination, or significant psychological harm to the subject.

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

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.

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.

Packaging & Shipment of Infectious Materials

The Principal Investigator is responsible for overseeing training and ensuring that all specimens packaged and shipped from TTUHSC comply with HSC OP 75.13, which states that:

“the shipment and transportation of all diagnostic and infectious materials is conducted in compliance with applicable rules, regulations, and guidelines governing the classification, description, labeling, marking, record keeping, training, and packaging of diagnostic and infectious materials.”

TTUHSC policy requires that all employees involved with the packaging or shipping of diagnostic or infectious materials undergo specific training in that discipline. The Principal Investigator is responsible for ensuring participation in the appropriate training. Documentation of training (i.e., certification) must be forwarded to the Safety Services Department. Additionally, it is the responsibility of supervisors to provide both initial and annual refresher training to all packers and shippers of diagnostics and infectious materials.

This training is available as a commercial shipping training program, *Saf-T-Pak* (CD-Rom), and is provided to supervisors by the Safety Services Department. *Saf-T-Pak's* comprehensive guide to shipping infectious substances and diagnostic specimens is updated annually and includes the 45th edition of the IATA dangerous goods regulations and the most current 49 CFR and U.S. Postal Service regulations.

HIPAA

AUTHORIZATION

Before an investigator can use or disclose protected health information (PHI), each subject must agree to sign the completed and IRB-approved TTUHSC form entitled “Authorization to Use and/or Disclose Your Protected Health Information for Research Study”. This form must also have the signature of a witness.

Such authorization shall satisfy the requirements of 45 CFR 164.508, except that the authorization may state that it does not expire, that there is no expiration date or event, or that it continues until the end of the research study.

HIPAA Waiver Request to Privacy Board

TTUHSC Principal Investigators may request to use and disclose specified PHI without an individual's authorization and/or without the necessity for an opportunity to agree or object for research purposes **if** the Principal Investigator submits a “Principal Investigator’s Request to Use and Disclose Protected Health Information Without Authorization for Research Purposes” form to TTUHSC or Institutional Privacy Board for review and decision.

For purposes of HIPAA, the TTUHSC Institutional Review Boards will act separately as Privacy Boards as defined by 45 C.F.R. Part 164.512(i). IRB Administrators shall verify Privacy Board Agreements with affiliated Entities.

Once the HIPAA documentation has been reviewed for compliance with TTUHSC policy, it does not need to be re-submitted for the duration of the study unless there are changes to study personnel or to the stated purpose of the research. These changes require the submission of an updated HIPAA Authorization form.

Duplicative HIPAA language shall not be included in the Informed Consent document. Sponsors requests to change HIPAA documents shall be submitted through the TTUHSC HIPAA Privacy Officer, but in general, shall not be considered.

Further information regarding HIPAA compliance, including approved forms, can be found at www.ttuhs.edu/hipaa.

Recordkeeping & Confidentiality

RECORDKEEPING

Every Principal Investigator is required by TTUHSC and federal regulations to maintain 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 must be maintained in the Principal Investigator's records. All records of human subject research are subject to inspection by federal authorities, TTUHSC officials, including but not limited to RIO and Compliance Officers, EVPR and the IRB. Research records (including data) are the property of TTUHSC and shall not be transferred to another entity without prior approval of the EVPR. All research records (including consent documents) must be kept for a minimum of three years after the close of the study at the local research site. Studies that involve drugs or devices seeking FDA approval must be kept for two years after the FDA has taken final action on the marketing application.

CONFIDENTIALITY

An issue of primary importance is the protection of subject confidentiality. The Principal Investigator must have sound plans to protect the subject's identity as well as the confidentiality of the research records. Care should be taken to explain the mechanisms that have been devised to protect confidentiality, for example, the use of numbering or code systems or safely locked files in private offices. Furthermore, the Principal Investigator should describe who has access to the data and under what circumstances a code system may be broken. Without appropriate safeguards, problems may arise from long-term retention of records.

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

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

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 <http://grants.nih.gov/grants/policy/coc/>.

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 http://grants.nih.gov/grants/policy/coc/appl_intramural.htm

Monitoring

The IRB and EVPR are authorized to monitor human subjects research approved by the IRB pursuant to the responsibilities and assurances made by TTUHSC under federal regulations (FWA 00006767) and TTUHSC policy (TTUHSC OP 73.06). The RIO shall be responsible for compliance activities on behalf of the IRB and EVPR, including audits and monitoring of IRB approved research.

