WEST TEXAS A&M UNIVERSITY

Standard Operating Manual
Human Research Protection Program/Institutional Review Board

September 2025

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1 Human Research Protection Program

West Texas A&M University (WTAMU) fosters a research environment that promotes respect for the rights and welfare of individuals recruited for, or participating in, research conducted by or under the auspices of the Organization. In support of this, WTAMU has established a Human Research Protection Program (HRPP). The WTAMU HRPP, in partnership with its research community, is responsible for ensuring the ethical and equitable treatment of all human subjects in research conducted under WTAMU's auspices.

1.1 Mission

The mission of the HRPP is to:

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

The HRPP includes mechanisms to:

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

1.2 Organizational Authority

The WTAMU Human Research Protection Program operates under the authority of the "Institutional Human Research Protection Program Procedure." As stated in that policy, the operating procedures in this document "…serve as the governing procedures for the conduct and review of all human research conducted under the auspices of WTAMU." The HRPP Policy and these operating procedures are made available to all WTAMU investigators and research staff and are posted on the IRB website.

1.3 Definitions

Common Rule. The Common Rule refers to the "Federal Policy for the Protection of Human Subjects" adopted by a number of federal agencies. Although the Common Rule is codified by each agency separately, the text is identical to DHHS regulations in 45 CFR 46 Subpart A. For the purposes of this document, references to the Common Rule will cite the DHHS regulations.

Clinical Trial. Per the Common Rule and NIH Policy, clinical trial means a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes.

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

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

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

In accordance with the Common Rule, the following activities are deemed not to be research:

(1) Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected.
(2) Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. Such activities are limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products). Such activities include those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters).
(3) Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes. (4) Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions.

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

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

- **Intervention** means both physical procedures by which information or biospecimens are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.
- **Interaction** means communication or interpersonal contact between investigator and subject.
- **Private information** means information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record).
- **Identifiable private information** means private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information. [45 CFR 46.102(e)(5)]. (NOTE: Federal guidance on the definitions of identifiable private information and identifiable biospecimen, as well as the list of technologies deemed to generate individual private information or an identifiable biospecimen [45 CFR 46.102(e)(7)] is likely to be revised. For a discussion of identifiability under HIPAA, please see Section 24.1.1.
- **Identifiable biospecimen** means a biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen [45 CFR 46.102(e)(6)].

  Note: FDA regulations have a different definition of "human subjects research". See Section 24.5 for the FDA definitions and details on FDA-regulated research.

Test Article. *Test article* means any drug for human use, biological product for human use, medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under FDA regulations. (See Section 24.5 for details on FDA regulated research.)

1.4 Ethical Principles

West Texas A&M University (WTAMU) is committed to conducting research with the highest regard for the welfare of human subjects and upholds and adheres to the principles of *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects in Research* by the National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research. These principles are:

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

The WTAMU HRPP, in partnership with its research community, including researchers and research staff, IRB members and chairs, IRB staff, the organizational official, employees and students, is responsible for ensuring the ethical and equitable treatment of all human subjects in research conducted under its auspices.

1.5 Regulatory Compliance

The HRPP facilitates compliance with federal regulations, state and local law and organizational policies (including tribal laws passed by the official governing body of an American Indian or Alaska Native tribe). Human subjects research at WTAMU is conducted in accordance with applicable regulations and requirements including, but not limited to, the following:

Research conducted, supported, or otherwise subject to regulation by any federal department or agency which adopts the Common Rule is reviewed and conducted in accordance with the Common Rule.

Research that involves dietary supplements, devices or biologics may be covered by FDA regulations. (See Section 24.5 for a detailed discussion of FDA-regulated research.) Research subject to **FDA regulations** is reviewed and conducted in accordance with applicable regulations including, but not limited to, 21 CFR 50, 21 CFR 56, 21 CFR 312 and 21 CFR 812.

Research involving the use of Protected Health Information is reviewed and conducted in accordance with the **Health Insurance Portability and Accountability Act** (HIPAA), 45 CFR Part 160, 45 CFR Part 162, 45 CFR 164. (See Section 24.1.1 for a detailed discussion of HIPAA.)

Research supported by the **Department of Defense (DoD)** is reviewed and conducted in compliance with 32 CFR 219, 10 USC 980, applicable parts of title 21 CFR 50, 21 CFR 56, 21 CFR 312, 21 CFR 812, DoD Instruction 3216.02, DoD Directive 3210.07, and applicable additional requirements from respective DoD component(s). (See Section 25.1 for a detailed discussion of DoD requirements.)

