TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER EL PASO

OFFICE OF RESEARCH
RESEARCH COMPLIANCE
PROGRAM MANUAL

Version 1.0

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ACRONYMS USED IN THIS MANUAL

Acronym	Meaning
AE	Adverse Event
BIS	Bureau of Industry and Security
CCL	Commodity Control List
CFR	Code of Federal Regulations
CITI	Collaborative Institutional Training Initiative
COIRC	Conflict of Interest in Research Committee
CRA	Clinical Research Associate
CRC	Clinical Research Coordinator
CRF	Case Report Form
CRO	Contract Research Organization
DCF	Data Collection Form
DHHS	Department of Health and Human Services
EAR	Export Administration Regulations
ECCN	Export Control Classification Number
eCRF	Electronic Case Report Form
eCRT	Effort Certification and Reporting Technology
EDC	Electronic Data Capture System
EMR	Electronic Medical Records
FCOI	Financial Conflict of Interest
FDA	Food and Drug Administration
FDAMA	Food and Drug Administration Modernization Act of 1997
FWA	Federal Wide Assurance
HIPAA	Health Insurance Portability and Accountability Act
HRPP	Human Research Protection Program
IACUC	Institutional Animal Care and Use Committee
IBC	Institutional Biosafety Committee
ICF	Informed Consent Form
ICH-GCP	International Conference on Harmonization – Good Clinical Practice
IO	Institutional Official
IP	Investigational Product
IRB	Institutional Review Board
iRIS	Integrated Research Information System
IRS	Internal Revenue Service
ITAR	Internal Traffic in Arms Regulations
MISC	Miscellaneous
NIFA	National Institute of Food and Agriculture
NIH	National Institutes of Health
NSF	National Science Foundation
OFAC	Office of Foreign Asset Control
OHRP	Office of Human Research Protections

- OP Operating Policy & Procedure
- OR Office of Research
- RC Research Committees
- SP Sponsored Programs
- PEC Primary Effort Coordinator
- PHI Protected Health Information
- PI Principal Investigator
- QIRB Quality Improvement Review Board
- RCC Research Compliance Committee
- RCO Research Compliance Officer
- RCR Responsible Conduct of Research
- RCU Research Compliance Unit
- RIO Research Integrity Officer
- RIU Research Integrity Unit
- RSC Radiation Safety Committee
- SAE Serious Adverse Event
- SARP Scholarly Activity and Research Program
- TTU Texas Tech University
- TTUHSCEP Texas Tech University Health Sciences Center at El Paso
- USDA United States Department of Agriculture
- USML United States Munitions List
- VPR Vice President for Research

Table of Contents

1. CHAPTER 1 : ORGANIZATION OF THE TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER AT EL PASO RESEARCH COMPLIANCE PROGRAM

1.1 Introduction

The Research Compliance Unit (RCU) is housed within the Research Integrity Unit (RIU) in the Office of Research (OR). It strives to support, advance and build a strong Research Community within Texas Tech University Health Sciences Center at El Paso (TTUHSC El Paso) through oversight and collaboration with researchers in order to provide education on compliance and research integrity as well as administrative support. The RCU is committed to serve as a central University resource for faculty and staff by providing regulatory guidance within institutional research conduct.

This manual describes the policies and procedures of the TTUHSC El Paso Research Compliance Program (RCP) that is implemented by the RCU. Its purpose is to communicate comprehensive information about institutional and federal research requirements including but not limited to those detailed on the TTUHSC El Paso Human Research Protection Program Manual (HRPP) and other TTUHSC El Paso research compliance committee manuals. This manual incorporates in one core document TTUHSC El Paso's program to promote and encourage research at our institution while upholding research integrity, human subject rights and protection, the humane care and use of animals, and the safe, legal, and ethical use of hazardous chemical and biological materials at our facilities . All members of TTUHSC El Paso conducting or engaged in research must be knowledgeable about the standards and requirements of the Office of Research (OR). Non-compliance can result in severe penalties to the institution, and in some instances, to the individual. It is the responsibility of faculty and staff to be familiar with TTUHSC El Paso's policies as they relate to these research compliance areas.

1.2 Goals and Objectives

Our overall objective is to ensure the quality and integrity of research conducted at our institution. We aim to adhere to federal and state regulations as well as institutional policies within research conduct.

As research and teaching are vital elements of TTUHSC El Paso, the RCU's mission is to advocate and share good clinical practice measures amongst the institution's research community, while encouraging open communication and guidance about ethical concerns and inquiries. This ensures that institutional and federal guidelines are met.

1.3 Research Covered by the Research Compliance Manual

This manual serves to inform TTUHSC El Paso research personnel about the different areas and components of research on our campus with a primary focus on research compliance. Throughout this manual we will review research compliance as it pertains to the following areas:

- Human Subjects
- Hazardous Chemicals and Biological Materials
- Recombinant/Synthetic DNA
- Financial Conflicts of Interest in Research
- Animals
- Export Controls
- Allowable Research Grant Expenditures
- Scientific Misconduct

More information regarding the areas listed above can be obtained through our TTUHSC El Paso website by reviewing each of their bylaws, operational policies, and administrative manuals. The website also includes additional resources and contact information.

**Refer to Appendix A for a full list of TTUHSC EP department names and links used as resources in completing this manual.*

2. CHAPTER 2 : ROLES AND RESPONSIBILITIES

2.1 Organizational Summary

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

2.1.1 Office of Research

The Office of Research (OR) is responsible for all aspects of research administration on campus. The OR houses the Vice President for Research (VPR), Sponsored Programs (SP), and the Research Ethics Committees. The VPR also serves as the Institutional Official (IO) for our institution. The OR uses Sponsored Programs and the Research Ethics Committees in order to provide campus-wide oversight.

In addition, the OR provides administrative and compliance oversight of research related services and of research activities conducted by TTUHSC El Paso faculty, staff, and students using TTUHSC El Paso facilities. The OR also serves as the point of contact for the Department of Health and Human Services' (DHHS) Office of Human Research Protection (OHRP). As mentioned previously, the Research Integrity Unit (RIU) is housed within the OR along with other services that will be mentioned later in this manual. This office utilizes the RIU to assure adherence to federal and state regulations as well as institutional policies in research conduct. The OR may also provide compliance oversight for activities taking place outside of TTUHSC El

Paso facilities when required by regulation, or when such oversight is agreed to in writing by TTUHSC El Paso.

2.2.2.1 Research Compliance Unit

As mentioned above, the Research Compliance Unit (RCU) is part of the RIU. The RIU currently consists of the RCU, the Research Ethics Committees, and the Clinical Research Support Program. The RCU itself has the Research Compliance Officer and the Research Compliance Senior Analyst. The RCU helps the research committees ensure that compliance is upheld by conducting audits to monitor adherence to applicable laws, regulations, Regents' Rules, and TTUHSC El Paso policies related to the appropriate conduct of research activities at or through TTUHSC El Paso.

Additionally, the RCU is responsible for monitoring and ensuring adherence to deadlines and/or submissions detailed in institutional policies and federal regulations for the supplementary research services that are provided by the OR. These services include but are not limited to the following:

- The TTUHSC El Paso Account on ClinicalTrials.gov
- Submissions to Regulations.gov
- Research Export Controls
- Certification and Processing in relation to time and effort reporting

The RCU also serves as a training resource for the Institution. The RCU creates and provides tailored and research-related training upon request, and offers trainings both in-person and online to internal and external participants for user convenience.

2.1.2.2 Research Compliance Officer

The Research Compliance Officer (RCO) is a designee assigned by the VPR. The RCO is responsible for conducting clinical research audits, monitoring of various compliance systems mentioned previously, creating and conducting trainings and is tasked with collaborating with appointed research committees, other divisions within the OR, the TTUHSC El Paso Office of Institutional Compliance, Texas Tech University System (TTU System) offices, and TTUHSC El Paso schools and departments on matters pertaining to research compliance. This individual also serves on and/or attends multiple institutional committees and meetings as an OR representative and in an effort to promote collaboration throughout the institution. These committees consist of, but are not limited to the following:

- Research Compliance Committee Meetings
- TTUHSC El Paso's Institutional Review Board Committee Meetings

- Conflict of Interest in Research Committee Meetings
- Institutional Compliance Committee Meetings
- Institutional Conflict of Interest Committee Meetings

The goal of RCO is to help facilitate research and to make sure it is done safely, ethically, and legally. RCO takes pride in being service-oriented. If you have questions or concerns, please contact the Research Compliance Officer at any time.

2.1.2.3 Research Compliance Senior Analyst

The Research Compliance Senior Analyst or designee is delegated specific responsibilities by the RCO. The Research Compliance Senior Analyst is responsible for maintaining some of the RCU's basic administrative functions while also conducting audits on exempt studies. Some examples of these functions consist of the following:

- Maintaining the institutional Clinicaltrials.gov system
- Recording, responding to, and processing all training requests and exam submissions
- Providing training certificates for any RCU training completions
- Maintaining the Research Compliance Webpage
- And assisting the RCO with other functions

Like the RCO, the Research Compliance Senior Analyst also creates and conducts trainings for the RCU. In addition, this individual is tasked with collaborating with other divisions within the OR, and other TTUHSC El Paso departments on matters pertaining to research compliance.

When the RCO is unavailable, the Research Compliance Senior Analyst becomes the RCO's back-up regarding clinical research audits. The Research Compliance Senior Analyst also provides the RCO with assistance in dealing more difficult and/or subject heavy audits.

The Research Compliance Senior Analyst is always available to provide assistance. If you have questions or concerns, please contact the Research Compliance Senior Analyst at any time.

2.1.3 Sponsored Programs

Sponsored Programs provides oversight during the pre and post award grant process for institutional, private, state, and federal grants. This office also houses the Research Contracts and Agreements (RCA) division, which coordinates and assists research personnel with non-disclosure/confidentiality agreements, industry-sponsored clinical trial agreements, and material transfer agreements. SP is responsible for overseeing and facilitating proper grant

management and research agreements, and for ensuring compliance with federal, state, and institutional guidelines. SP does not step in until after the award application has been prepared and is being submitted. In addition to this, SP does not oversee SEED grant funding for medical student projects related to the TTUHSC EP Scholarly Activity and Research Program (SARP). The SARP office provides guidance and assistance to students applying for SEED grant funding SARP projects. The SARP office is housed within the Department of Medical Education.

It should be noted that the Office of Institutional Advancement is responsible for providing information regarding grants that may be available to researchers at our institution. They are also able to provide guidance in reaching out to corporations who support the type of research that investigators are interested in conducting, and in assisting to gather all institutional documents required for submission.

2.1.4 Office of Contracts and Grants Accounting

The Office of Contracts and Grants Accounting (CGA) is located within the Department of Business Affairs and is responsible for providing support in administering contracts and grants related to research amongst many other services. The CGA and the RCA work hand-in hand to implement and oversee our institution's grant, financial, contractual processes for Federal, State, Local and Private Contracts and Grants related to research. In addition, this office oversees the accounting and financial reporting for other types of restricted funds.

2.1.5 Clinical Research Support Program (CRSP)

The OR has established a program to provide clinical research support to investigators on campus that wish to initiate a clinical research study but do not have adequate and direct support to do so. The purpose of this program is to encourage investigators that are not normally able to conduct research on their own to initiate research studies in order to promote the growth of sponsored and clinical research at our institution. This program is housed within the RIU in the Office of Research, but is not part of the Research Compliance Unit or the Research Ethics Committees and works independently of these groups. More information about this program can be obtained on the CRSP webpage found in on our main research page in our TTUHSC EP Website.

3. CHAPTER 3: INSTITUTIONAL REQUIREMENTS

3.1 HSC Policies and Procedures

All research compliance policies and procedures listed throughout this manual are governed by institutional, state, and federal regulations. These policies abide by and correlate with the information presented in the information listed throughout the HSC Ops, the TTUHSC El Paso Human Research Protection Program Manual, and the research compliance committee OPs and bylaws. There are some standards and instructions mentioned within this document that are not state and/or federal mandates. These standards and instructions are based on the collaborative efforts of the OR and institutional research compliance committees with the intention to standardize and improve the quality of our research.

**Please note that nothing in this manual shall supersede or replace TTUHSC El Paso policies addressing a specific research area.*

4. CHAPTER 4 : RESEARCH COMPLIANCE COMMITTEES/ETHICS COMMITTEES

4.1 TTUHSC El Paso Research Ethics Committees

A number of standing ethics committees have been established, each with specific areas of responsibilities. The various institutional committees have the authority to approve or disapprove any research and research related activities based on their discretion and also in accordance to federal, state and institutional policies and guidelines. These committees were established to protect the rights and safety of research participants, employees, and animals involved in research.

4.1.1 Institutional Review Board for the Protection of Human Subjects (IRB)

TTUHSC El Paso has established IRBs to review research involving human subjects. Chairpersons and members of each TTUHSC El Paso IRB are appointed by the VPR and serve at the discretion of the VPR. TTUHSC El Paso has established multiple IRBs to manage the workload, and they report to the VPR through the OR.

The TTUHSC El Paso IRB members, IRB administrative staff, the Sr. Director, the OR Managing Director, and the VPR are responsible for ensuring that all TTUHSC El Paso personnel, students and affiliated entities comply with applicable federal regulations and institutional policies regarding the conduct of research with human subjects. In order to ascertain that compliance is upheld, the IRBs are authorized to monitor research involving human subjects approved by the IRB. The IRBs also have the authority to inspect research facilities, obtain records and other relevant information relating to the use of human subjects in research by way of audits. These audits are implented by the Research Compliance Unit. In addition no research involving human subjects may commence until all required institutional approvals (including IRB approvals) are obtained. This prohibition includes data collection for research involving human subjects, which meets the criteria for exemption from formal IRB review.

As outlined in the current HRPP Manual, each TTUHSC El Paso IRB is responsible for reporting to the Institutional Official (IO) any unanticipated problems involving risks to subjects or serious and continuing noncompliance with IRB requirements, and any decision to suspend or terminate approval of research involving human subjects. The VPR, in consultation with the OR Managing Director, is responsible for ensuring that required reporting of such events are made to appropriate entities such as the Office for Human Research Protections (OHRP), Food and Drug Administration (FDA) or the National Institutes of Health (NIH).

4.1.1.1 The Research Compliance Unit's Responsibilities to the IRB

Audit findings are typically reviewed by the IRB Chair, designated committee members, and/or the full board. For routine audits, the IRB Chairperson or designee will conduct an initial review of the audit report. If both the research compliance officer and IRB Chairperson/designee agree that the audit report contains no findings related to serious or continuing non-compliance, the audit report can be accepted as written on behalf of the IRB. A copy of the audit report may be placed on the next agenda for IRB members to review for informational purposes. The IRB then takes such actions that are in its judgment necessary to enforce compliance with applicable federal and state law, regulations, or guidelines. A final audit report is then distributed by the IRB administration to all listed on the study, and IRB and compliance representatives. The IRBs may or may not require additional information, a formal response, and/or a corrective action plan depending on the severity of the findings uncovered during the audit.

The research compliance officer may also be asked to work with the PI to implement any recommendations that were included in the audit report. Failure by the PI to communicate with the research compliance officer regarding implementation of recommendations may lead to a "for-cause" audit or could be reported to the IRB as continuing non-compliance. All audit reports that result from "for-cause" audits, regardless of the findings, and any audit reports that either the research compliance officer or the IRB Chairperson/designee (or both) determine to include findings of serious or continuing non-compliance will be placed on the next IRB agenda for review at a convened meeting of the IRB. Audit reports will be available for review by all IRB members. At the convened IRB meeting the pre-liminary audit report, findings, and recommendations will be reviewed. The IRB will make a final determination as to whether the findings meet the definition of serious and/or continuing non-compliance. Recommended corrective actions are based on HRPP Manuanl and *Appendix B* of this manual and can include action up to suspension and/or termination of approval of research that is not being conducted in accordance with IRB requirements or that has been associated with unexpected serious harm to subjects.

Following the IRB's review of the audit findings and any additional determinations that they have made, the PI will be notified through iRIS of the outcome of the review. If the IRB offers a plan of correction, the specific changes to be implemented will be communicated, as well as a time frame for implementing the changes. If the IRB has determined that the project is to be suspended or terminated, this information will be communicated to the principal investigator as well. The VPR and Managing Director of the OR will also be notified of any IRB determinations of serious or continuing non-compliance and any decision to suspend or terminate a research project. The IO will then be responsible for notifying federal and/or sponsoring oversight agencies.

4.1.2 Institutional Biosafety Committee (IBC)

TTUHSC El Paso has established an Institutional Biosafety Committee (IBC) to fulfill the requirements of the NIH Guidelines. IBC members are appointed by the VPR, but the VPR is ultimately responsible for the implementation of guidelines and regulations through the provision of necessary resources, and the establishment of appropriate policies and procedures.