The EVPR is responsible for the development and implementation of a research compliance program at TTUHSC. (TTUHSC OP 10.16) The TTUHSC Research Integrity Office (RIO) has been established by the EVPR to provide administrative support to the IRB and to maintain research compliance at TTUHSC with applicable laws, regulations, and TTUHSC policy.

The PI shall make available all research records for review or audit upon request of the IRB, the EVPR, and RIO or authorized designee. Routine compliance audits shall be conducted as part of the monitoring process. Special audits may also be conducted on behalf of the IRB at the request of the IRB Chair, Director of RIO and/or the EVPR in response to allegations that research is not being conducted in accordance with IRB requirements or has been associated with unexpected serious harm to subjects or others.

Monitoring and/or auditing activities may include, but are not limited to the following:

- Study file for required elements including the presence of required documentation; protocol and amendments; approved consent forms and IRB documentation
- Subject eligibility
- Informed Consent Documentation
- Unanticipated and Adverse Event reporting
- Accuracy and completeness of Case Report Forms
- Confidentiality of records
- Drug and Device handling and accountability
- Laboratory data
- Concomitant medications/therapy
- Subject history
- Progress reports from PIs
- Contact research subjects
- Audit advertisements and other recruiting materials as deemed appropriate by the IRB
- Other Research conducted by PIs
- Other monitoring or auditing activities deemed appropriate by the IRB
- Any additional information determined necessary by the EVPR.

Allegations of Non Compliance or Harm to Subjects

The Research Integrity Office (RIO) shall document the receipt of allegations of non-compliance with IRB approved protocol or harm to research subjects or others. Information received by the RIO shall be reviewed in a timely manner and assigned to research compliance personnel for audit pursuant to criteria and procedures established in the TTUHSC Research Compliance Office Procedure Manual. Audit findings and reports will be sent to the PI, IRB Chair, RIO Director and EVPR. The IRB may report findings of non-compliance or IRB decisions to the PIs direct supervisor or others as it deems necessary.

The IRB Chair will determine the need for full IRB review of audit reports. The report may be placed on the agenda of the next regularly scheduled meeting for notification or discussion, as appropriate. The Full Board may vote to suspend/terminate the research if it is found that a human subject has been exposed to unexpected serious harm or that research is not being conducted in accordance with IRB approved protocol. In addition, shall the EVPR conclude that the research does not fully comply with policies or obligations of TTUHSC, the research may be disapproved, or suspended/terminated on behalf of TTUHSC.

Compliance reports summarizing all IRB compliance activities including audits shall be submitted to each IRB and EVPR by the RIO on a pre-determined schedule. Compliance reports are confidential and privileged Medical Committee documents.

Research Without IRB Approval

If research is or has been conducted by TTUHSC faculty, staff, or students without IRB approval, any person with knowledge about this shall immediately report it to the EVPR and/or the IRB. Corrective steps will be taken to ensure that the researcher is aware of all federal, state, and local policies and procedures. Researchers will be asked to immediately stop all research and inform any journals, meetings, etc. where research was presented or where presentation is pending that the research was conducted without IRB approval.

Federal Regulatory Agency Audits

PI shall notify RIO Research Compliance Officer immediately upon receipt of impending notice of audit or investigation.

Sponsor Monitoring Reports

PI shall send a copy of external sponsor monitoring reports to RIO Research Compliance Officer within 5 days of receipt.

Glossary

ADMINISTRATIVELY CLOSED Decision of the IRB based on PI non-responsiveness to IRB requests. This can occur prior to initial IRB approval or any time following IRB approval.

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 considered 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.*

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.

ASSENT Agreement by an individual not competent to give legally valid informed consent (e.g., a child or cognitively 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.

BELMONT REPORT A statement of basic ethical principles governing research involving human subjects issued by the National Commission for the Protection of Human Subjects in 1978.

BENEFIT A valued or desired outcome; an advantage.

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

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.

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 TRIAL A controlled study involving human subjects, designed to evaluate prospectively the safety and effectiveness of new drugs or devices or of behavioral interventions.