Research conducted or supported by the U.S. **Department of Education (ED)** is subject to the Common Rule with regulations published at 34 CFR 97. In addition to the Common Rule, human subjects research involving education records conducted at institutions receiving ED funding must comply with additional requirements, including the Family Educational Rights and Privacy Act (FERPA) (34 CFR 99) and the Protection of Pupil Rights Amendment (PPRA) (34 CFR 98). Investigators should consult these regulations and resources provided by ED when developing their research protocol. The IRB will evaluate the research in accordance with these regulations when applicable. (See Section 25.2 for a detailed discussion of ED requirements.)

The U.S. **Department of Energy (DOE)** is a signatory to the Common Rule with regulations equivalent to 45 CFR 46 published under 10 CFR 745. Research conducted or supported by DOE, or performed in DOE facilities, is subject to additional requirements for investigators and for reviewing IRBs. These requirements are outlined in this section.

DOE Order 443.1B Chg 1 establishes DOE-specific policy and principles for the protection of human subjects. DOE Notice 443.1 outlines requirements that must be met for classified research. DOE provides additional resources on its website that investigators and IRBs may also find helpful. (See Section 25.3 for a detailed discussion of DOE requirements.)

Department of Justice. DOJ is not a signatory to the revised common rule. Per notice on NIJ's website, DOJ is considering next steps. Applicants are advised to monitor and follow the instructions on this website. (Also see Section 25.4.)

The **Environmental Protection Agency (EPA)** is a signatory to the Common Rule with regulations equivalent to 45 CFR 46 published under 40 CFR 26 (Subpart A). (See Section 25.5 for a detailed discussion of EPA requirements.)

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

For research subject to the Common Rule (whether due to support or organization policy) the following outlines when the old rule or the revised rule will apply to research conducted at [Institution].

A. **Research subject to the old rule (pre-2018 requirements).** The old rule will apply to the following studies, unless a study is transitioned to comply with the revised rule as described in Sections B or C below.
   - All studies initially approved, waived under .101(i), or determined exempt before January 21, 2019 will be subject to the old rule through the close of study.

B. **Research subject to the revised rule (2018 requirements).** The revised rule will apply to the following studies.
   - All studies initially approved, waived under .101(i), or determined exempt on or after January 21, 2019, will be subject to the revised rule.
   - On or after January 21, 2019, Institutions have the flexibility to transition individual studies described in section A and agree to comply with the new rule if they so choose. The study must comply with the revised rule on the datethe determination

to transition is documented. [This section should describe procedures and requirements for implementing this option at the Institution].

1.6 Federalwide Assurance (FWA) and IRB Registration

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

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

Likewise, federal regulations require IRBs to register with DHHS if they will review human subjects research conducted or supported by DHHS or research subject to FDA regulations. WTAMU's IRB office maintains its FWA and IRB registration(s) in accordance with applicable regulations and guidance provided by OHRP .

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

WTAMU's Federal Registration Numbers	
FWA	FWA000012607
IORG	IORG 0001611
IRB Registration	IRB 00002071

1.7 Research under the Auspices of West Texas A&M University

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

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

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

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

The Institutional Official, IRB Chair, and Vice Chair, with the assistance of the AREHS Director and staff and TAMUS legal counsel as needed, are authorized to determine whether WTAMU is engaged in a particular research study. Investigators and other institutions **shall not** independently determine whether WTAMU is engaged in a particular research study.

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

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

1.8 Written Procedures

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

The WTAMU IRB will keep the research community apprised of new information that may affect the human research protection program, including laws, regulations, policies, procedures, and emerging ethical and scientific issues on its website, through email, and other forums. These SOPs will be available on the WTAMU IRB website. Changes to the SOPs are communicated to investigators and research staff, and IRB members and IRB staff by way of the IRB Website.

1.9 WTAMU HRPP Structure

The HRPP consists of individuals, departments, and committees with responsibilities for human research protections such as the Institutional Official (IO), the Institutional Review Board (IRB), the Institutional Biosafety Committee (IBC), the Research Conflict of Interest Official, TAMUS Legal Counsel, AREHS Director and staff, investigators, research staff, and others. The objective of this system is to assist the organization in meeting ethical principles and regulatory requirements for the protection of human subjects in research.

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

1.9.1 Institutional Official

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

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

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

The IO is also responsible for:

- Fostering, supporting and maintaining an culture that supports the ethical conduct of research involving human subjects and compliance with applicable regulatory and other requirements;

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

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

The IO must complete CITI training modules for Institutional/Signatory Official: Human Subjects Research. The AREHS Office will support the continuing education of the IO by providing information and updates on topics related to human research protections.

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

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

1.9.2 AREHS Office

In addition to the leadership structure described above, the staffing for the AREHS Office includes a director and staff. The AREHS director and staff for WTAMU must comply with all ethical standards and practices. The duties and responsibilities for all staff are found in their respective job descriptions, and their performance is evaluated on an annual basis. The AREHS Director reports to the Vice President of Research and Compliance and AREHS staff report to the AREHS Director, who has day-to-day responsibilities for AREHS operations.