The IBC provides local oversight of all A/BSL3 research activities, and oversight of all research involving biologically hazardous and acutely hazardous chemical materials (excluding radioactive materials or radiation producing devices) as used by TTUHSC El Paso faculty at TTUHSC El Paso facilities. The committee also monitors compliance with applicable federal, state, and local rules, regulations, and laws with regard to research involving biologically and chemically hazardous materials, and Recombinant or Synthetic Nucleic Acid Molecules. The IBC and the Office of Safety Services work together to review all of TTUHSC El Paso's research that involve biologically and chemically hazardous materials, and Recombinant or Synthetic Nucleic Acid Molecules.

4.1.2.1 The Research Compliance Unit's Responsibilities to the IBC

The IBC has the authority to inspect research facilities, obtain records and other relevant information related to the use of hazardous chemicals and biological materials used in research. The IBC takes such actions that are in its judgment necessary to enforce compliance with applicable federal and state law, regulations, or guidelines, including action to suspend or terminate approval of research that is not being conducted in accordance with IBC requirements or that has been associated with unexpected serious harm to others.

In addition, routine and random inspections of the approved research areas are conducted by Safety Services. This information is reported to the IBC and discussed at the committee meetings. There are varying degrees of non-compliance, as well as an

escalation process and relevant disciplinary action(s), pertaining to PI's, research personnel, and their respective IBC protocols.

The RCU is also responsible for compliance activities on behalf of the IBC and the VPR, including audits and monitoring of IBC approved research. Currently the RCO will review IBC licenses associated with IRB protocols during audits. These licenses involve the use of working in a laboratory and/or handling, collecting, and/or shipping of any kind of tissue sample or specimen. The IBC licenses are reviewed to ensure that they are not expired and that the appropriate personnel have been added along with the materials that will be handled. Evidence of non-compliance is reported to the IRB and may be reported to the IBC depending on the severity of the finding.

4.1.3 Institutional Animal Care and Use Committee (IACUC)

The IACUC was established by the TTUHSC El Paso President and is responsible for reviewing animal research and teaching protocols, animal research facilities, and to support and to protect the officially sanctioned use of animals in research, teaching and service at TTUHSC El Paso. The IACUC is overseen by the IO.

All research or teaching involving animals and conducted by or under the direction of any employee or agent of TTUHSC El Paso using any TTUHSC El Paso property or facility in any way is governed by the policies and procedures set in place by the IACUC. These policies apply regardless of whether the research is subject to Federal regulation or funded by a sponsor.

Failure to comply with any of the laws or regulations, or any of the TTUHSC El Paso IACUC Policies and Procedures may result in possible action under applicable institutional policies, including but not limited to IACUC Complaints of Mistreatment of Animals and Policy Noncompliance at TTUHSC El Paso. Any perceived violation shall be reported in accordance with policy even if immediate harm to animals is not present.

4.1.3.1 The Research Compliance Unit's Responsibilities to the IACUC

Allegations of non-compliance and/or mistreatment of the animals is reportable by any person with concerns involving the care and use of animals at our institution. The IACUC does include a list of reportable incidents within their policies and how to report the incident. For complaints or to report any incidents of mistreatment please refer to **IACUC Policy #11 - Complaints of Mistreatment of Animals and Policy Noncompliance at TTUHSC El Paso** available on the IACUC's Policy Page (https://elpaso.ttuhsc.edu/research/committees/iacuc/policies.aspx). Complaints received by the IACUC will result in a full investigation and proper assessment of the nature, extent, and urgency of the concern. Investigations are currently being

conducted by the IACUC Chair and/or the Institutional Veterinarian (IVet) and do not involve the RCU.

4.1.4 Conflict of Interest in Research Committee (COIRC)

The TTUHSC El Paso COIRC was established by the VPR and is considered a medical committee that reviews disclosures of significant financial interests to determine the presence of a Financial Conflicts of Interest (FCOI) as it relates to the research being conducted by the individual with the FCOI. The COIRC also reviews the nature and magnitude of the conflict, the degree to which the conflict is related to the research, and the extent to which research might be affected by this financial interest.

In accordance with the TTUHSC EP Conflict of Interest in Research Policy, all research personnel are required to disclose any financial conflicts of interest as outlined in the policy. These disclosures are to be made at least annually, and are to be updated more frequently as circumstances change.

Determinations of conflict require conflict management that can include but are not limited to Conflict Management Plans, divestments, and removal as the Principal Investigator for the particular research study. The COIRC is charged with working with the investigator/research personnel to manage the conflict and/or create a CMP and conduct periodic review of previously approved Conflict Management Plans (CMPs) and works with investigators/research personnel to develop appropriate CMPs, provide copies of the CMPs to appropriate review committees and administrators, and obtains and reviews annual reports regarding ongoing CMPs.

In addition, the IRB will not continue the review of a submission until the COIRC has met and made its recommendations, and the investigator has adequately addressed these.

Non-financial conflicts of interest (conflicts of commitment, nepotism, etc.) may also interfere with objective conduct of research activities. Such conflicts are addressed as indicated in HSCEP OP 10.05 Conflicts of Interest and Commitment Policy.

A conflict of interest determination by the COIRC and the CMP may be appealed to the VPR within thirty (30) days of the date that the COIRC notifies the faculty, staff, or student(s) of the COIRC's decision. Once the appeal is submitted to the VPR, the VPR's decision and final determination will be final.

Investigators and/or research personnel who have ongoing CMPs are also responsible for providing annual written reports (or at any time upon request from the COIRC) regarding any action taken under the CMP. Reports should be submitted to the COIRC chairperson or designee. Annual reports should be submitted on or before the anniversary date that the CMP was last approved by the COIRC. The chairperson will then review the reports and will provide a written summary to the COIRC at their next convened meeting. The COIRC may choose to

review the report in its entirety. These written reports will be required until the completion of the research project for which the conflict was identified

4.1.4.1 The Research Compliance Unit's Responsibilities to the COIRC

The VPR or COIRC may also request interim compliance audits of the monitoring plans be conducted by the OR or the TTU System Office of Audit Services. These audits may be requested either for cause or on a routine basis.

A breach of the Conflict of Interest in Research policy is considered a form of noncompliance and may include, but is not limited to:

- Significant financial interest(s) not disclosed in a timely manner;
- Disclosing inaccurate erroneous or misleading information;
- Failure to provide additional information to the COIRC or VPR regarding a disclosure; or
- Violation of the terms of an approved CMP.

Once a breach has been identified, the COIRC will review the breach and its relation to the research project in question within 30 days of discovery. This can result in an interim management plan. Within 120 days of discovery of the breach, the COIRC will conduct a retrospective review of the investigator's activities in relation to the research project in order to identify all noncompliance. Once the review has been completed, the results are reported to the sponsor and/or funding agency if bias is found.

Breaches can result in, but are not limited to, a review and investigation by the COIRC, the creation of a CMP, additional training, and the reporting of a breach. Intentional breaches can result in the recommendation of additional sanctions to the VPR. The VPR shall make the final determination regarding which sanctions, if any, shall be imposed on the investigator or research personnel.

5. CHAPTER 5 : EDUCATION AND TRAINING

5.1 TTUHSC El Paso Research Education and Training as it Pertains to iRIS

All principal investigators, co-investigators, and research personnel are required to receive specific training regarding the type of research that they will be conducting prior to obtaining an iRIS account and/or prior to beginning any research-related activities. This training will be verified prior to iRIS access being granted and prior to the initial or continuing approval of a research study.

5.1.1 Institutional Review Board for the Protection of Human Subjects (IRB)

To obtain an iRIS account for clinical research, the following trainings will need to be completed:

- Human Subject Research Course (Available on CITI Training)
- Conflict of Interest Training (Available on CITI Training)

The following will be mandatory after an iRIS account is obtained, and will need to be completed as soon as possible and on an annual basis:

- Financial Disclosure
  - The disclosure form may be accessed through iRIS via the Conflict of Interest Module under "My Workspaces" at the top left of the iRIS dashboard.

The following are mandatory trainings that are required under specific circumstances:

- Informed Consent Course (Only mandatory if you will be working on a study that uses Informed Consent - https://elpaso.ttuhsc.edu/research/compliance/Training.aspx)
- Good Clinical Practices (Only mandatory if you will be working on a drug or device study or an NIH-funded study – Available on CITI)
- Responsible Conduct of Research (Only mandatory if you will be working on a sponsored study or a government-funded study that requires this training – Available on CITI)
- Clinical Research Coordinator Training (Only mandatory if you will be working in the capacity of a Research Assistant or a Clinical Research Coordinator on a study – Available on CITI)

5.1.2 Institutional Biosafety Committee (IBC)

To obtain an iRIS account for laboratory research, the following trainings will need to be completed:

- Lab Safety Essential (LSE) training
  - Each person conducting or assisting with a research project involving biohazardous materials must receive training regarding laboratory safety prior to conducting any work in any TTUHSCEP laboratory or approved area. Access to the training is obtained through Safety Services by emailing Jacqueline.lomeli@ttuhsc.edu. In addition, yearly in-person and/or online refresher training specific to approved agents will be required and conducted by Safety Services.
- Conflict of Interest Training (Available on CITI Training)

The following will be mandatory after an iRIS account is obtained, and will need to be completed as soon as possible and on an annual basis:

- Financial Disclosure

- The disclosure form may be accessed through iRIS via the Conflict of Interest Module under "My Workspaces" at the top left of the iRIS dashboard.

Any employee of TTUHSC El Paso who ships or will be shipping hazardous items must first be trained and certified to do so. Although HazMat Shipping Training is not mandatory in order to obtain an iRIS account, it is required in order to package, ship, sign-off, or offer packages for transportation. All hazmat shippers must provide copies of training certificates and copies of any shipping declaration forms to Safety Services. A hazmat shipper is any employee who handles, offers for transport, transports, or causes hazardous materials to be transported.

Multiple training programs are maintained at TTUHSC El Paso so that employees may focus their certification to the types of shipments that apply to them. Each program requires initial training, followed by recurrent refresher training every two years. The Department of Safety Services offers and coordinates training classes for TTUHSC hazmat employees. The HazMat Shipping Training Program offers the following courses in the form of either classroom training or self-study modules:

- HazMat Shipping
- Infectious Substances and Dry Ice
- Dry Ice
- Exempt Human Specimens

Shipments of hazardous materials are regulated by the United States Department of Transportation (DOT), and the International Air Transport Association (IATA) in order to promote safe and secure transportation of hazardous materials and to ensure minimal threats to life, property, and the environment.

**For more details and information on training, contact the Department of Safety Services at 915-215-4820.*

5.1.3 Institutional Animal Care and Use Committee (IACUC)

IACUC does not require training before obtaining an account:

- Training status will be verified when joining a study and at the schedules review period of active studies.
- Minimum requirements to participate in research involving animal subjects:
  - Working with the IACUC Course
  - Reducing Pain and Distress in Laboratory Mice and Rats Course
  - Working with (Species) in Research Settings Course
  - Conflict of interest Course
  - Submission of a Research Financial Disclosure
  - Occupational Health Safety (OHS) Clearance

* More information can be obtained on the IACUC's Training Requirements page: https://elpaso.ttuhsc.edu/research/committees/iacuc/training-requirements.aspx

5.1.4 Conflict of Interest in Research Committee (COIRC) and Financial Disclosures (FD)

All investigators and research staff are required to renew their Conflict of Interest training every 4 years. New iRIS accounts cannot be obtained without Conflict of Interest Training (Available on CITI Training), and new projects shouldn't be submitted or approved without up to date training for all study personnel. Additionally, approval of continuing reviews may be denied if training of any study personnel has lapsed. All research staff must also have a current Annual Financial Disclosure statement on file with the OR according to the TTUHSC EP OP 73.09 Financial Conflicts of Interest in Research. The annual disclosure form may be accessed through iRIS via the Conflict of Interest Module under "My Workspaces" at the top left of the iRIS dashboard.

TTUHSC El Paso investigators and study personnel are bound to the policies set forth in TTUHSC EP OP 52.06 Standards of Conduct and Ethics, TTUHSC EP OP 10.05 Conflicts of Interest and Commitment and TTUHSC EP OP 73.09 Financial Conflicts of Interest in Research. Unaffiliated investigators are normally asked to complete the requirements as well. Affiliated entities should submit documentation to the IRB specifying how the identified conflict of interest will be managed.

5.2 TTUHSC El Paso Research Education and Training Provided by the OR

The Research Compliance Unit (RCU) creates and provides trainings in an effort to promote on-the-job training, educational opportunities on basic and advanced clinical research activities, and revised institutional, state, and federal policy awareness. The trainings are provided at scheduled intervals and on demand, and are available through an online platform and in-person. A list of available training presentations is available on the TTUHSCEP Research Compliance Training webpage. Training requests can be submitted on the same webpage by selecting the "Training Request Form" button on the same webpage. Specialized training requests involving the development of specific training that are not currently being offered can also be submitted on that page.

5.2.1 RCU Trainings Provided Through the ACME Portal

Training requests submitted for access to on-line trainings are received as general notifications through the TTUHSC El Paso Research Compliance Outlook inbox. These notifications do not contain any specific information regarding the requestor or the information that has been submitted on the request form. The training request form itself is received and saved onto the REDCap system. Training Request Forms can be submitted for one's self, on behalf of another individual, or on behalf of a group of individuals. Upon submitting the training request, the requestor can expect to receive an immediate notification from the TTUHSC El Paso Research Compliance Outlook inbox letting them know that the request form has been received and

providing them with general and basic information regarding the accessibility of the training. Even though the research compliance inbox automatically sends out a notification, the process of assigning the requested training is currently very manual. The act of submitting the Training Request Form does not automatically allow the requestor to access the training(s) that has or have been requested.

All on-line training requests are reviewed and fulfilled as soon as a member of the Research Compliance Unit is available, but are given priority. Because of this, the RCU does require up to 24 hours to fulfill any training request submitted within regular work hours from Monday through Thursday. Requests submitted on Friday, Saturday, and/or Sunday should expect to be reviewed and processed no later than Monday at end of day unless this day falls on a holiday. Training Request Forms submitted during holidays will not be reviewed and/or processed until after the holiday.

Once the request has been processed, the requestor will receive an email from the ACME system with a link to the training. In some cases, the requestor may also receive an email from the TTUHSC El Paso Research Compliance Outlook inbox indicating that the training has been made available.

The ACME system requires an eRaider in order to assign a training and in order for a learner to access the ACME system. Online training requests made for individuals that do not have an eRaiders are processed by emailing the individual learner with instructions, and an attached electronic copy of the PowerPoint presentation, and MS Word version of the test. Certificates are then manually created for the learner upon successfully passing the test. Training certificates received in this manner will differ from those received from the ACME system.

Each training is made available for up to 30 days regardless of whether or not the training was made available on ACME or through email. ACME and the RCU allow the learner to take the test associated with each training up to three times. After three test failures, the ACME system is set to lock the learner out of being able to re-take the test. In order to unlock a test or request an extension to the deadline, the learner must send an email to the TTUHSC El Paso Research Compliance Outlook inbox. If the learner is locked out a second time due to failures or if the learner fails the test a total of 6 times, the Research Compliance Officer is notified and may require the learner to take the training in person. The RCO may also require the learner to complete multiple observed activities in order to ensure that the training has been understood. This process is mostly enforced with failures involving the Basic Informed Consent Training, but is enforceable with other trainings as well. Once a training has been completed through ACME, the system will automatically provide the user with a training certificate that should be kept for future reference.

5.2.2 RCU Trainings Provided In-Person

Training requests submitted to request in-person trainings are received and stored in the same manner as the requests for on-line training. Upon submitting the training request, the requestor will still receive an immediate notification from the TTUHSC El Paso Research Compliance Outlook inbox letting them know that the request form has been received and that a member of the RCU will email them shortly.

The Training Request Form for in-person trainings varies a little from the on-line training request form. The form requires a minimum of five attendees per in-person training request. Once the RCU reviews the request form and the date or range of dates that are being requested, the requestor is then contacted to schedule the training. Note that in-person training requests must be received at least **30 days in advance** of the date that is being requested for the training. Training requests received less than 30 days in advance will not be given priority and may or may not be possible depending on the availability of the trainer. Each training also takes a specific amount of time to present. Trainings with activities normally take longer than an hour. It is the requestor's responsibility to plan around the required length of each training accordingly.

Note: The presenter is also able to present via WebEx if necessary, but this must be specified when the training request is submitted.

At the beginning of each training, the RCU trainer is required to obtain attendance, and will typically bring a mandatory sign-in sheet unless the requestor chooses to provide an attendance sheet of their own to the trainer. At the end of each presentation, the trainer will typically pass around an evaluation. These forms are anonymous and voluntary. Their purpose is to help the trainer improve their process and training materials.