CLOSURE See *Study Closure*

COGNITIVELY IMPAIRED Legally competent persons who may be compromised in any way in their ability to make decisions in their best interests.

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.*)

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.

CONFLICT OF INTEREST COMMITTEE *See TTUHSC OP 10.8*

CONSENT *See: Informed Consent.*

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. (*45CFR 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.

DATA AND 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.

DEVICE (MEDICAL) *See: Medical Device.*

DHHS A federal agency: U.S. Department of Health and Human Services; formerly the Department of Health, Education and Welfare (DHEW).

DISAPPROVED The IRB has reviewed the study and determined that it is not approved and may not receive further review. *See also Request for Reconsideration*

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.

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.

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

EXEMPT RESEARCH Research determined by person(s) designated by the IRB Chairperson or designee to involve human subjects in one or more of certain minimal risk categories [38 CFR 16.101(b)].

EXTERNAL ADVERSE EVENT (ALSO CALLED IND SAFETY REPORT) Adverse events experienced by subjects enrolled by investigators at other sites participating in the same clinical trial as investigators at TTUHSC/Affiliates.

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

EXPEDITED REVIEW Review of proposed research by the IRB chair or a designated voting member or group of voting members rather than by the entire IRB. Federal rules permit expedited review for certain kinds of research involving no more than minimal risk and for minor changes in approved research.

EXPERIMENTAL Term often used to denote a therapy (drug, device, procedure) that is unproven or not yet scientifically validated with respect to safety and efficacy. A procedure may be considered "experimental" without necessarily being part of a formal study (research) to evaluate its usefulness.

FDA Food and Drug Administration; an agency of the federal government established by Congress in 1912 and presently part of the Department of Health and Human Services.

FEDERALWIDE ASSURANCE (FWA) An agreement between a federally funded entity and OHRP that stipulates methods by which the entity will protect research participants (66 Fed Reg 19139, 19141(April 13, 2001))

FETUS The product of conception from implantation until delivery [45 CFR 46.202].

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 nonscientific areas. For the research to be approved, it must receive the approval of a majority of those voting members present at the meeting.

GRANT Financial support provided for research study designed and proposed by the Principal Investigator(s). The granting agency exercises no direct control over the conduct of approved research supported by a grant.

GUARDIAN An individual who is authorized under applicable state or local law to give permission on behalf of another to general medical care [45 CFR 46.402(3)]

HIPAA Health Insurance Portability and Accountability Act of 1996

HUMAN IN VITRO FERTILIZATION Any fertilization involving human sperm and ova that occurs outside the human body.

HUMAN SUBJECTS Individuals whose physiologic or behavioral characteristics and responses are the object of study in a research project. Under the federal regulations, human subjects are defined as: living individual(s) about whom an investigator conducting research obtains: (1) data through intervention or interaction with the individual; or (2) identifiable private information.

IDE *See: Investigational Device Exemptions.*

INCAPACITY A person's mental status leads to the inability to understand information presented, to appreciate the consequences of acting (or not acting) on that information, and to make a choice. Often used as a synonym for incompetence. (*See also: Incompetence.*)

INCOMPETENCE Technically, a legal term meaning inability to manage one's own affairs. Often used as a synonym for incapacity. (*See also: Incapacity.*)

IND *See: Investigational New Drug.*

IND SAFETY REPORT *See: External Adverse Event.*

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.

INSTITUTIONAL REVIEW BOARD (IRB) A specially constituted review body established or designated by an entity to protect the welfare of human subjects recruited to participate in biomedical or behavioral research. At TTUHSC, the IRB is deemed to be a medical committee.

INSTITUTIONALIZED Confined, either voluntarily or involuntarily (e.g., a hospital, prison, or nursing home).

INTERNAL ADVERSE EVENT Any adverse events experienced by a single subject enrolled in TTUHSC or TTUHSC IRB affiliate research project. (reverse words)

INVESTIGATIONAL DEVICE EXEMPTION (IDE) An unapproved medical device that is used to save the life of a patient or to help a patient suffering from a serious disease or condition for which there no other alternative therapy exists. Patients/physicians faced with these circumstances may have access to investigational devices under one of four main mechanisms by which FDA may make an unapproved device available: Emergency Use, Compassionate Use (or Single Patient/Small Group Access), Treatment Use, or Continued Access.