The requestor is responsible for reserving and providing the room and equipment for each training presentation requested. The requestor is also responsible for providing copies of the training presentation to their attendees. The requestor can ask the RCU to provide a copy of the training material prior to the training; otherwise, the RCU will typically provide an electronic copy of the training materials after the training presentation. The RCU will also email electronic copies of the training certificates for each attendee. It will be up to the requestor to distribute the training material and certificates to the attendees.

5.2.3 RCU Special Training Requests

New ideas for trainings are always welcome, but it is important to remember that training presentations require a lot of time, effort, and research to put together. Requests for customized trainings can be submitted by using the "Comments" section at the end of the "Training Request Form" unless a "Special Training Request" form is made available on the Research Compliance Webpage. These requests will be reviewed by the RCU, the OR Managing Director, and any other applicable unit or personnel. If a customized training, that is not already available, is being requested, the request must be submitted at least two months in advance.

Requests received less than two months in advance will not be given priority and may or may not be rejected depending on the workload and availability of the trainer.

Special training requests should include a description of the training being requested, length of training, whether or not they would like the training to include an activity, date of training, number of attendees and any additional information they would like to include to help the trainer understand the request.

A minimum of 10 attendees are required per request. If 10 attendees are not available, the requestor must allow the RCU to make the training session available to other individuals and departments at or involved with TTUHSCEP. Even though the requestor is responsible for reserving and providing the room and equipment for the training presentation, they will only be required to provide a copy of the training materials and certificates to their attendees.

5.3 Responsible Conduct of Research Training (RCR)

At TTUHSCEP we currently provide the RCR training through CITI Program only. This training includes information regarding:

- Research Misconduct
- Research Integrity
- Mentoring, Authorship and Peer Review
- Data Management
- Conflict of Interest
- Collaborative Research
- Research Involving Human Subjects
- Using Animal Subjects in Research
- Export Controls and National Security

Although this training is not currently mandatory at TTUHSCEP, certain pharmaceutical sponsors require RCR training. Research involving the National Institutes of Health (NIH), National Science Foundation (NSF), and U.S. Department of Agriculture (USDA), also require that certain categories of researchers receive this training.

In addition, the NIH implemented a policy that requires a more extensive version of the RCR training than the one provided by CITI Program. The NIH's RCR policy also prohibits a training program that relies entirely on online instruction except in special instances of short-term training. The CITI Program RCR Basic course can be used to complement an in-person training experience but cannot be used to replace it. Because of this, one of the RCU's goal is to eventually install and offer an RCR program involving an 8-hour one to two day workshop that will fulfill the requirements for all federally-funded research.

5.3.1 Responsible Conduct of Research Training for NIH Requirements

NIH policy requires that all trainees, fellows, participants, and scholars receiving support through any NIH training, career development award (individual or institutional), research education grant, and dissertation research grant receive instruction in responsible conduct of research as of January 25, 2010. The required guidance provided below is taken directly from the NIH grant policy and is directed at formal instruction in responsible conduct of research:

- **Format**: Substantial face-to-face discussions among the participating trainees/fellows/scholars/participants and a combination of didactic and small-group discussions are highly encouraged. *On-line courses can be used to supplement instruction in responsible conduct of research only.*
- **Subject Matter**: Responsible conduct of research training must include the following areas:
  - conflict of interest – personal, professional, and financial
  - policies regarding human subjects, live vertebrate animal subjects in research, and safe laboratory practices
  - mentor/mentee responsibilities and relationships
  - collaborative research including collaborations with industry
  - peer review
  - data acquisition and laboratory tools; management, sharing and ownership
  - research misconduct and policies for handling misconduct
  - responsible authorship and publication
  - the scientist as a responsible member of society, contemporary ethical issues in biomedical research, and the environmental and societal impacts of scientific research

Note that according to the NIH policy, courses related to professional ethics, ethical issues in clinical research, or research involving vertebrate animals may form a part of instruction in responsible conduct of research, they generally are not sufficient to cover all of the above topics.

- **Faculty Participation**: Training faculty and sponsors/mentors are highly encouraged to contribute both to formal and informal instruction in responsible conduct of research. Informal instruction occurs in the course of laboratory interactions and in other informal situations throughout the year. Training faculty may contribute to formal instruction in responsible conduct of research as discussion leaders, speakers, lecturers, and/or course directors.

Per the policy, rotation of training faculty as course directors, instructors, and/or discussion leaders may be a useful way to achieve the ideal of full faculty participation in formal responsible conduct of research courses over a period of time.

- **Duration of Instruction**: Instruction should involve substantive contact hours between the trainees/fellows/scholars/participants and the participating faculty. Acceptable programs generally involve at least eight contact hours. A semester-long series of seminars/programs may be more effective than a single seminar or one-day workshop because it is expected that topics will then be considered in sufficient depth, learning will be better consolidated, and the subject matter will be synthesized within a broader conceptual framework.

- **Frequency of Instruction**: Per the policy, reflection on responsible conduct of research should recur throughout a scientist's career: at the undergraduate, post-baccalaureate, predoctoral, postdoctoral, and faculty levels. The policy explains that instruction must be undertaken at least once during each career stage, and at a frequency of no less than once every four years.

Note that per the NIH, instruction in responsible conduct of research may take place, in appropriate circumstances, in a year when the trainee, fellow or career award recipient is not actually supported by an NIH grant.

The NIH also provides special considerations determined by the type of award being received.

Contact our TTUHSC EP Sponsored Programs (SP) to find out how to apply to receive an NIH award.

- More information regarding the NIH policy can be found at the following link: https://grants.nih.gov/grants/guide/notice-files/not-od-10-019.html

5.3.2 Responsible Conduct of Research Training for USDA NIFA Requirements

Per United States Department of Agriculture (USDA) National Institute of Food and Agriculture (NIFA) policy 2 CFR Part 422, any institution completing research funded by the USDA must "foster an atmosphere conducive to research integrity, bear primary responsibility for prevention and detection of research misconduct, and maintain and effectively communicate and train their staff regarding policies and procedures". The regulations mandate that all individuals participating in a project funded by a USDA grant complete RCR training once every three years. This regulation extends to and includes:

- Program directors
- Faculty members
- Undergraduate students
- Graduate students
- Postdoctoral researchers
- Any staff involved in designing, conducting, or recording research

The awardee does not have to submit an RCR plan as part of the application, but they must provide documentation supporting compliance with the training requirement at the request of the funder.

USDA NIFA mandates that the general content of the ethics training, at a minimum, emphasize three key areas of research ethics: authorship and plagiarism, data and research integration, and reporting misconduct. The CITI Program RCR training covers these three key areas, and thus can be used by researchers to fulfill the training requirement. Contact our TTUHSC EP Sponsored Programs (SP) to find out how to apply to receive a USDA NIFA award, and how to provide proof of RCR training per USDA NIFA requirements.

More information regarding the USDA's RCR requirements can be found at the following link: https://nifa.usda.gov/responsible-and-ethical-conduct-research

5.3.3 Responsible Conduct of Research Training for NSF Requirements

The National Science Foundation (NSF) does not detail specific methods required in order to meet their RCR training requirements, instead it leaves it up to the institution to either utilize existing training resources or to develop new educational methods or content to meet training needs. NSF regulations mandate that individuals participating in a project funded by an NSF grant complete RCR training once every three years. The NSF, requires education and training in responsible conduct of research to anyone who will be supported by NSF grants to conduct research:

- Students (undergraduate and graduate)
- Postdoctoral scholars
- Principal investigators
- Key personnel
- Sub-awardees
- And anyone else who may be listed on the grant, even if they do not directly receive funds from the grant

In order to meet the NSF mandate, TTUHSCEP has determined that the CITI Program RCR training can be used to satisfy the NSF's RCR training requirements, but the role of the Principal Investigator and other senior faculty in mentoring students and trainees and in providing other opportunities for discussion, such as workshops, lectures, and courses, is always encouraged.

At the time of proposal submission, the TTUHSCEP must certify via its authorized representative that it has a plan to provide training and oversight to all researchers, regardless of career stage, who are supported by funds from an NSF grant. It is not required to submit a training plan as a part of a proposal application, but the funding agency may request it at any time.

The institutional training plan must be in place at the time of the proposal, but the actual training of individuals can take place at a later time, as long as that expectation is listed in the institutional training plan. Contact our TTUHSC EP Sponsored Programs (SP) to find out how to apply to receive an NSF award.

More information regarding the NSF's RCR requirements can be found at the following link: https://www.nsf.gov/pubs/policydocs/pappg19_1/pappg_9.jsp#IXB

6. CHAPTER 6: RESPONSIBLE CONDUCT OF RESEARCH

6.1 Responsible Conduct of Research at TTUHSC El Paso

Responsible conduct of research refers to the general responsibility of research personnel to exhibit good citizenship in their professional lives. Researchers who report their work honestly, accurately, efficiently, and objectively are considered to be implementing responsible conduct. Researchers who are dishonest, knowingly report inaccurate results, waste funds, or allow personal bias to influence scientific findings are not considered to be conducting themselves within the boundaries of responsible conduct of research.

There is no specific or detailed guidance on exact best practices when it comes to displaying good citizenship in the research profession. Instead, the ideals behind responsible conduct must be internalized and fully understood by all personnel in order to show proper judgement in the face of varying situations. Responsible conduct of research should incorporate local, state, and Federal regulations in its practice and may vary from field to field and in different settings. TTUHSCEP works hard to integrate these regulations into its institutional guidelines, Human Research Protection Program and operating policies and procedures. *Refer to Section 5.3 in this manual for information regarding Responsible Conduct of Research training requirements.*

6.1.1 Research Misconduct

Research misconduct falls within responsible conduct of research guidelines. This type of misconduct was added due to historical incidents involving egregious misbehavior. Public concerns were raised as a result of these incidents and the lack of corrective action that was implemented at that time. Because of this, Congress required Federal agencies and research institutions to develop research misconduct policies defining the following three areas:

- Falsification - Making up data or results and recording or reporting them.
- Fabrication - Manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record.
- Plagiarism - The appropriation of another person's ideas, processes, results, or words without giving appropriate credit.

Stipulations were also added to limit the Federal Government's role in research misconduct to well-documented, serious departures from accepted research practices. The stipulations stated that the actions must include:

- Significant departure from accepted practices
- Must have been committed intentionally, or knowingly, or recklessly
- And must be proven by a preponderance of evidence

TTUHSC El Paso's policy and procedures are intended to describe the Institution's responsibilities under the Public Health Service (PHS) Policies on Research Misconduct, 42 CFR

Part 93 (Code of Federal Regulations, Title 42, Part 93) and the National Science Foundation (NSF) Policy on Research Misconduct, 45 CFR 689. Please refer to HSCEP OP 73.07 "Integrity in Research and Allegations of Scientific Misconduct (*Attachment A*)" in order to review TTUHSCEP's policies on research misconduct and details on reporting allegations of research misconduct. **Remember that it is our responsibility to report research misconduct and non-compliance with institutional and federal policy in order to ensure that research integrity is upheld, and to ensure that the health and safety of research subjects are protected.**

Allegations of research misconduct and workplace abuse can be reported to EthicsPoint on the following link: https://secure.ethicspoint.com/domain/media/en/gui/44534/index.html

Allegations of research misconduct can also be reported to our TTUHSCEP appointed Research Integrity Officer (RIO) or to our Compliance Hotline at 1-866-294-9352 (toll free).

7. CHAPTER 7 : GOOD CLINICAL PRACTICES

7.1 Good Clinical Practices at TTUHSC El Paso

Good Clinical Practice (GCP) is an international ethical and scientific quality standard for clinical trials. This guideline was defined by the International Conference on Harmonization (ICH) for investigational drug and device trials, but is typically applied to all research as an industry standard and is recommended by the FDA. The ICH is an international body that defines a set of standards, which governments can then transpose into regulations for clinical trials involving human subjects. GCP follows the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use of GCP guidelines, and is sometimes referred to as ICH E6 Good Clinical Practice Guidelines or ICH-GCP guidelines.

GCP also serves to protect the rights, integrity and confidentiality of trial subjects. It is important because it provides assurance that the data and reported results are credible and accurate, and that the rights, integrity and confidentiality of trial subjects are respected and protected. GCP guidelines also help ensure that only adequately planned and conducted clinical trials are performed by enforcing strict guidelines and high standards on ethical aspects of a clinical study including comprehensive documentation for the clinical protocol, record keeping, training, and facilities, including computers and software. GCP aims to ensure that the studies are scientifically authentic and that the clinical properties of the investigational product are properly documented.

GCP is a standard for the following portions of a clinical trial:

- Design
- Conduct
- Performance

- Monitoring
- Auditing
- Recording
- Analyses
- Reporting

Historically, the first version of the ICH E6 Good Clinical Practice (GCP) Guideline was finalized in 1996, and described the responsibilities and expectations of all participants in the conduct of clinical trials. Descriptions of responsibilities and expectations also including investigators, monitors, sponsors and IRBs. The guidelines were revised in 2016 with an integrated addendum to encourage implementation of improved and more efficient approaches to clinical trial design, conduct, oversight, recording and reporting while continuing to ensure human subject protection and reliability of trial results. The guidelines were also revised to include standards regarding electronic records and essential documents intended to increase clinical trial quality and efficiency of clinical research studies.

At TTUHSCEP, ICH-GCP guidelines have been incorporated into our Human Research Protection Program and our audits, and should be implemented for all research at the Institution. International and multi-site clinical trials conducted at TTUHSC El Paso are conducted in accordance with ICH-GCP guidelines.

7.1.1 Research Integrity

Research integrity refers to active adherence and adoption of ethical principles and practices as professional standards that are essential for the responsible conduct of research. According to the NIH, research integrity includes:

- The use of honest and verifiable methods in proposing, performing, and evaluating research
- Reporting research results with particular attention to adherence to rules, regulations, and guidelines
- Following commonly accepted professional codes or norms

The codes or norms mentioned above refer to shared values in the scientific community that consist of:

- Honesty - conveying information truthfully and honoring commitments
- Accuracy - reporting findings precisely and take care to avoid errors
- Efficiency - using resources wisely and avoid waste
- Objectivity - letting the facts speak for themselves and avoid improper bias

TTUHSCEP defines principal investigator responsibilities as promoting 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. Adherence to the principles of research integrity is expected from all principal investigators at TTUHSCEP and their research personnel.

8. CHAPTER 8: DATA INTEGRITY

8.1 Data Integrity at TTUHSC El Paso

Data integrity is defined as the extent to which all electronic or paper-based data are complete, consistent, accurate, trustworthy, and reliable throughout the lifecycle of data. This refers to its creation, through its archival status and until its destruction. Regulatory agencies and sponsors rely on data to ensure subject rights and safety are upheld along with the scientific value of clinical studies.

At out Institution, we strongly encourage the use of Good Documentation Practices and have systems and trainings in place to educate and assist researchers with tool development and guidelines for data collection. TTUHSCEP encourages the implementation of ALCOA, the development of data collection forms, the use of electronic data capture systems, and the creation of regulatory binders and subject files in order to improve Good Documentation Practices and ensure data integrity is upheld.

8.2 Good Documentation Practices at TTUHSC El Paso

Good Documentation Practices (GDP) refer to methods and systemic procedures for recording, correcting and managing data, documents and records, to ensure the reliability and integrity of information and data collected throughout all aspects of research. Roots of good documentation principles can be found in the ICH-GCP guidelines within their definitions of source data and source documents. In addition, our TTUHSCEP Human Research Protection Program (HRPP) manual describes that it is the principal investigator's (PI) responsibility to assure the validity of the data and the documentation of all study-related processes and procedures. For more information regarding principal investigator responsibilities, please refer to the TTUHSCEP IRB's HRPP Manual.

There are several important factors that researchers will want to consider in trying to uphold good documentation practices for their research. A list of suggestions is being provided below, but these are not mandatory and researchers should not feel restricted to this list:

- There should be a record of every visit and conversation with the subject in each subject file.
- E-mails and faxes and any other sponsor or study-related correspondence should be printed, signed/dated, and filed in the Regulatory Binder.
- There should be logs for the different procedures that are required within the protocol.
- Records of calibration of study-required equipment, including temperature logs, should be kept and filed appropriately.

- Screening and recruitment logs should be retained to demonstrate that inclusion/exclusion criteria were performed according to the protocol.
- For sponsored research, site visit monitoring logs should be kept to document the purpose and frequency of the monitoring visits.
- Records of missing or unobtainable data required by the protocol should be explained appropriately in a Note-to-File.
- If information must be added to a previous entry, it should be inserted and noted as a late entry or addendum at the end of the text in the subject's study record or data collection form. *It should not be squeezed in between previously written notes.*
- If data must be changed, the entry should be lined through (single strikethrough). The new entry or correction should be written above or close to the original entry, initialed and dated.
- Entry errors that do not require a new entry, just to be deleted, should be lined through (single strikethrough), initialed and dated.
- All changes and entries should be evident and obvious during an audit. If further clarification is required, this can be done in the form of a Research Note or Note-to-File.

8.2.1 ALCOA

ALCOA refers to a set of guidelines describing how data should be documented and maintained. The FDA first used this acronym on their 2003 guidance with the implementation of their 21 CFR Part 11 rule for data integrity. Since its implementation, ALCOA has become a standard for research documentation, and is now common practice amongst research sites. ALCOA stands for and is described as follows:

- Attributable - It should be clear who has documented the data.
- Legible - Entries should be readable and signatures should be identifiable.
- Contemporaneous - The information should be documented in the correct time frame along with the flow of events.
- Original or true copy - Original documents where the data or information was first recorded should be used; if the original documents are not available then an exact copy should be used. The investigator should have and maintain the original source documents.
- Accurate - Data should be correct and consistent, and should be a real representation of facts.

Although this rule applies to FDA-regulated research, research personnel are encouraged to implement ALCOA into their research documentation practices.

In recent years, an additional four attributes have been added to emphasize that the data should also be:

- Complete - Data collection forms and regulatory documents should be complete until that point in time. The data and study documentation should be backed up by evidence.
- Consistent - Documentation should demonstrate the required attributes consistently. Data and information should be based on real and reliable facts (Ex: Date and time).
- Enduring - Data and documentation should be long-lasting and durable throughout its lifecycle.
- Available - Regulatory documents should be easily available for review by treating physicians and auditors during audits or inspections. The documents should also be retrievable in reasonable time.

These attributes apply to both paper and electronic records and represent the foundation of data integrity.

8.2.2 Data Collection Forms

Data Collection Forms (DCF) are the backbone of any research study. DCFs allow researchers to collect all protocol-required data and help meet data integrity and code of federal regulation requirements and expectations. DCFs are required for most studies and are expected for sponsored and federally-funded research. In addition, DCFs can be electronic and in paper form depending on the need and the type of document. There are a variety of documents that are considered data collection forms including:

- Source documents – These are the first recording or observations made or data generated about a study subject during their participation on a trial. Source documentation is the foundation of all clinical trials.
    - Examples of source documents include but are not limited to:
        - Original signed and completed informed consent form (ICF)
        - Physical exam notes
        - Adverse event (AE) lists
        - Investigation product (IP) logs
        - Subject pill diaries
        - Research notes
        - Certified copies of electronic medical records (EMR)
        - Study-specific checklists
        - Hospital admission and discharge summaries
        - Birth and death certificates
- Case Report Forms (CRF) – These are preprinted forms that allow the PI and the clinical research coordinator (CRC) to write appropriate data regarding demography, efficacy, safety, medication use, and other aspects of the study. CRFs can sometimes serve as source

documents, but this is typically decided by the sponsor and whether or not they want the researcher to collect data directly onto a specific form that they've created. Recently CRFs were printed on carbon copy paper and would require the researcher to legibly and carefully transcribe the data from the source documents onto the CRFs. The CRF would then be provided to the clinical research associate (CRA) or study monitor for the sponsor.

- Examples of CRFs can include but are not limited to:
  - Adverse event logs
  - Study visit assessments
  - Concomitant medication logs
  - Lab and vital entries
  - Inclusion/Exclusion forms
- Note that researchers should have a clear understanding of what data the protocol is attempting to collect. Sometimes sponsors provide CRFs and sometimes they don't. In cases where study sponsors don't provide CRFs but have an electronic data capture (EDC) system, the researcher may decide to create their own CRFs based on the forms available on the sponsor's EDC system. This should be discussed with the study sponsor prior to implementation. CRFs created in this manner must not collect additional data that has not been approved by the IRB for collection. Researchers involved on investigator-initiated studies that decide to create CRFs should have the PI approve each CRF for use, and must submit each CRF to the IRB for review and approval. This is done in an effort to prevent the unauthorized collection of unapproved data.

- Electronic Data Capture (EDC) system – This is a platform that contains sponsor-prepared protocol-specific electronic case report forms (eCRF). EDC systems have taken the place of carbon copy CRFs in an effort to reduce the amount of labor-intensive work that was historically required for paper CRFs. EDC systems are secure, password-protected, and limited access systems that serve to connect the researcher directly with the sponsor's Data Management team. The sponsor's Data Managers work to review all of the entries submitted by researchers and query errors, data requiring clarification, missing fields, etc. eCRFs are the manner in which a sponsor collects data for final statistical analysis. Many different systems and platforms exist and require specific training and registration prior to use. Temporary access is typically granted to members of the research team after training takes place. Print-outs of eCRFs and instructions are typically provided in regulatory binders sent to the research site with a sponsored study. EDCs should not be used to record original source data and should be a secondary point of entry for transcribed data. *Remember that it is the PI and each researcher's responsibility to maintain accurate and complete subject case histories and source documentation for each study. Data submitted to a sponsor through an EDC system must be backed by source data which is maintained at the site. Failure to maintain complete and correct case histories can result in determinations of serious non-compliance by internal and external auditors.*

- EDC systems and external systems that are requiring TTUHSC EP employees to create a login are now being reviewed to ensure that they abide by new Texas State Laws. A formal submission process is still being finalized, but not submitting a system for review could result in the system being blocked by firewall.

- Electronic Data Capture Systems at TTUHSCEP –TTUHSCEP does have electronic data capture systems for investigator-initiated studies. These systems not only allow users to create their own eCRFs, but are also able to collect and manage PHI which differs from sponsor EDCs.
  - EDC Systems at TTUHSCEP include but are not limited to:
    - REDCap – This stands for "**R**esearch **E**lectronic **D**ata **Cap**ture" and is fairly customizable. This system has limited-access, is password-protected, and has been deemed as secure with a closed network at our campus. PHI data input fields are defined differently on this system for easy removal at the end of a study, since removal of PHI and de-identification at the end of a study are required for all IRB-approved research. IRB-approval to use this system for specific research studies must be obtained through the submission of an initial application or an amendment prior to its implementation on a study. For access to this system, you must reach out to the Research IT Department housed within the Office of Research (OR).
    - iMedRIS (aka: iRIS) – This stands for "**I**ntegrated **Med**ical **R**esearch **I**nformation **S**ystem" and is a web-based system that is used to process all of the research applications that are submitted to our Institutional Review Board (IRB). It enables online application submission, real-time submission tracking, review, post-approval of compliance activities of all study regulatory documentation for research studies. The system also functions as a document repository, providing investigators with easy access to submission records and study documents. In addition, iRIS allows researchers to create eCRFs within the subject management tab on each main study submission page. As with REDCap, use of subject management on iRIS needs to be approved by the IRB for each study prior to its implementation.
    - CloudLIMS - This is a cloud-based "**L**aboratory **I**nformation **M**anagement **S**ystem" that is offered as software as a service (SaaS). This system enables laboratories to automate their workflows and manage samples through their complete life cycle. It also assists in managing complex laboratory operations. It facilitates collaborative studies, sample requisition, and inventory management. CloudLIMS access is not made readily available as with REDCap and iRIS. Account requests must be submitted through the TTUHSC EP Office of Research for approval prior to being given system access. As with REDCap, the Research IT Department is responsible for maintenance this system at our campus.

Note that TTUHSC EP does have a specific drive that is designated for the collection of any and all research subject PHI. Forms and documents that are used to maintain subject PHI,

such as data collection spreadsheets and Master Identification Logs, should not be saved on the researcher's desktop or laptop, and should instead be saved on this access-restricted drive. Access to this drive must be requested through the Research IT Department.

9. CHAPTER 9: FEDERAL REPORTING OF APPLICABLE RESEARCH TRIALS

9.1 Federal Reporting Requirements for Applicable Research Trials at TTUHSC El Paso

In 1997, Congress passed the first U.S. Federal law to require trial registration. This was the Food and Drug Administration Modernization Act of 1997 (FDAMA). Section 113 of FDAMA (FDAMA 113) required the NIH create a public information resource on certain clinical trials regulated by the Food and Drug Administration (FDA). The information in the registry was intended for a wide audience, including individuals with serious or life-threatening diseases or conditions, members of the public, health care providers, and researchers. Specifically, FDAMA 113 required that the registry include information about federally or privately funded clinical trials conducted under investigational new drug applications to test the effectiveness of experimental drugs for patients with serious or life-threatening diseases or conditions. (*Source:* https://clinicaltrials.gov/ct2/about-site/history#CongressPassesLawFDAMA)

9.1.1 ClinicalTrials.gov

ClinicalTrials.gov was launched by the NIH in February 2000 as a result of FDAMA 113. It is a directory of federally and privately supported research trials designed to test the effect of experimental drugs, devices and procedures for many diseases and conditions. The FDA mandates the registration of all "Applicable Clinical Trials" on this registry in order to ensure that compliance with FDAMA 113, FDAAA 801, the Final Rule and additional regulations are upheld.

If an IRB-approved study is a clinical trial which has not been registered by the study sponsor, it may be the Principal Investigator's responsibility to register the trial. The Protocol Registration and Results System website provides specific information regarding how to register a new trial. 564BIn addition, FDA regulations (21 CFR 50.25c) requires the following statement in informed consent documents for all applicable clinical trials overseen by the agency:

"A description of this clinical trial will be available on http://www.ClinicalTrials.gov as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time."

The statement is included in the TTUHSC biomedical informed consent template. Different federal agencies and policies fluctuate in terms of which clinical research trials must be submitted to ClinicalTirals.gov per their specific requirements. More information regarding these registration requirements are detailed in the subsequent sections below.

9.1.1.1 FDAAA 801 and the Final Rule Requirements

Section 801 of the Food and Drug Administration Amendments Act (FDAAA 801) was passed by Congress in 2007. This law expanded the requirements for clinical trial registration and submission o ClinicalTrials.gov. Section 801 of FDAAA (FDAAA 801) required the registration of more types of trials, additional trial registration information, and the submission of summary results, including adverse events for certain trials. The law also included penalties for noncompliance, such as the withholding of NIH grant funding and civil monetary penalties of up to $10,000 a day.

In September 2016, the U.S. Department of Health and Human Services (HHS) issued a Final Rule for Clinical Trials Registration and Results Information Submission (42 CFR Part 11). The Final Rule clarified and expanded the regulatory requirements and procedures for submitting registration and summary results information of clinical trials on ClinicalTrials.gov, in accordance with FDAAA 801. The final rule was intended to clarify which trials must be submitted, when they must be submitted, and whether compliance has been achieved to sponsors, investigators, and the public. The Final Rule provided the definition of an Applicable Clinical Trial and provided structured criteria for determining which studies are considered to meet the definition. In addition, the Final Rule also expanded the FDAAA 801 requirements by requiring the submission of results information for trials of unapproved products. The regulation was made effective on January 18, 2017 and compliance was enforced as of April 18, 2017.

Registration is required for studies that meet the definition of an "applicable clinical trial" (ACT). ACTs are defined as follows:

- Controlled clinical investigations (other than phase 1 investigations) of any U.S. Food and Drug Administration (FDA)-regulated drug or biological product for any disease or condition
- Certain studies of FDA-regulated medical devices, excluding small clinical trials to determine feasibility and certain clinical trials to test prototype devices, but including FDA-required pediatric post-market surveillances of a device product
- Interventional studies (with one or more arms) of FDA-regulated drug, biological, or device products that meet one of the following conditions:
    - The trial has one or more sites in the United States
    - The trial is conducted under an FDA investigational new drug application or investigational device exemption
    - The trial involves a drug, biological, or device product that is manufactured in the United States or its territories and is exported for research

Note that the responsible party (the sponsor or designated PI) for an ACT must submit the required clinical trial information no later than 21 days after enrollment of the first participant.

ClinicalTrials.gov created an "ACT Checklist" to assist researchers in determining if their trials were applicable and needed to be registered. This checklist is available by copying and pasting the following link: https://prsinfo.clinicaltrials.gov/ACT_Checklist.pdf

9.1.1.2 NIH and the Final NIH Policy Requirements

In November 2014, the NIH proposed a policy to ensure that every clinical trial that received NIH funding was registered on ClinicalTrials.gov. Additionally it proposed to have summary results submitted and posted in a timely manner, whether subject to FDAAA 801 or not. Following that, in January 2015 the NIH National Cancer Institute (NCI) issued its Policy Ensuring Public Availability of Results from NCI-supported Clinical Trials. This policy proposed that all extramural or intramural NCI-Supported Interventional Clinical Trials (Covered Trials) report final trial results in a publicly accessible manner within twelve (12) months of the Trial's Primary Completion Date regardless of whether the clinical trial was completed as planned or terminated earlier.

In September 2016, the NIH issued its final policy encouraging broad and responsible distribution of information from NIH-funded clinical trials through ClinicalTrials.gov. Under this policy, every clinical trial fully or partially funded by the NIH is expected to be registered onto ClinicalTrials.gov and have summary results information submitted and posted in a timely manner. These requirements apply to all NIH-funded trials whether subject to FDAAA 801 or not.

Note that the NIH requires the responsible party (the sponsor or designated PI) for an ACT to submit the required clinical trial information no later than 21 days after enrollment of the first participant.

This policy was made effective for applications for funding, including grants, other transactions, and contracts submitted on or after January 18, 2017. For the NIH intramural program, the policy applies to clinical trials initiated on or after January 18, 2017. (Source: https://clinicaltrials.gov/ct2/about-site/history#DraftNIHPolicy)

9.1.1.3 ICMJE Requirements

In 2005 the International Committee of Medical Journal Editors (ICMJE) began requiring trial registration as a condition of publication. In June 2007 the ICMJE adopted the World Health Organization's (WHO) definition of clinical trial: "any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes." The ICMJE's

interpretation of "health-related interventions" include any intervention used to modify a biomedical or health-related outcome (Ex: drugs, surgical procedures, devices, behavioral treatments, dietary interventions, and process-of-care changes). Per the ICMJE, "health outcomes" include any biomedical or health-related measures obtained in patients or participants, including pharmacokinetic measures and adverse events. *Purely observational studies (those in which the assignment of the medical intervention is not at the discretion of the investigator) will not require registration. Those who are uncertain whether their trial meets the expanded ICMJE definition should err on the side of registration if they wish to seek publication in an ICMJE journal. (Source: http://www.icmje.org/about-icmje/faqs/clinical-trials-registration/)*

The ICMJE is a small working group of general medical journal editors who meet annually and fund their own work on the Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals. The current members of the ICMJE are listed below:

- Annals of Internal Medicine
- British Medical Journal
- Bulletin of the World Health Organization
- Deutsches Ärzteblatt (German Medical Journal)
- Ethiopian Journal of Health Sciences
- Iranian Journal of Medical Sciences
- JAMA (Journal of the American Medical Association)
- Journal of Korean Medical Science
- New England Journal of Medicine
- New Zealand Medical Journal
- The Lancet
- Revista Médica de Chile (Medical Journal of Chile)
- Ugeskrift for Laeger (Danish Medical Journal)
- U.S. National Library of Medicine
- World Association of Medical Editors

Note that ICMJE requires the responsible party (the sponsor or designated PI) for an ACT to submit and post the required clinical trial information prior to the enrollment of the first participant.

9.1.2 Regulations.gov

The 2018 Revised Common Rule was available on July 19, 2018 and was made effective on January 20, 2019. (Note that institutions were not permitted to implement the entirety of the revised Common Rule until January 20, 2019.) Information regarding the 2018 Revised Common Rule is available on the Electronic Code of Federal Regulations website and states the following:

"**§46.116 General requirements for informed consent.**

(h) Posting of clinical trial consent form.

(1) For each clinical trial conducted or supported by a Federal department or agency, one IRB-approved informed consent form used to enroll subjects must be posted by the awardee or the Federal department or agency component conducting the trial on a publicly available Federal Web site that will be established as a repository for such informed consent forms.

(2) If the Federal department or agency supporting or conducting the clinical trial determines that certain information should not be made publicly available on a Federal Web site (e.g. confidential commercial information), such Federal department or agency may permit or require redactions to the information posted.

(3) The informed consent form must be posted on the Federal Web site after the clinical trial is closed to recruitment, and no later than 60 days after the last study visit by any subject, as required by the protocol."

This requirement pertains to any clinical research studies that were initiated on or after January 21, 2019, and for studies initiated before January 21, 2019 but approved after that date. Older studies that have adopted the 2018 Revised Common Rule must also meet this requirement.

Instructions on how and where to upload a consent can be found on the following links:

- To upload the informed consent document onto Regulations.gov: https://www.hhs.gov/ohrp/regulations-and-policy/informed-consent-posting/index.html
- To upload the informed consent document onto ClinicalTrials.gov: https://clinicaltrials.gov/ct2/manage-recs

According to the common interpretation of the federal regulations, studies already registered on ClinicalTrials.gov and/or sponsored studies whose ClinicalTrials.gov record is maintained by the sponsor must still upload their informed consent document within 60 days after the last study visit. Please note that principal investigators are responsible for ensuring that this process has been completed for all of their clinical research studies (including sponsored studies).