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 nonclinical data on the investigational product(s) which is relevant to the study of the investigational product(s) in human subjects.

IN VITRO Literally, "in glass" or "test tube;" used to refer to processes that are carried out outside the living body, usually in the laboratory, as distinguished from in vivo.

IN VIVO Literally, "in the living body;" processes, such as the absorption of a drug by the human body, carried out in the living body rather than in a laboratory (in vitro).

IRB See: *Institutional Review Board*.

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.

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.

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.

MEDICAL DEVICE A diagnostic or therapeutic article that does not achieve any of its principal intended purpose through chemical action within or on the body. Such devices include diagnostic test kits, crutches, electrodes, pacemakers, arterial grafts, intraocular lenses, and orthopedic pins or other orthopedic equipment.

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)].

MONITORING The collection and analysis of data as the project progresses to assure the appropriateness of the research, its design and subject protections.

NONAFFILIATED MEMBER Member of an Institutional Review Board who has no ties to the parent entity, its staff, or faculty. This individual is usually from the local community (e.g., minister, business person, attorney, teacher, homemaker).

OFFICE FOR HUMAN RESEARCH PROTECTIONS (OHRP) The office within the U.S. Department of Health and Human Services, responsible for implementing DHHS regulations [45 CFR Part 46] governing research involving human subjects.

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

PI See: *Principal Investigator*.

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 with 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 BOARD IRB or another review body which reviews requests to use or disclose Private Health Information (PHI) for research purposes without authorization under HIPAA.

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 DEVIATION 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.

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 Systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge [45 CFR 102(d)].

RESEARCH INTEGRITY OFFICE (RIO) Office responsible for the oversight and direction of the human research protection program at TTUHSC, which includes administrative oversight of the IRB, the TTUHSC Research Compliance Program, and TTUHSC Educational requirements for human research.

RESPECT FOR PERSONS An ethical principle discussed in the Belmont Report requiring that individual autonomy be respected and that persons with diminished autonomy be protected.

RETROSPECTIVE STUDIES Research conducted by reviewing records from the past (e.g., birth and death certificates, medical records, school records, or employment records) or by obtaining information about past events elicited through interviews or surveys.

REVIEW (OF RESEARCH) The oversight of research on a periodic basis by the IRB. In addition to the at least annual reviews mandated by the federal regulations, reviews may, if deemed appropriate, also be conducted on a continuous or periodic basis.

RISK The probability of harm or injury (physical, psychological, social, or economic) occurring as a result of participation in a research study. Both the probability and magnitude of possible harm may vary from minimal to significant. Federal regulations define only "minimal risk".

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.

SPONSOR A person or other entity that initiates a clinical investigation, but that does not actually conduct the investigation, i.e., the test article is administered or dispensed to, or used involving, a subject under the immediate direction of another individual. A person other than an individual (e.g., a corporation or agency) that uses one or more of its own employees to conduct an investigation that it has initiated is considered to be a sponsor (not a sponsor-investigator) and the employees are considered to be investigators.

STUDY All components of a research project.

STUDY CLOSURE Study approved by the IRB that may be closed by the investigator, the sponsor, the IRB, TTUHSC, or by an affiliated entity. (*See: Section 5.5*) (*See: Administratively Closed*).

STUDY COMPLETED Study completed as approved by IRB, including data analysis, and finalized.

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 noncompliance with 45 CFR Part 46; or the requirements or determinations of the IRB (See Sections 5.6, 5.7). Requires prompt reporting to federal regulatory authorities and TTUHSC pursuant to federal Assurance and 45 CFR Part 46.

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

TABLED The IRB has reviewed the study and determined that extensive changes are necessary. The study will be re-reviewed by once changes have been made.

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;
- (2) related or possibly related to a subject's participation in the research; and
- (3) suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) related to the research than was previously known or recognized.

UNEXPECTED ADVERSE EVENT Any adverse event occurring in one or more subjects in a research protocol, the nature, frequency, or severity of which is not consistent with either:

- (1) the known or 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.

Appendices (Useful Tools)

I. PI Responsibilities

This document briefly outlines the responsibilities of the Principal Investigator (including responsibilities related to clinical trials).

II. Documentation of the Consent Process

In addition to the signed informed consent document, this form is a useful tool to document the process of obtaining informed consent in accordance with TTUHSC policy and Good Clinical Practice (GCP) guidelines.