9.1.3 The RCU's Responsibilities to TTUHSCEP's Federal Reporting Requirements

Institutions are required to create a single institutional account for their university or agency with ClinicalTrials.gov. Each institution maintains one or more on-site PRS administrators that maintain the institutional account and provide access to research personnel upon request. The TTUHSCEP Research Compliance Unit administers the TTUHSC El Paso ClinicalTrials.gov account

four our institution, and they should be contacted to facilitate account set-up, to reset passwords, and for general questions.

Along with administering the TTUHSCEP ClinicalTrials.gov account, the RCU is also responsible for ensuring that compliance is upheld by each research team. Studies are monitored on an annual basis, or more often, to ensure that all applicable studies have been submitted to ClinicalTrials.gov and/or Regulations.gov. Studies are also reviewed to ensure that informed consent forms have required language. The TTUHSCEP ClinicalTrials.gov account is also monitored on a weekly basis to confirm that there are no errors or items pending updates or corrections.

TTUHSCEP PRS administrators can also provide guided assistance with determining how records need to be submitted and with interpreting PRS Review comments and stipulations from ClinicalTrials.gov. TTUHSCEP PRS administrators may not, however, create, update or complete records on behalf of a researcher. TTUHSCEP institutional guidelines on ClinicalTrials.gov are available along with more information on our TTUHSCEP Research Compliance webpage.

For additional information, researchers can also reach out the Research Compliance Unit. Contact information is available on the TTUHSCEP Research Compliance Webpage.

10. CHAPTER 10: RESEARCH EXPORT CONTROLS

10.1 Research Export Controls at TTUHSC El Paso

Transfers of information, commodities, technology and software to a foreign national or entity within or outside the U.S. are regulated by the U.S. government in the interest of national security, economic and foreign policy concerns. The policies that control these transfers are known as "Export Controls". In addition, the federal export control laws (EAR, ITAR and OFAC) prohibit the export (including deemed export) of controlled technology and information without an export license, unless an exception applies. It is important for all institutional personnel to report activities that might trigger export controls. Below is a list of research and research related activities that could trigger export controls:

- Research that contains restrictions on publications or access by foreign nationals;
- Research where controlled technology or information is provided to and used by researchers in a laboratory that would require a license for foreign nationals to participate;
- Shipment of controlled technology or information outside the United States;
- Technical assistance agreements where U.S. citizens or permanent residents are providing training to foreign nationals where a controlled technology or information is involved;
- Taking laptop computers, GPS systems or their associated software to another country;

- Travel to embargoed, sanctioned or boycotted countries, or shipment, transport or other provision of equipment, goods, services or anything of value to embargoed, sanctioned or embargoed countries or individuals therein.
- Under ITAR, an export also includes the performance of a defense service on behalf of or for the benefit of a foreign person within or outside the United States.

There are two exceptions from the export license requirements that may be applicable to TTUHSCEP researchers. These exceptions only apply to deemed exports, not to shipments of controlled technology or information outside the U.S. The exceptions apply if the research is defined as fundamental research and/or if the information is in the public domain and is publicly available and accessible.

Lack of compliance can result in the Institution not being allowed to collaborate with international researchers, and can severely limit the research opportunities of our faculty and their students and staff. Failure to comply with export controls can also result in criminal penalties against both an individual and the University. This can, in turn, result in the loss of research contracts, governmental funding, and the ability to export items. In order to comply with export controls individuals may need to obtain required governmental licenses, monitor and control access to restricted information and materials, and notify specific departments and individuals prior to any export-related activity. TTUHSCEP and its employees are required to comply with applicable export control laws and regulations.

For more information, please refer to HSCEP OP: 73.16 or contact our appointed Research Export Control Administrator, Jacqueline Roberts. For information regarding Export Controls not related to Research, please contact the Institutional Compliance Office.

10.1.1 Foreign Influence

According to 32 CFR 147.4 and 32 CFR 147.5, “foreign influence” refers to security risks that may exist when an employee's family is subject to duress, and/or when an employee may prefer a foreign country over the United States. Federal agencies have expressed concern that foreign entities may be using university research enterprises to compromise our economic competitiveness and national security. This can include “the sharing of confidential information by peer reviewers with others, including in some instances foreign entities, or otherwise attempting to inappropriately influence funding decisions” according to NIH Director, Dr. Francis Collins.

Behaviors that cause concern include:

- Foreign visitors entering our institution without being vetted
  - There are currently no attestation requirements to record and approve their visit, but departments are encouraged to inform Human Resources prior to the visit and document the visitor’s contact information and credentials
- Investigators traveling and collaborating with institutions in different countries where there is limited control and awareness in terms of what is shared

  - Investigators are reminded to review foreign sanctions and to contact the Research Compliance Unit for information on Research Export Controls
- Ensure that there is proper implementation and oversight of the "Checklist & Certification for Export Controls" provided by the Visa and Immigration Services Administration housed in the Department of Human Resources
  - This is a form that is filled out by departments when foreign students or employees are added
- In addition, there are concerns about foreign students accessing and downloading research data.

Significant penalties may result from non-compliance with institutional and federal regulations such as:

- Federal warning letters, Denial Orders and Interim Suspensions
- Seizure & Forfeiture of commodities or technical data
- Debarment and termination of export privileges which includes the revocation of contracts, loss of funding, debarment from government contracts or implementation of additional compliance measures
- Significant harm to the integrity and reputation of the institution and the individual
- Severe criminal and monetary fines to both the individual and the University
- Protracted and intensive investigations involving federal agencies
- Fines of up to $1,094,010 per violation
- Prison sentences of up to 20 years per violation

For questions, please contact the Research Compliance Unit for information on Foreign Influence and Research Export Controls.

11. CHAPTER 11: EFFORT CERTIFICATION

11.1 Certifying Time and Effort at TTUHSC El Paso

Time and effort certification serves to ensure that the salary and wages of employees charged to a sponsored project are allocable, allowable, consistently treated, and reasonable. Employees who are receiving compensation from a sponsored project, and are committing effort on a sponsored project, or are spending time/effort towards a sponsored project are required to have an Effort Statement certifying their effort in accordance with the HSCEP OP 65.07. This policy is based on OMB 2 CFR 200.400.

At TTUHSCEP, the Effort Certification and Reporting Technology (eCRT) system is used to document the effort put forth on a sponsored project and to confirm that the project warrants the financial compensation provided by the sponsor. The eCRT system is accessible at https://ecrt.texastech.edu/ecrt. Effort statements are meant to be used as an after-the-fact method of

confirming the amount of effort performed on a sponsored project. The eCRT system reflects an individual's payroll distribution to various institutional funds, including sponsored project funds, and provides an estimation of actual time spent on activities such as instruction and research. It documents the distribution of salaries and wages based on a reasonable estimate of time worked, distinguishing between institutional activities and sponsored projects.

Primary Effort Coordinators (PEC) are responsible for facilitating the entire effort certification process for their department. They assist PIs and Certifiers with the certification process, and review the payroll data within eCRT and verify accuracy compared to estimated employee effort. PECs are also responsible for processing Labor Redistributions as needed, including sufficient justification for the adjustment. Principal Investigators and Project Directors are then responsible for certifying the effort of staff and/or non-faculty paid from each of their sponsored projects and any faculty with commitments to a sponsored project but not paid from any sponsored FOP. Certification is required of all personnel whenever a portion of their salary is charged to a sponsored project; this includes other faculty (non-PI) paid from a sponsored project. Non-PI faculty must certify their own effort. After the certification process occurs, PECs are required to process all certified statements.

Principal Investigators and Project Directors are responsible for understanding the effort certification requirements of the projects for which they apply and for which they are awarded funding. Both Principal Investigators/Program Directors and PECs are responsible for monitoring time and effort for employees. Principal Investigators and Program Directors monitor and review their projects' time and effort to ensure that it is accurate and compliant; PECs monitor effort statements to identify employees whose pay has exceeded specified salary and cap limitations and to prepare labor redistributions and more. It is the PECs responsibility to notify SP if the certified effort of an individual falls short of their committed effort by more than 25% to determine if sponsor notification is required. Principal Investigators and Program Directors are responsible for ensuring that the reported level of effort is accurate and commensurate with commitments to sponsors, that other activities will not conflict with effort commitment and that certifications are made in an accurate and timely manner. Principal Investigators and Program Directors are also tasked with maintaining sufficient documentation to verify the effort expended.

**For more information, you can review HSCEP OP 65.07 or visit the* Contracts and Grants Accounting Reference Material webpage.

11.1.1 The Research Compliance Unit's Responsibilities Toward Effort Reporting

Effort statements are due on a quarterly basis. At the beginning of the certification period for each quarter, the eCRT system sends out general notifications to remind each department to certify and process their efforts. To further encourage timely submissions, the RCO has been tasked with monitoring effort submission compliance.

Because the RCO has limited administrative access to the eCRT system, they are not able to provide assistance with any questions or concerns regarding the eCRT system and certification

process. Questions and/or changes to certification/processing responsibilities and temporary proxy assignments are addressed by specific individuals located in the Contracts and Grants Accounting department that work closely with the eCRT system.

The RCO's main purpose is to imposing the escalation of non-compliance in accordance with our institutional policy (HSCEP OP 65.07). After the certification/processing deadline has passed, PECs, PIs, and certifiers are required to enter a note in the "Note" section of each effort statement that is being submitted after the deadline in order to explain why the effort is being submitted late. If a department has not submitted their effort and/or responded to the RCU administrators' notifications during the course of the certification period, the RCU initiates escalation by informing the PECs and certifiers that their situation has been escalated to the RCO. If there is no response or action from the PEC or the certifiers then the situation is escalated to the department chair then the Vice President for Research is notified. Continued non-compliance is then escalated to the VPR and can be further escalated to the CFO.

12. CHAPTER 12: RESEARCH COMPLIANCE

12.1 Research Compliance at TTUHSC El Paso

All TTUHSC El Paso faculty, staff, students, volunteers, and vendors are expected to follow federal and state laws and TTUHSC El Paso policies regarding research activity conducted on behalf of TTUHSC El Paso and/or using TTUHSC El Paso facilities. At TTUHSCEP, the VPR is responsible for the oversight of the research compliance program at TTUHSC El Paso, with specific compliance oversight responsibilities delegated to the OR. The OR house the appointed research ethics committees on campus and in collaboration with monitoring activities performed by each committee, the OR is authorized to monitor compliance with applicable laws, and TTUHSC El Paso policies related to the appropriate conduct of research activities at or through TTUHSC El Paso. In addition, the OR works with other divisions within the Office of Research, the TTUHSC El Paso Office of Institutional Compliance, Texas Tech University System (TTU System) offices, and TTUHSC El Paso schools and departments on matters pertaining to research compliance.

The VPR, OR and appointed research ethics committees on campus rely on audits and monitoring approved research in order to ensure that research compliance is upheld. The research ethics committees can delegate authority to the Research Compliance Officer and the Research Compliance Unit in order to inspect research facilities, obtain records and other relevant information relating research. Each committee takes such actions that are in its judgment necessary to enforce compliance with applicable federal and state law, regulations, or guidelines, including action to suspend/terminate approval of research that is not being conducted in accordance with committee requirements.

The OR provides compliance oversight for the research activities listed below, which are conducted by TTUHSC El Paso faculty, staff, and students using TTUHSC El Paso facilities. The OR may also provide compliance oversight for activities taking place outside of TTUHSC El Paso facilities when required by

regulation, or when such oversight is agreed to in writing by TTUHSC El Paso. Compliance-specific activities related to each type of research may be found in HSCEP OPs, administrative manuals, or bylaws for the following research activities:

- Animals: HSCEP OP 73.03 and IACUC policies
- Human Subjects: HSCEP OP 73.06 and HRPP Administrative Manual
- Hazardous Chemicals and Biological Materials: HSCEP OP 73.05, HSCEP OP 73.12, and IBC Manual available at: https://elpaso.ttuhsc.edu/research/committees/ibc/_documents/IBC_Manual.pdf
- Recombinant/Synthetic DNA: HSCEP OP 73.05 and IBC Manual available at: https://elpaso.ttuhsc.edu/research/committees/ibc/_documents/IBC_Manual.pdf
- Financial Conflicts of Interest in Research: HSCEP OP 73.09 and COIRC Manual available at: https://elpaso.ttuhsc.edu/research/committees/coirc/COIRC%20Manual.pdf
- Export Controls: HSCEP OP 73.16
- Allowable Research Grant Expenditures: HSCEP OP 65.04
- Scientific Misconduct: HSCEP OP 73.07

12.1.1 Non-Compliance

Non-compliance is defined as a situation, event or process in research that is inconsistent with:

- The ethical principles of human and animal subjects in research
- University policies regarding posing a threat to individuals, the university, or the environment
- Federal, state, and/or local regulations applying to research under the jurisdiction of the TTUHSC El Paso research committees
- TTUHSC El Paso policies and procedures governing institutional research
- Research activities as approved by the TTUHSC El Paso research committees.

Note: Data collected by activities determined to be in “non-compliance” cannot be described in publications or presentations as having been obtained with research committee approval. In addition, research personnel are highly encouraged to conduct routine self-monitoring of their studies. A self-monitoring tool for human subject research has been created for this purpose and is available on the TTUHSC El Paso Research Compliance webpage.

12.1.2 Serious and Continuing Non-Compliance

Serious non-compliance is defined as a situation, event or process which could significantly:

- Increase risks to subjects
- Jeopardize the safety, welfare, or rights of subjects, research personnel, and/or others
- Decrease the potential scientific integrity of the research

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

Continuing non-compliance is a pattern of repeated non-compliance, which continues:

- After initial discovery
- After research committee approval of corrective action plan
- Without intervention
- To increase the risk of serious non-compliance
- And significantly increases risks to, or jeopardizes the safety, welfare, and/or rights of subjects, research personnel, and/or others
- To decrease potential benefits or scientific integrity of the research

12.1.2.1 Protocol Violations

Protocol violations are a serious form of non-compliance. Protocol violations are a type of deviation from the protocol that reduces the quality or completeness of the data affecting research integrity. Violations can also make the Informed Consent Form inaccurate, or can impact a subject's safety, rights, or welfare. Examples of protocol violations include but are not limited to the following:

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

12.1.3 Reporting Allegations of Non-Compliance

All TTUHSC EP research personnel, participants, and others are encouraged to report non-compliance. Reports of non-compliance can include but are not limited to protocol deviations, unanticipated events involving risks to subjects or others, complaints from participants or

others regarding treatment by research staff, reimbursement issues, issues of data integrity, or any other compliance concerns including animal mistreatment and abuse and risks to environmental and personnel safety. All complaints and allegations of research non-compliance are reviewed and result in necessary action as required.

When potential non-compliance is reported, efforts are taken to maintain confidentiality but confidentiality cannot be guaranteed. The name of the reporter is not disclosed to the individuals involved in the complaint, unless disclosure is required to reconcile the situation. If a translator is necessary for participants to state the allegation(s), arrangements for a translator can be made.

The Research Compliance Officer can receive allegations of non-compliance by any means including, but not limited to:

- Voluntary notification by the principal investigator or research staff, through iris or direct communication with the Research Compliance Officer or OR staff
- Information given by other staff of the institution,
- Information given by other members of the research staff,
- Monitoring reports provided by the study sponsor,
- Reports of non-compliance by the research subjects via the TTUHSC El Paso Research Protection Hotline number listed on all approved informed consent documents.
- Anonymous reports to the TTUHSC El Paso Research Protection Hotline or to EthicsPoint.

Initial assessment of the validity of an allegation is made by the research compliance officer in consultation with the Managing Director of the OR, the research committee Chairperson, and/or the Research Committee Senior Director. This initial assessment will generally be conducted within one business day. The initial assessment depends on the nature of the allegation and may include, but is not limited to, review of the approved documents, speaking with study staff, and/or review of financial records associated with the study fund.

If the initial assessment indicates that the allegation has no basis in fact or cannot be adequately investigated given the information received, the Research Compliance Officer can create a personal “Note to File” and no further action will be taken.

If the allegation does have a basis in fact, and the PI has not implemented suitable corrective action, a “for cause” regulatory compliance audit may be initiated by the Research Compliance Officer.

All institutional members should report non-compliance. Observed, suspected, or apparent research misconduct, however, should be to the RIO or to the Compliance Hotline at 1-866-294-9352 (toll free).

12.1.3.1 Institutional Notification and Reporting Requirements

If an individual is unsure whether a suspected incident falls within the definition of non-compliance, the individual may meet with the RCO. For research misconduct, he or she may meet with or contact the RIO (or designee), to discuss the suspected research misconduct informally, which may include discussing it anonymously and/or hypothetically. If the circumstances described by the individual do not meet the definition of research misconduct, the RIO will refer the individual or allegation to other offices or officials with responsibility for resolving the problem. The RCO may also be asked to conduct a for-cause audit by the RIO, the IRB, or by the OR.

Audit findings detected during for-cause audits are shared with the IRB and applicable personnel. The IRB Chair, Research Committee Senior Director, and the OR may conduct a preliminary review in order to determine if the findings must be submitted for full-board review. If findings are submitted to the full board, then corrective actions are decided upon and added to a report. This report is then shared with the PI, applicable research personnel and the OR (if needed), and corrective actions are also implemented by the IRB at this time if it is required.

Investigators are normally provided with a 30- day deadline by which they need to meet all of the corrective actions listed on the report. The investigators may also be asked to submit a corrective action preventative plan in response to the report, which explains what actions have been completed and how they were completed.

12.2 RCU Open-door Policy at TTUHSC El Paso

The RCU has an open-door policy and is available to:

- Answer questions from the research community on campus regarding the University's research-related policies and procedures
- Confidentially receive reports and/or allegations of research non-compliance
- Respond to research-related questions and provide guidance and resources
- Facilitate and discuss training as needed
- Review audit findings, queries and concerns

12.3 OR Research Compliance Committee

A Research Compliance Committee (RCC) has been established to advise on issues and concerns related to funded grants and/or research activities conducted at or through TTUHSC El Paso. The RCC is considered a "medical committee," thus all documents generated by the RCC, submitted to the RCC, or created for the purposes of fulfilling the RCC's duties are confidential.

The RCC consists of the following members:

- OR Research Compliance Officer or his/her designee – committee chairperson

- OR Managing Director or his/her designee
- Sponsored Programs (SP) Associate Managing Director or his/her designee
- OR Senior Director of research committees
- Senior Director of Safety Services or his/her designee
- Chairperson of each TTUHSC El Paso research oversight committee:
  - Institutional Review Board
  - Institutional Animal Care and Use Committee
  - Institutional Biosafety Committee
  - Conflict of Interest in Research Committee
- Representative from General Counsel, appointed by the associate general counsel
- Institutional Compliance Officer

The RCC has the following responsibilities:

- Review and provide input on research-related policies and procedures.
- Provide input regarding general research compliance activities not under the authority of other research oversight committees.
- Provide guidance, including identification of possible research risk areas.
- Review reports of investigations of concerns and/or complaints related to research compliance, provided that such review does not conflict with other TTUHSC El Paso policies, bylaws, or guidelines.
- Serve as liaisons for their schools/departments to communicate non-confidential information to faculty and staff concerning research compliance duties and responsibilities.
- Review and provide input on trainings and training requirements for faculty and staff.
- Provide input on criteria for and frequency of audits.
- Request audits for case-specific investigators, grants, and protocols.

The RCC meets quarterly to address research compliance matters not otherwise the responsibility of other TTUHSC El Paso research oversight committees.

13. CHAPTER 13: RESEARCH AUDITS

13.1 Regulatory Compliance Audits

An audit, as it pertains to regulatory compliance audits, is an investigation of every aspect of a research study. This investigations includes but is not limited to research personnel educational prerequisites, trial-related activities, documents, and data. Its purpose is to ensure that the research study is being

conducted in adherence to the protocol, sponsor's standard operating procedures (if applicable), GCP, and institutional and federal regulatory requirements.

At TTUHSC El Paso, the RCU conducts different types of regulatory compliance audits on research approved by the TTUHSC El Paso IRB. These audits are conducted due to allegations and on a routine basis. Although the other research committees at TTUHSC El Paso are able to request audits on the research that they oversee, they are currently in charge of monitoring and reviewing their research and may conduct investigations without the help of the RCU. Instead, the RCU's primary focus regarding research that is overseen by other research committees is to ensure that research covered and approved by the IRB meets the basic submission, notification, and approval requirements set by the additional research committees.

As we continue to build our Research Compliance Program, we hope to start conducting regulatory compliance audits on all TTUHSCEP approved research.

13.1.1 Routine Regulatory Audits

Routine regulatory audits refers to clinical trials that are audited on a routine basis are selected based on the following but are not limited to these criteria:

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

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

Special circumstances that might delay an audit for more than 30 days are always considered.

Each audit may include a targeted educational component that teaches research faculty and staff how to correct their mistakes and prevent the same mistakes in the future. Final interviews are no longer being conducted by the RCO, and a detailed list of findings and possible deviations is no longer shared at the end of each audit.

Also note that the Research Compliance Senior Analyst can serve as emergency back-up to the RCO if the RCO is unavailable and an audit cannot be rescheduled. The Research Compliance Senior Analyst can also assist the RCO in research studies that are more difficult or have a large subject population to review.

13.1.2 Special Regulatory Audits

Aside from "Routine Regulatory Audits" and "For-Cause Audits", OR admin realized that there was a need to specify an additional type of audit called a "Special Audit". A special audit is a tightly-defined audit that focuses on a specific area of concern regarding a research study and its activities. This type of audit may be initiated if areas of concern have been brought to the attention of the OR without the submission of any formal allegations. Special audits are conducted by the RCU or by ad hoc committees as set forth in specific HSCEP OP 73.14, guidelines, or bylaws, or at the request of the VPR or OR directors, the RCC, the institutional compliance officer, or other TTUHSC El Paso or TTU System administrators.

13.1.3 For-cause Regulatory Audits

Clinical trials audited on a for-cause basis are done so based upon the receipt of an allegation or a request from the IRB to review the research. Potential triggers may also contribute to a for-cause audit and include, but are not limited to:

- PI's with prior adverse events;
- Novel or new interventions in a biomedical study;
- Investigators submitting protocols requiring expedited or full board review who have no prior research experience;
- Especially high risk protocols (as determined by the IRB);
- Protocols involving especially high risk/vulnerable populations and/or groups highly susceptible to coercion;
- Protocols that substantially overlap with major Privacy Rights statutes, such as HIPAA or FERPA;
- A protocol to be conducted over an unusually long period of time;
- PI's who are chronically late in filing for continuing review; and/or
- PI's who submit multiple drafts of informed consent forms;
- PI's who submit informed consent forms which clearly do not apply to the study being reviewed; or
- PI's who submit informed consent forms from other sites or facilities.

Principal investigators will not be given significant prior notification for a for-cause or directed audit. PI can expect notice to be less than 24 hours in advance to several week in advance, but these types of audits should take place as soon as possible. In addition, the RCO may require individual recorded interviews from research and non-research personnel regarding the research study in order to complete an investigation.

13.1.4 Retrospective Chart Review & Exempt Study Audits

Retrospective chart review and exempt studies are audited on a routine basis, and are selected based on the following but are not limited to these criteria:

- New investigators to the institution
- New coordinators to the institution
- If the study is a result of a SARP Project
- Research in departments which have had previous compliance concerns
- Research conducted by investigators with previous compliance concerns

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

13.1.5 Documents and Activities Reviewed During an Audit

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

- observation of the consent process
- observation of the data collection process
- regulatory 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 data collection sheets
- confidentiality of records
- drug and device handling, accountability, and storage
- laboratory data
- study progress reports
- contacting of research subjects
- study advertisements and recruiting information
- research instruments
- request that the PI(s) submit what data or analysis has been done to date to the IRB for review

- subject compensation information
- any additional information determined necessary by the research compliance officer

13.1.6 Reporting Audit Findings

Findings are submitted to the IRB with corrective action recommendations after preliminary review and approval by the Senior Director of the RIU.

Mandatory escalation can be initiated by the RCO at any moment in cases of suspected research misconduct.

The IRB Chair and the Research Committee Senior Director review findings and corrective action recommendations to determine whether or not findings require further review by the Full Board. The IRB Full Board is given time to review a final draft of an audit report that is generated to contain audit findings, corrective action recommendations, and study details. The RCO is generally invited to attend Full Board meetings that will include audit review in order to provide additional information that may not be included in the final draft of the audit report. The IRB Full Board will conclude their audit revision by not approving or by approving some or all of the corrective action recommendations. The final audit report is then completed by IRB administrators and includes any additional criteria required by the IRB. For violations and serious non-compliance, additional actions requested by the IRB full board are also implemented during this timeframe. The report is then submitted via iRIS to the PI and the contact personnel in the PI's research team with an email containing additional instructions on deadlines and/or corrective action preventative plans that must be submitted.

For-cause and routine audits are fairly similar in the way that findings are reported to the IRB and in the way that the IRB provides the audit report to the PI and the research team.

Routine audits are conducted by the Research Compliance Senior Analyst

13.1.5.1 Corrective Actions Resulting from Audit Findings

The audit report will include corrective actions that must be completed by the study personnel, with approval by the principal investigator **no more than 30 days** after the audit report is received by the research team. The IRB might also implement additional stipulations and/or requirements as part of the corrective actions. Possible corrective actions recommended may include, but are not limited to:

- request for more information before a final decision can be made;
- protocol or informed consent document changes;
- changes to, or outside monitoring of the informed consent process;
- suspension or termination of IRB approval of the study;

- more frequent review by the IRB;
- follow-up audits to be conducted on a regular basis for a specified period of time;
- additional training or certification of the PI and the research staff;
- disqualification of the PI or members of the research staff from conducting research at TTUHSC El Paso;
- disallowance of research use of data collected;
- notification of current and/or past research participants regarding study problems;
- re-consent of current study participants;
- notification of other TTUHSC EP committees or administrators; or
- notification of outside entities (DHHS, FDA, NIH, study sponsor) of the compliance issues.

14. CHAPTER 14: RETROSPECTIVE MEDICAL CHART REVIEW & EXEMPT STUDIES

14.1 Retrospective Medical Chart Review Study

To answer clinical queries, a study team may choose to conduct a medical record review study. These types of studies are also known as retrospective chart review studies. The process of a medical record review study consists of obtaining retrospective data and recording the data in a secured structure database for analysis. The previously recorded data is studied, subjected to statistical analysis that leads to drawing conclusions. Carrying out retrospective chart review studies can evaluate the characteristics of a disease running its course through a certain time period along with the treatment outcomes. Other reasons to conduct a retrospective chart review study includes determining appropriate diagnosis, effectiveness of treatments and care plans, and to access standard guidelines.

Please note that with the revised common rule, there is no requirement for data to be in existence. They can conduct a chart review of information that will be collected for clinical purposes in the future as long as it meets the criteria.

14.1.1 Conducting Medical Retrospective Chart Review Studies

There are challenges to performing a retrospective chart review study, particularly data reliability. Unlike prospective studies in which study teams can plan on what type of data to collect and how the data collection process will occur, retrospective record data already exists and may be insufficient or incomplete. A variety of data sources can be used to collect data for a retrospective chart review study. These data sources include hard copy medical records, electronic medical records, disease registries, case files, pharmacy records, and many more.

Every type of data source has its particular advantage and challenges. Data extraction may require an extensive amount of time and certain permission requirements may need to be fulfilled prior to accessing the data. Some data sources require clearances to use the data for academic research or publication. Please note that it is best to be aware of the research terms and conditions of the data source or registry chosen for the retrospective chart review study.

Depending on the nature of the research study, there will be multiple steps to conducting a retrospective chart review study. Some basic steps include: formulating a research question, identifying the most appropriate data source, deciding on which data variables to collect, realizing methods of extracting the data, and lastly formulating statistical methods to use for data analysis. As mentioned before, it is important to take into consideration any clearances that may need to be obtained once a data source is selected. The importance of knowing which data collection variables are appropriate for the research study will assist with data extraction from case records. Examples of variables include types of ICD-9 codes, medical diagnoses, medical terminologies, demographics, etc. The extraction of data should be carried out in accordance with the research study protocol. Addressing clearly what variables are needed for the research study with data managers allow more absolute values. A study team can extract a subsample set to evaluate discrepancies or inaccuracies. Analysis of the data can range in complexities depending on what is most appropriate for the research question at hand.

Please ensure that any change in variables, data extraction, or data analysis is modified on the research study's protocol and is approved by the IRB prior to executing the changes.

14.1.2 Ethical Considerations for Chart Review Studies

The most common question of whether or not an informed consent is needed when conducting a retrospective chart review study is often asked. The requirement for requesting a waiver of consent no longer applies as per the revised common rule. Exempt research is not subject to the requirements of the Common Rule and therefore is not required to meet the requirements for informed consent, to include waiver of informed consent. Sometimes research studies t will not want or need to collect PHI; however, a record review from UMC will typically always have PHI. Most chart reviews normally have at least one identifier in order to be able to complete the review and/or verify data. An example of PHI that is often used is the medical records number. In addition, if a study team needs access to data, then a waiver of HIPAA will also need to be requested during the application process even if PHI is not being collected. The study team will need to justify on the study application why they are requesting a HIPAA waiver.

There are ethical aspects to consider when conducting a retrospective chart review study. Although a waiver of HIPAA can be obtained for a research study, a subject's data is still at risk of being compromised or misused. Data may fall in the hands of individuals not approved to work on the research study or additional data may be extracted without approval. Only approved study personnel should be involved in the process of data collection and analysis.

Also, the data that is to be collection should only be data listed in the protocol and application, and must be approved by the IRB. Please note that data which has previously been IRB-approved for collection and analysis can later be used to answer a different question on another retrospective chart review study without obtaining IRB approval; however, identifying information must first be removed from the data set before other researchers can use it.

A retrospective chart review study can be conducted ethically following certain standards. First, only collecting and analyzing IRB-approved data to answer the research question should be done. Also, if a HIPAA waiver is obtained and PHI is being collected for the research study then the research study team will need to de-identify any PHI from the data set before it is used for analysis. For example, de-identifying PHI can include coding subject's names to an alpha-numeric format to conceal identities. Safeguard measures must be set in place to protect the data that is being collected for the research study. Safeguard measures, such as password protected computers and files should only be accessed by authorized research study personnel. Most importantly, please be aware that although a research study may be time sensitive and have its urgency to begin data collection, the process of data collection cannot begin until IRB approval and other facility or institutional clearance (if applicable) has been received.

When considering a retrospective chart review research study, a study team will need to weigh in its advantages and disadvantages. Some advantages include, for example, the cost effectiveness of the study, the study's potential of identifying risk factors, and not having to deal with loss to follow-up subjects. The disadvantages include incomplete data variables, the need to collect large amounts of data if the outcomes are rare, and even errors in data recording may be encountered. In order to receive the best outcome when conducting a retrospective chart review research study, a study team will need to clearly specify the clinical questions they seek to answer, adequately plan the data collection process and its source or sources, and have a systematic methodology to analyze outcome measures. All of these aspects have to be met along with ethical standards of obtaining the appropriate approvals, clearances, and have data safeguard measures in place. Appropriately conducting a retrospective chart review study has the potential to find clinical based evidence that may not be available by any other resources.

14.2 Exempt Research Study

The term "exempt" is used to refer to human subject studies that present no greater than minimal risk to subjects and fit into one or more exempt categories as determined by the IRB. Although studies that qualify for exempt status do not have the same federal requirements for research involving human subjects as non-exempt studies, investigators still have a responsibility to protect the rights and welfare of their subjects. In addition, investigators must continue to adhere to TTUHSC EP policies, and conduct their research in accordance with the ethical principles of Justice, Beneficence, and Respect for Persons as described in the Belmont Report.

Principal investigators and their study team do not have the authority to determine whether or not a research project qualifies as exempt, and may not begin the research until the IRB has provided an initial notification of approval for the study.

The Office for Human Research Protections has additional information and categories of criteria that fall under exempt status. When a research study is determined to be exempt, it is submitted for expedited review as opposed to full board review. This means that the research is able to be reviewed and approved without convening a meeting of the IRB.

15. CHAPTER 15 RESEARCH VOLUNTEERS

15.1 Research Volunteer

A research volunteer is defined as a non-compensated person who performs low risk department functions for research purposes. These individuals typically have limited duties and scope of responsibilities, and may participate in laboratory or laboratory-related activities and in human research-related activities with appropriate permissions. All research volunteer opportunities are accepted without promise or expectation of compensation, future employment, or other tangible benefit.

15.1.1 Research Volunteer Registration Process

Persons who are interested in becoming research volunteers must visit the Research Volunteer page available through the OR webpage. An application is available on the Research Volunteer page and must be submitted to designated personnel along with a resume and proof of identification. Individuals who apply must be vetted through the Human Resources TTUHSC El Paso volunteer office and the OR.

After the initial registration process, volunteers must complete online safety training courses, successfully pass a criminal background check, attend orientation, complete HIPAA training, and complete immunization review. Research Volunteers are only allowed to volunteer for a period of one year and may not exceed more than 20 hours per week. If the department wants to request that a volunteer work more hours, they need to consult with Human Resources, and they may need to consider the possibility of creating a paid position in order to fulfill the department's needs.

15.1.2 Acceptable Applicants

Volunteers may include visiting professors, researchers and/or medical personnel who are not employed by, or do not have faculty appointments at TTUHSCEP. Volunteers must also be at least 17 years of age and have authorization to work in the United States. TTUHSCEP volunteers are part of the TTUHSCEP workforce, but are not considered employees for any purpose and are not covered by the Fair Labor Standards Act. They are not eligible for any TTUHSCEP benefits and are not covered by or eligible for Workers Compensation, as a result of this volunteer association with TTUHSCEP.