III. Designation of Authorized Personnel

This form can be utilized to designate research personnel and identify the specific research activities that each member of the team is authorized to perform. It clarifies authorized personnel for auditors and other personnel involved. It should be kept with the Principal Investigator's study documents.

IV. Regulatory Files Checklist

This checklist outlines the study-related documents that should be maintained in the Principal Investigator's files to maintain compliance with applicable regulations. Commercial sponsors typically require this documentation to be maintained in a "regulatory binder."

I. PI Responsibilities

SUMMARY OF PRINCIPAL INVESTIGATOR RESPONSIBILITIES

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 and storage of the investigational product(s) at the trial site
- reviewing the proper use of the study article(s) by the subject(s)

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 and appropriate 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

II. Documentation of the Consent Process

Subject Identifier: _____

Protocol: _____

Principal Investigator: _____

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

The Informed Consent Document was explained and questions were discussed in
English Spanish Other _____.

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

The Informed Consent Document was explained and voluntary consent or assent was obtained at
_____ AM PM on ____/____/_____, before any research procedures were performed.

Informed consent or assent was obtained using International Council on Harmonization Good Clinical Practice Guidelines.

Risks and benefits of this research were explained to the subject subject's family designated representative and all questions were answered.

Alternative treatments or therapies were discussed with the subject subject's family designated representative and all questions were answered.

All procedures included in the research protocol have been discussed with the subject subject's family designated representative and all questions were answered.

The subject's rights while participating in a research study were discussed with the subject subject's family designated representative and all questions were answered.

The subject subject's family designated representative reviewed the consent form and verbalized an understanding of the study consent, the study procedures and study participant role.

After all questions were answered, and prior to any study related procedures, Informed Consent or Assent was voluntarily provided by: subject subject's family designated representative.

A copy of the signed and dated consent form has been placed in the medical record and also given to the: subject subject's family designated representative and they were informed to treat it as a legal document.

Name(s) of patient's family member & relationship: _____

Name(s) of designated representative: _____

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

HIPAA Authorization Form signed: Yes No N/A
(explain) _____

Printed Name of Person Obtaining Consent

Signature

Date

III. Designation of Authorized Personnel

As Principal Investigator for the following study:

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

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

 Signature

_____/_____/_____
 Date

IV. Regulatory Files Checklist

📁 INVESTIGATOR'S BROCHURE

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

📁 PROTOCOL and CASE REPORT FORMS

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

📁 PROTOCOL AMENDMENTS

Retain copies of any amendments to the original final protocol made by the sponsor or the investigator. Modifications may be in the form of new pages to be inserted in the protocol, an addendum to the protocol in the form of a letter, or contained in the body of an amended protocol.

Note that all protocol amendments must be reported to your Institutional Review Board (IRB). Also, protocol amendments that increase the risk to the subject in any way must receive IRB approval prior to implementation.

📁 FORM FDA 1572

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

📁 INVESTIGATOR CVs

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

📁 IRB CORRESPONDENCE

Contains all correspondence between the investigator and the IRB regarding this protocol. Examples of documents to retain are comments from the IRB on the consent form or the protocol, the IRB approval letter(s), advertisements for the study approved by the IRB, yearly renewals of approval, site updates to the IRB, serious adverse event reports, notification to the IRB of IND safety reports, and a letter notifying the IRB of the completion of the study.

📁 IRB-APPROVED INFORMED CONSENT FORM

Has the original approved IRB consent form(s), as well as any amended or renewed consent forms.

📁 LABORATORY CERTIFICATION

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

📁 RANGE OF NORMAL VALUES for the REFERENCE LABORATORY

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

📁 SAE REPORTS (Internal and External)

All serious adverse events must be reported promptly to the sponsor and to the IRB. Contains copies of all IND safety reports sent by the sponsor.

 **DRUG ACCOUNTABILITY**

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

 **MONITORING LOG**

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

 **INCLUSION/EXCLUSION LOG**

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

 **SIGNATURE LIST**

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

 **FINAL STUDY REPORT**

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

 **SPONSOR CORRESPONDENCE**

Contains all correspondence between the investigator and sponsor, except for items dealing with protocol changes and financial matters (which are filed separately).