The following is a list of individuals that may not be considered volunteers and/or may not be eligible to apply for volunteer positions:

- Individuals acting as members of officially-sanctioned university support organizations
- Individuals who are enrolled as students at TTUHSCEP or are accepted into a residency program at TTUHSCEP for the purpose of providing services to meet course requirements or to earn course credit
- Individuals who are enrolled in academic programs at TTUHSCEP who are participating in activities as part of their TTUHSCEP course curriculum
- Students from institutions of secondary or higher education that are participating as a part of an officially sanctioned educational agreement with TTUHSCEP, or are engaged in an educational tour conducted by TTUHSCEP staff
- Individuals who are visiting fellows
- Individuals who seek unpaid academic or research faculty appointments at TTUHSCEP
- Individuals who serve on TTUHSCEP Committees as a community representative members
- Individuals who have been dismissed previously for cause from employment at TTUHSCEP
- TTUHSCEP employees whose employment is essentially the same as, or is similar to, their regular work at TTUHSCEP
- Foreign nationals who require an export license where the volunteer services involve access to export controlled information or equipment

15.1.3 Time Sheet Requirements and Access

Volunteers must submit monthly timesheets to their volunteer supervisor. They should then be submitted to the OR on a monthly basis, but no later than the 2nd working day of each month. At that time, timesheets are reviewed for completeness and submitted to HR. Volunteers are terminated if timesheets are not submitted to the OR for three consecutive months.

Volunteers must be added to research projects through iRIS, and the amendment must be approved by the designated ethics committee prior to allowing the volunteer participate on the project. It is the volunteer's supervisor's responsibility to provide the volunteer with departmental orientation and protocol-specific training. The supervisor must also implement

start and completion dates, goals and anticipated activities, and potential areas of security/confidentiality. The supervisor is also responsible for providing the volunteer with informal performance evaluations for improvement and to ensure adherence to institutional policies.

Volunteers are not authorized to have TTUHSCEP equipment, keys and employee badges. Volunteers who need access to the Medical Science Building (MSBI) in order to complete their volunteer experience can obtain a temporary badge with preprogrammed general building access to these restricted buildings on a daily basis. Badges are only available at the MSBI Front Desk during regular business hours (M-F, 8 am-5pm) and are only valid for that business day. *Badges must be returned to the Front Desk by the end of each day*. Badges are not issued during any other timeframe including after regular business hours, holidays or weekends. Volunteers issued an access card are prohibited from providing unauthorized access to another person. Any unauthorized use, loss or malfunction of a badge must be reported to the Front Desk immediately. The OR will monitor volunteer start and end dates. Volunteers must be supervised by their respective volunteer supervisor at all times. In addition, volunteers under 18 years old cannot be allowed access to BSL2 or above.

Once the research volunteer has completed the work and their service to TTUHSCEP is being discontinued, it is the supervisor's responsibility to communicate this to the OR and to HR.

16. CHAPTER 16: CHANGES AND ALLOWANCES DUE TO COVID-19

16.1 COVID-19 and Research

The pandemic has brought about significant repercussions that have fundamentally changed clinical research. This has put a lot of pressure on researchers, regulators, and policy makers to move quickly and implement changes in order to continue to conduct quality research while upholding safety for subjects and research personnel alike. In the interest of clinical research conducted at TTUHSCEP, certain allowances and recommendations have been made to assist research personnel in addressing the challenges that have come up. Please keep in mind that deviations are expected due to missed visits and other restrictions, this is where documentation is instrumental since it is important to capture specific information that will be helpful to understand what happened and why.

16.1.1 Virtual CRA Visits

Our HIPAA Privacy Officer is requesting that any and all regulatory documentation be shared through TTUHSCEP's approved account. A file should be created on the TTUHSC El Paso approved system and access to that specific file should be shared with the CRA or study sponsor. Access must be limited to a specific number of days and all regulatory documents must be de-identified prior to being scanned and uploaded. Clinical Trial Agreements must be

amended to state that CRAs and study sponsors may not print and may only view documents from the record on TTUHSC El Paso's approved system. Documents that can be scanned and uploaded include documents from TTUHSCEP EMR and any other study documentation that a CRA or sponsor is requesting to view. TTUHSCEP is not currently allowing TTUHSCEP EMR and regulatory research records to be viewed through WebEx.

At this time, UMC's Research Committee is only allowing the use of WebEx. Documents from UMC EMR (CERNER) may only be viewed by CRAs and study sponsors through WebEx. UMC is not allowing items from its EMR to be uploaded onto Box.

TTUHSCEP does not currently have a specific virtual platform in which regulatory documents can be shared with study sponsors and CRAs. Researchers are also not allowed to use any temporary sponsor platforms to conduct virtual visits. This does not refer to EDC systems and is specific to source documentation. There are discussions in place to purchase and install a system that will allow research personnel to create, maintain, and share access to regulatory documentation for individual studies; this should resolve the difficulties that researchers are facing with virtual study visits.

16.1.2 Conducting Informed Consent on Patients in Isolation

Informed consent is required for trial participation, and consent must be documented by the use of a written and IRB-approved informed consent document. When feasible, the traditional method of obtaining informed consent is preferred, but the FDA has recommended the following procedures that are considered to still satisfy the FDA's requirement. Please note that the following items were taken directly from the FDA's "Conduct of Clinical Trials of Medical Products During the COVID-19 Public Health Emergency; *Guidance for Industry, Investigators, and Institutional Review Boards*" https://www.fda.gov/media/136238/download.

- "**Method 1:** A photograph of the signed informed consent document can be transmitted to the trial staff.
  - An unsigned consent form is provided to the patient by a person who has entered the room.
  - The investigator/designee arranges a telephone call or video conference call with the patient (and, if desired and feasible, additional individuals requested by the patient (e.g., next of kin)).
  - To ensure that patients are approached in a consistent fashion, a standard process should be used that will accomplish the following:
    - Identification of who is on the call.
    - Review of the informed consent document with the patient by the investigator/designee and response to any questions the patient may have.

        - Verbal confirmation by the patient that their questions have been answered, that they would like to participate in the trial, and that they have signed and dated the informed consent document that is in their possession.
    - The patient (or an individual in the room) takes a photograph of the signed informed consent document and sends it to the investigator/designee.
    - A trial team member enters the photograph into the trial records along with an attestation that states how that photograph was obtained and that it is a photograph of the informed consent document signed by the patient.

- **Method 2:** A witness can attest to the signature, but a photograph of the signed informed consent document cannot be transmitted
    - An unsigned consent form is provided to the patient by a person who has entered the room.
    - The investigator/designee arranges a three-way telephone call or video conference call with the patient, a witness who is not otherwise connected with the clinical investigation, and, if desired and feasible, additional individuals requested by the patient (e.g., next of kin). Alternatively, in lieu of using a witness, a recording of the conversation can be made.
    - To ensure that patients are approached in a consistent fashion, a standard process should be used that will accomplish the following:
        - Identification of who is on the call.
        - Review of the informed consent document with the patient by the investigator/designee and response to any questions the patient may have.
        - Verbal confirmation by the patient that their questions have been answered, that they would like to participate in the trial, and that they have signed and dated the informed consent document that is in their possession.
            - When using a witness, documentation in the trial records includes: (1) a signed and dated attestation by the witness who participated on the call that the patient confirmed their agreement to participate in the trial and signed the informed consent document; and (2) a signed and dated attestation by the investigator/designee stating why the informed consent document signed by the patient was not retained (e.g., due to potential contamination of the document by infectious material).
            - When using a recording in lieu of a witness, documentation in the trial records includes: (1) the recording of the conference call; and (2) a signed and dated attestation by the investigator/designee who participated on the call stating why the informed consent document signed by the patient was not retained (e.g., due to potential contamination of the document by infectious material).

When either Method 1 or 2 is used to document informed consent, the resulting documentation should be: (1) collected and archived, as either original paper copies or appropriately certified electronic copies (e.g., using a validated process for scanning paper

copies), and (2) retained according to applicable FDA record retention requirements as part of the trial record.

If the patient is unable to provide informed consent and there is a legally authorized representative, investigators must obtain written consent from the patient's legally authorized representative in accordance with 21 CFR 50.27(a)."

16.1.3 Conducting Virtual Informed Consent on Prospective Subjects

In addition to the current challenges that the pandemic and risk of infection has created, there has been a push towards decentralization of research within the world clinical research. Decentralization of clinical research refers to conducting clinical research through telemedicine and using processes and technologies differing from traditional processes. Because of this, the FDA added additional guidance on conducting virtual informed consent with prospective subjects. The following items represent the FDA's recommendations that were taken directly from the FDA's "Conduct of Clinical Trials of Medical Products During the COVID-19 Public Health Emergency; *Guidance for Industry, Investigators, and Institutional Review Boards*" https://www.fda.gov/media/136238/download.

- "Where a prospective trial participant (or legally authorized representative) is unable to print the informed consent document provided electronically by the investigator/designee, an electronic signature process is not available, and the prospective trial participant must meet time-sensitive eligibility criteria, the investigator may consider using the following alternative process to satisfy FDA requirements for obtaining and documenting informed consent:
    - The investigator/designee provides the prospective participant (or legally authorized representative) with an electronic version of the informed consent document.
    - The investigator/designee arranges a telephone call or video conference call with the prospective participant (or legally authorized representative), the investigator/designee, a witness who is not otherwise connected with the clinical investigation and, if desired and feasible, additional participants requested by the prospective participant (e.g., next of kin). Alternatively, in lieu of using a witness, a recording of the conversation can be made.
    - To ensure that the prospective participant (or legally authorized representative) is approached in a consistent fashion, a standard process should be used that will accomplish the following:
        - Identification of who is on the call.
        - Review of the informed consent document with the prospective participant (or legally authorized representative) by the investigator/designee and response to any questions the prospective participant (or legally authorized representative) may have.

        - Verbal confirmation by the prospective participant (or legally authorized representative) that their questions have been answered and that they would like to participate in the trial.
    - Verbal confirmation by the participant (or legally authorized representative) that they signed and dated a blank piece of paper with a written statement that they voluntarily agree to participate in the protocol, noting both the Protocol 'NUMBER' and brief protocol title.
    - After signing and dating the newly created document, the trial participant (or legally authorized representative) sends a photograph of the signed and dated statement by facsimile, text message, or email to the investigator/designee; OR returns the document to the investigator by mail at a later date, or at a future study visit that might occur in person.
    - When using a witness, documentation in the trial records includes a signed and dated attestation by the witness who participated on the call that the patient confirmed their agreement to participate in the trial and signed the document referenced above.
    - When using a recording in lieu of using a witness, documentation in the trial records includes the recording of the conference call.
    - After the signed and dated document is received by trial staff, it should be appended to a copy of the consent document that was reviewed with the trial participant (or their legally authorized representative) and retained in the trial records as would normally be done for a signed informed consent document.

Additionally, a note in the trial records should be made explaining the circumstances of why informed consent was obtained through an alternative method. The case history for each trial participant must document that informed consent was obtained prior to participation in the trial.

This alternative approach must be reviewed and approved by the IRB overseeing the trial as required under FDA regulations."

16.2 Informing the IRB

Changes in process and procedures are to be expected, but it is imperative that the IRB be notified of these changes prior to their implementation. In addition to changes in informed consent procedures, recommendations have been printed by the FDA and other government agencies on conducting remote patient visits and on the shipping of investigational drugs and products to subjects.

Regardless of the change, the IRB should be informed when feasible. Situations do exist in which emergencies may not allow notification of changes prior to implementation, but these situations and more are explained in the TTUHSCEP Human Research Protection Program Manual.

17. CHAPTER 17: ESCALATIONS

17.1 Escalations Due to Non-Compliance

Often, the Research Compliance Unit and other research administrators may research out to principal investigators and personnel for a variety of reasons including but not limited to: Problems with a record on ClinicalTrials.gov, expired training requirements, information regarding research export controls, questions about an upcoming audit, etc… Due to the many aspects of research, some of these inquiries may be time-sensitive and contingent on a response from research staff and faculty. In the event that the RCU reaches out to a principal investigator and/or their research personnel, three attempts to communicate will be made by email and/or by phone. If all attempts at communication are unsuccessful, then the Managing Director of the Office of Research will be made aware and the situation will be escalated to the principal investigator's department chair. If communication is still unsuccessful, then the situation will be escalated to the Vice President for Research. The VPR will then implement follow-up corrective action.

18. APPENDIX

HELPFUL RESOURCES

TTUHSC El Paso Research Compliance Webpage

TTUHSC El Paso Human Research Protection Program Manual

TTUHSC El Paso Research Compliance Training Webpage

TTUHSC El Paso Research Compliance Resources Webpage

TTUHSC El Paso Research Compliance ClinicalTrials.gov Webpage

TTUHSC El Paso Research Compliance Research Export Controls Webpage

TTUHSC El Paso Operating Policies and Procedures

EthicsPoint Compliance Reporting

TTUHSC El Paso Office of Research (OR)

TTUHSC El Paso Research Committees

TTUHSC El Paso Sponsored Programs (SP)

TTUHSC El Paso Contracts and Grants Accounting (CGA)

TTUHSC El Paso CGA Time and Effort Reporting Reference Material

iRIS System Log-In and Access

TTUHSC El Paso Safety Service Manuals

GLOSSARY OF COMMONLY USED RESEARCH TERMS

Please refer to the TTUHSCEP HRPP Manual for the definition of the following terms:

ADMINISTRATIVELY CLOSED STATUS
ADVERSE EVENT (AE)
ALCOA
APPROVED
APPROVED DRUGS
ARM
ASSENT
AUDIT
AUTHORIZED OFFICIAL
AUTONOMY
BASELINE
BELMONT REPORT
BENEFICENCE
BENEFIT
BIOLOGIC
BLINDING (OR MASKING)
CANCELLED
CASE REPORT FORM (CRF)
CHILDREN
CLINICAL RESEARCH ASSOCIATE (CRA)
CLINICAL RESE CLINICAL TRIAL
CLINICALTRIALS.GOV IDENTIFIER (NCT NUMBER)
CLOSED TO ACCRUAL
CLOSURE
COLLABORATIVE RESEARCH
COMMON RULE
COMPETENCE
COMPLETED
COMPLIANCE
CONFIDENTIALITY
CONFLICT OF INTEREST
CONFLICT OF INTEREST IN RESEARCH COMMITTEE
CONSENT
CONTINUING NON-COMPLIANCE
CONTINUING REVIEW
CONTRACT
CONTRACT RESEARCH ORGANIZATION (CRO)

PRIVACY BOARD IRB
PROSPECTIVE STUDIES
PROTOCOL
PROTOCOL AMENDMENT
PROJECT
PROTOCOL DEVIATION
PROTOCOL VIOLATION
PUBLIC DOMAIN/PUBLICLY AVAILABLE
QUALITY ASSURANCE
QUALITY IMPROVEMENT
QUORUM
RANDOMIZATION
RECRUITMENT
RELIANCE AGREEMENT
RELYING IRB
REPRESENTATIVE
REQUEST FOR ADDITIONAL INFORMATION
RESEARCH
RESPECT FOR PERSONS
REVIEW (OF RESEARCH)
SECONDARY USE
SERIOUS ADVERSE EVENT (SAE)
SERIOUS NON-COMPLIANCE
SINGLE-BLIND STUDY
SOURCE DATA/DOCUMENTS
SPECIMEN
SPONSOR
STANDARD TREATMENT
STANDARDS OF CARE
STUDIES
STUDY
STUDY CLOSURE
STUDY STATUS
SUBJECT IDENTIFICATION CODE
SURVEY
SUSPENDED
SUSPENSION/TERMINATION
TABLED
TERMINATED
UNANTICIPATED ADVERSE DEVICE EFFECTS
UNANTICIPATED PROBLEMS INVOLVING RISK TO SUBJECTS OR OTHERS (UPIRSO)

UNEXPECTED ADVERSE EVENT
VOLUNTARY
VULNERABLE SUBJECTS
WITHDRAWN

The following terms are primarily defined in this manual:

BIAS A point of view or preference which prevents impartial judgment in the way in which a measurement, assessment, procedure, or analysis is carried out or reported.

BLANKET CONSENT Refers to a process by which individuals donate their samples without any restrictions.

BROAD CONSENT Refers to a process by which individuals donate their samples for a broad range of future studies, subject to specified restrictions.

CLINICAL RESEARCH NIH defines clinical research as:

- Patient-oriented research. Research conducted with human subjects (or on material of human origin such as tissues, specimens and cognitive phenomena) for which an investigator directly interacts with human subjects. Excluded from this definition are in vitro studies that utilize human tissues that cannot be linked to a living individual. Patient-oriented research includes: (a) mechanisms of human disease, (b) therapeutic interventions, (c) clinical trials, or (d) development of new technologies.
- Epidemiologic and behavioral studies.
- Outcomes research and health services research.

COHORT STUDY A study conducted on a group of people. These studies are a type of medical research used to investigate the causes of disease and to establish links between risk factors and health outcomes.

CONCOMITANT MEDICATION Prescription and over-the-counter drugs and supplements a study participant has taken along with the study intervention. This information may be collected as a history item as well as during the study. Some studies may collect only those medications that may interact with the study or intervention or that may exclude an individual from participating in a study.

CONTROLLED TECHNOLOGY AND/OR INFORMATION This includes goods, services and related technology identified on the CCL and governed under EAR, 15 CFR Parts 730-774, and defense articles or services and related technical data listed in the United States Munitions List (USML) and governed under ITAR, 22 CFR §§120-130.

DATA MANAGEMENT The processes of handling the data collected during a clinical trial from development of the study forms/CRFs through the database locking process and transmission to statistician for final analysis.

Data Management Plan (DMP) A plan that documents the processes for handling the flow of data from collection through analysis. Software and hardware systems along with quality control and validation of these systems, as relevant are described.

DATA AND SAFETY MONITORING PLAN (DSMP) Plan included with the grant application for clinical trials which establishes the overall framework for data and safety monitoring, how adverse events will be reported to the IRB and the NIH and, when appropriate, how the NIH Guidelines and FDA regulations for INDs and IDEs will be satisfied.

DEEMED EXPORT A deemed export occurs when Controlled Technology or Information is disclosed (written, oral or visual inspection) to foreign persons within the United States. Examples of a deemed export include tours of laboratories that have Export Controlled Technology or Information, or laboratories in which foreign nationals (i.e., students or visiting scientist) are working on an research project involving Export Controlled Technology or Information.

DIAGNOSTIC TRIALS determine better tests or procedures for diagnosing a particular disease or condition.

ELIGIBILITY CRITERIA List of criteria guiding enrollment of participants into a study. The criteria describe both inclusionary and exclusionary factors, (e.g. inclusion criterion - participants must be between 55 and 85 years old; exclusion criterion – must not take drug X three month prior to the study).

EXPORT An export is the transfer by any means of technology, information (written, visual or oral), equipment (including visual inspection), software or codes, or services to anyone, including a U.S. citizen, outside the United States. This includes actual shipment outside the U.S., visual inspection, or making the information or software available over the Internet.

FOREIGN PERSON OR ENTITY These are persons or entities who:

- are not U.S. citizens (foreign nationals), “Lawful Permanent Residents” (Green Card), or “Protected Individuals” under the Immigration and Naturalization Act designated an aslyee, refugee, or a temporary resident under amnesty provisions;
- are any foreign corporation, business association, partnership or any other entity or group incorporated under the laws of a foreign state if either its principal place of business is outside the U.S. or its equity securities are primarily traded on foreign exchange(s); or
- are any foreign government.

FUNDAMENTAL RESEARCH Basic and applied research in science and engineering, the results of which ordinarily are published and shared broadly within the scientific community, as distinguished from proprietary research and from industrial development, design, production, and product utilization, the results of which ordinarily are restricted for proprietary or national security reasons.

GOOD DOCUMENTATION PRACTICES (GDP) A systematic procedure of preparation, checking, verifying, recording, issuing, storing, reviewing, correcting and managing data, documents and records, to ensure the reliability and integrity of information and data collected.

HEALTH INSURANCE PORTABILITY AND ACCOUNTABILITY ACT (HIPAA) PRIVACY RULE The first comprehensive Federal protection for the privacy of personal health information. The Privacy Rule regulates the way certain health care groups, organizations, or businesses, called covered entities under the Rule, handle the individually identifiable health information known as protected health information (PHI).

HEALTHY VOLUNTEER Is a person with no known significant health problems who participates in clinical research to test a new drug, device, or intervention.

INFORMED CONSENT FORM A document that describes the rights of a study participant and provides details about the study, such as its purpose, duration, required procedures, and key contacts. Risks and potential benefits are explained in the informed consent document.

INTERVENTION A procedure or treatment such as a drug, nutritional supplement, gene transfer, vaccine, behavior or device modification that is performed for clinical research purposes.

NATURAL HISTORY STUDIES Provide valuable information about how disease and health progress.

OBSERVATIONAL STUDY MONITORING BOARD (OSMB) The safety and data monitoring body for observational studies with large or vulnerable populations or risks associated with tests or standard of care.

PATIENT VOLUNTEER Has a known health problem and participates in research to better understand, diagnose, treat, or cure that disease or condition.

PHARMACOKINETICS The process (in a living organism) of absorption, distribution, metabolism, and excretion of a drug or vaccine.

PLACEBO A placebo is an inactive pill, liquid, powder, or other intervention that has no treatment value. In clinical trials, experimental treatments are often compared with placebos to assess the treatment's effectiveness.

PLACEBO CONTROLLED STUDY A method of investigation in which an inactive substance/treatment (the placebo) is given to one group of participants, while the test article is given to another group. The results obtained in the two groups are then compared to see if the investigational treatment is more effective in treating the condition.

PREVENTION TRIALS Look for better ways to prevent a disease in people who have never had the disease or to prevent the disease from returning.

QUALITY CONTROL (QC) The internal operational techniques and activities undertaken within the quality assurance system to verify that the requirements for quality of trial related activities have been fulfilled (e.g., data and form checks, monitoring by study staff, routine reports, correction actions, etc.).

QUALITY OF LIFE TRIALS (or supportive care trials) explore and measure ways to improve the comfort and quality of life of people with a chronic illness.

RECRUITMENT PLAN The plan that outlines how individuals will be recruited for the study and how the study will reach the recruitment goal.

RESPONSIBLE CONDUCT OF RESEARCH (RCR) Is defined as the practice of scientific investigation with integrity.

RETENTION PLAN The plan that details the methods in which the study will use in order to retain study participation in the clinical trial.

RETROSPECTIVE STUDY/RETROSPECTIVE COHORT STUDY Is a backward-looking type of cohort study and the opposite of a prospective study, where researchers look at data that already exist and try to identify risk factors for particular conditions. Interpretations are limited because the researchers cannot go back and gather missing data.

SAFETY MONITORING PLAN A plan that outlines the oversight of a clinical trial.

SCREENING LOG An essential document that records all individuals who entered the screening process. The screening log demonstrates the investigator’s attempt to enroll a representative sample of participants.

SCREENING PROCESS A process designed to determine individual’s eligibility for participation in a clinical research study.

SCREENING TRIALS Test the best way to detect certain diseases or health conditions.

STANDARD OPERATING PROCEDURE (SOP) Detailed written instructions to achieve uniformity of the performance of a specific function across studies and patients at an individual site.

STOPPING RULES Established safety criteria that would either pause or halt a study due to reasons including but not limited to futility or risk(s) to the participants.

STRATIFICATION Separation of a study cohort into subgroups or strata according to specific characteristics such as age, gender, etc., so that factors which might affect the outcome of the study, can be taken into account.

LIST OF ITEMS THAT FALL UNDER NON-COMPLIANCE AND THEIR APPROVED CORRECTIVE ACTIONS

- A **note-to-file** is a memo created to identify a discrepancy or problem in the conduct of the clinical research study. This memo can be written to identify the root cause of a problem, to identify the corrective action taken to prevent recurrence of the problem, and to document that the corrective action has resolved the problem.
- A **deviation** is a less serious form of non-compliance. Protocol deviations are unplanned or unforeseen changes in the implementation of an IRB-approved protocol. They generally refer to a modification of procedures that has already occurred for a single subject; they are not intended to modify the protocol.
- A **violation** is serious non-compliance. Violations are a divergence from the protocol that materially (a) reduces the quality or completeness of the data, (b) makes the Informed Consent Form inaccurate, or (c) impacts a subject's safety, rights, or welfare. Examples of protocol violations may include the following [3]:
  - Inadequate or delinquent informed consent
  - Inclusion/exclusion criteria not met
  - Unreported serious adverse events
  - Improper breaking of the blind
  - Use of prohibited medication
  - Incorrect or missing tests
  - Mishandled samples
  - Multiple visits missed or outside permissible windows
  - Materially inadequate record keeping
  - Intentional deviation from protocol, Good Clinical Practice, or regulations by study personnel
  - Subject repeated non-compliance with study requirements

Informed Consent and HIPAA

- All of the following items should be reported as **Note-to-files**:
  - Items involving the **subject**:
    - The subject did not add “AM” or “PM” to the time on the consent.
    - Random marks and scribbles on consent/HIPAA form
    - Subject did not initial or checkmark all pages of the consent (as needed)
    - Subjects not receiving a copy of the consent/HIPAA

        - Subjects do not print their name on the consent/HIPAA
        - Subjects do not add a date to the HIPAA
        - Subjects adding additional signatures to various pages of consent/HIPAA
        - Subjects did not answer questions to give permissions on consent
        - Subject or representative added information to the wrong lines on the consent
        - Subject dates and/or times written on consent/HIPAA are not accurate or do not match other times or dates on consent/HIPAA
        - Dates or times written in a different style than what is normally used on the study or different from the style used by the consenting research personnel. (For example: dd/mm/yyyy or military time) (No penalty for differences in the way date or time is entered)
        - Adding the parent's name to the consent/HIPAA but not the child's when the child is the subject
        - Adding the child's name to the consent/HIPAA but not the parent's when the parent is the subject
        - Signature of second parent not obtained for good reason but not documented, (with the research team trying to reach the subject's 2nd parent)
    - Items involving the **research personnel administering the consent**:
        - The research personnel did not add "AM" or "PM" to the time on the consent.
        - Several signatures at the bottom of a consent with no explanation
        - HIPAA signed several weeks after the consent was signed
        - Unnecessary impartial witness signed consent, but didn't checkmark box stating that it was necessary or some variation of this
        - Investigator retaining photocopy of consent and not original
        - Research personnel did not print their name on the consent
        - Research personnel do not add a date to the consent
        - Research personnel do not add a time to the consent
        - Research personnel adding additional signatures to various pages of consent/HIPAA
        - Adding notes or information to consent/HIPAA after the subject has signed and been given their copy
        - Adding subject PHI to signed subject informed consent documentation
        - Research personnel added information to the wrong lines on the consent
        - Research personnel dates and/or times written on consent/HIPAA are not accurate or do not match other times or dates on consent/HIPAA
        - Printing the consent on VOID paper
        - Adding the wrong date to the consent/HIPAA
        - Research personnel did not fill out everything required of them on the consent
        - Research personnel fills out date and/or time the on consent/HIPAA on behalf of the subject
- All of the following items should be reported as a **Deviation**:
    - Research personnel do not sign consent
    - Subjects do not add a date to the consent (for minimal risk or lower risk level studies)

  - Subjects do not add a time to the consent (for minimal risk or lower risk level studies)
  - Subjects completing unapproved surveys and questionnaires
  - Subject diaries are left blank, missing information, or not done
  - Research personnel do not sign consent on multiple consents
  - Research Personnel filling out the date and/or the time on the consent/HIPAA on behalf of the subject on multiple consents or maybe just once or twice but on a high-risk studies
  - Subjects not signing HIPAA before medical records are accessed
  - Expired consents/assents used to consent subjects (minor changes to the consent if any)
- All of the following items should be reported as a **Deviation and require re-consent**:
  - Subjects not adding a date to the consent (for greater than minimal risk studies)
  - Subjects not adding add a time to the consent (for greater than minimal risk studies)
  - Subjects consented with Spanish consents, but taking surveys in English due to lack of translations
  - Legally authorized representatives not signing their names, adding a date, and/or adding the time to the consent/HIPAA section
  - Research personnel using unapproved methods to consent subjects (for example: Skype, group consents, etc…)
  - Crooked and illegible subject signature on a consent without explanation - (consent can be deemed invalid and subject must be re-consented)
  - Subjects not being re-consented when a new version of a consent is approved (new consents that contain pertinent information or change in risk or procedures)
  - Expired consents/assents being used to consent subjects
- All of the following items should be reported as a **Protocol Violation**:
  - Unapproved (unstamped) consents are used to consent subjects
  - Unapproved personnel conduct consent and sign consent form
  - Subject signed the consent several hours after the research personnel
  - Study procedures are done before subjects sign consent

<u>iRIS, Protocol Non-Compliance and EMR</u>

- All of the following items should be reported as a **Deviation**:
  - Research personnel have not been added to study on iRIS, but have been working on the study
  - More subjects are enrolled onto the study than what was approved by the IRB
  - Inaccurate information listed on the iRIS application when compared to other study documents and study procedures For example: this includes major differences like the study requiring an IBC license because samples are handled and processed by TTUHSC EP personnel)
  - Procedures being done out-of-window per protocol study calendar
  - Procedures not being done according to protocol
  - Serious adverse events reported to the IRB after the 10 day mark designated on the HRPP manual

- Procedures that are not listed on application or the protocol are being implemented (For example: The administration of a demographics questionnaire that was never mentioned or submitted to the IRB for prior approval)
- Major procedures listed on the application are not being followed (For example: Questionnaires that have been mentioned on the application and other study documents are not being done)
- Major procedures listed on the protocol are not being followed (ex: Protocol-mandated lab tests are not being implemented)
- Conducting research at other institutions without obtaining proper approvals

- All of the following items should be reported as a **Protocol Violation**:
  - Providing external or unapproved personnel with access to EMR with one's personal name and password
  - Unreported serious adverse events
  - Inaccurate information listed on the iRIS application when compared to the other study documents and study procedures (For example: Serious non-compliance that puts subjects at risk or procedures that are being done without proper consent like the principal investigator deciding to give the subject and extra dose of the investigational product based on a the application versus the protocol or consent)
  - iRIS-approved personnel which have not been added to a study in iRIS, that have been working on study with subjects
  - Unapproved procedures conducted on subjects
  - Lack of investigator oversight
  - Providing EMR access to unauthorized personnel with one's own personal account
  - Personnel that do not have the required trainings or an iRIS account that have been working on the study with subjects and/or have consented the subjects

Subject Documentation

- All of the following items should be reported as **Note-to-files**:
  - Retrospective chart review data collection spreadsheet has blank fields, where no data has been entered including "N/A" and/or "Unknown". – JR 6/26/19
  - Surveys and questionnaires are missing information that subject did not want to give
  - Subjects signing the consent/HIPAA in one language but completing the surveys in a different language
  - Research personnel lining-through subject entry
  - Subjects being lost to follow-up with the research team trying to reach the subject via phone call and/or certified letter
  - Procedures being done out-of-window without strict protocol guidance
  - Surveys and questionnaires are missing information
  - Subject diaries are missing information
  - Surveys and questionnaires are missing information
- All of the following items should be reported as a **Deviation**:

  - Subject files being missing documents
  - Results not being documented at the moment of data collection (results recalled and documented from memory at a later date)
  - Subject documents being missing protocol-mandated information that can only be collected at specific times
  - Surveys and questionnaires being missing left blank or not done
  - Surveys/questionnaires orally translated to subjects instead of having a Spanish version available
  - No Spanish versions of documents available on iRIS with Spanish-speaking subjects enrolled on a study
  - Subjects being lost to follow-up with the research team not trying to reach the subject
  - Some missed subject visits
- All of the following items should be reported as a **Protocol Violation**:
  - Multiple missed subject visits

Study Documentation

- All of the following items should be reported as **Note-to-files**:
  - Lack of proper compensation records
- All of the following items should be reported as a **Deviation**:
  - There are surveys/questionnaires in the binder that are not on iRIS and have not been submitted for IRB review (for example: data collection forms)
  - Collecting unapproved or unnecessary data from EMR (labs, tests, insurance info, etc…)
  - Using an electronic system for data capture without prior approval (for example: REDCap)

Study Investigational Product and Subject Samples

- All of the following items should be reported as a **Deviation**:
  - Subject samples are not being maintained in an approved location or condition
  - Study investigational product are not being maintained in an approved location or condition
  - Personnel handling samples without obtaining proper approvals
  - Subjects missing dose of investigational drug or taking more drug than instructed
- All of the following items should be reported as a **Protocol Violation**:
  - Multiple missing tests and procedures for subjects
  - Unapproved study personnel administering investigational drug and following subject

Subject Payment

- All of the following items should be reported as **Note-to-files**:
  - 30% not withheld from non-residents
- All of the following items should be reported as a **Deviation**:
  - Lack of compensation
  - Subject receiving different amounts of compensation than what is listed on consent

- All of the following items should be reported as a **Protocol Violation**:
  - Lack of documentation in subject files (inadequate case histories)
  - Inclusion/exclusion criteria not met by subject(s)
  - Research personnel not continuing to follow subjects after initial research visit

Training

- All of the following items should be reported as a **Deviation**:
  - Research personnel do not have Basic Lab Essentials Training and have handled samples
  - Research personnel handling samples without first having their Shipping and Handling Training as required by Safety Services
  - Research personnel do not have required trainings or an iRIS account and have worked on study but have not worked with subjects