1.9.3 Institutional Review Board (IRB)

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

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

Research that has been reviewed and approved by the IRB may be subject to review and disapproval by the IO. However, the IO may not approve human research that has not been approved or has been disapproved by the IRB.

WTAMU may also use the services of external IRBs, in which case it will enter into a reliance agreement, for example, when a single IRB is required as a term or condition of a grant.

1.9.4 Legal Counsel

The WTAMU HRPP relies on Texas A&M University System's Legal Counsel or designee for the interpretation of state law and the laws of other jurisdictions where research is conducted as they apply to human subjects research. Counsel is available to provide guidance on other relevant topics as needed. When there are any conflicts between federal or national law and other applicable laws, the Legal Counsel will determine the appropriate resolution.

1.9.5 Principal Investigators

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

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

The PI for human subjects research under the auspices of WTAMU must be actively employed at WTAMU. Students, even if employed as either a student worker, staff technician, or graduate student, are not eligible to serve as a PI.

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

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

1.9.6 Sponsored Research Services

Sponsored Research Services (SRS) staff review all research agreements with grantors and sponsors including federal, foundation, industry, and non-profit. This review ensures that all terms of the award (grant or contract) are in compliance with organizational policies. The Executive Director of the Office of Sponsored Research reviews all grants and sponsored research contracts and, upon approval, submits the documents to the Vice President for Research and Compliance for execution on behalf of WTAMU. The Vice President of Research and Compliance has the institutional authority to approve funding proposals and to execute research agreements on behalf of the organization.

Sponsored Research Services has access to the IRB submission to confirm that the contract and the consent documents are consistent in terms of costs to subjects and who pays in case of injury. SRS and the IRB office coordinate efforts to ensure that all applicable individuals have filed appropriate COI disclosures to meet investigator COI policies.

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

1.9.7 Relationship among Components

There is an expectation of coordination and communication between the various units that comprise the HRPP. To facilitate this communication, the Vice President of Research and Compliance/Institutional Official, the AREHS Director and the IRB Chair will meet with various administrative groups, as needed, including the President's Cabinet, Deans' Council and the Department Head/Direct Supervisor Committee.

1.9.8 Study-Specific Coordination

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

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

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

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

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

2 Quality Assurance

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

2.1 External Monitoring, Audit, and Inspection Reports

When research is under the oversight of the WTAMU IRB, all reports from auditors, or inspectors must be submitted to the IRB for review. The IRB Chair or designee will review such reports to monitor for issues that could impact the rights or welfare of human subjects and for

issues indicative of possible serious or continuing noncompliance. If such issues are identified, the report will be forwarded to the convened IRB to determine what additional actions are necessary, if any.

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

2.2 Investigator Compliance Reviews

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

Compliance reviews are conducted to assess investigator compliance with federal, state, and local law, TAMUS policies and regulations, and WTAMU rules and procedures, and to identify areas for improvement, and to provide recommendations based on existing policies and procedures. The results of compliance reviews will be reported to the WTAMU IRB, the investigator, and other WTAMU leadership, as appropriate. Any IRB reporting and evaluation of noncompliance will be handled according to the procedures described in Section 14, Noncompliance.

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

If issues are identified that indicate possible misconduct in research, the procedures in the WTAMU Ethics in Research, Scholarship and Creative Work: Research Misconduct rule will be initiated. If the potential research misconduct also involves potential noncompliance with the IRB approved protocol, any investigations will be coordinated between the IRB according to the instructions section 14, Noncompliance.

Compliance reviews may include:

- Requesting progress reports from investigators;
- Examining investigator-held research records;
- Reviewing the recruitment process and materials;
- Reviewing consent materials and the documentation of consent;
- Observing the consent process and other research activities;
- Interviewing investigators and research staff;

- Interviewing research subjects; and/or
- Conducting other monitoring or auditing activities as deemed appropriate by the IO or IRB.

2.3 IRB Compliance Reviews

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

Review activities may include:

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

AREHS and the IRB Chair will review the results of IRB compliance reviews with the IRB and the Institutional Official. If substantive deficiencies are identified in the review, a corrective action plan will be developed by AREHS and approved by the IO. The AREHS Director will have responsibility for implementing and reporting progress on the corrective action plan, the results of which will be evaluated by the IO.

2.4 HRPP Quality Assessment and Improvement

Annually, a meeting is held by the IO, IRB Chair and AREHS Director and staff to assess the compliance and the quality, efficiency, and effectiveness, of the HRPP. The plan is included in the WTAMU Institutional Annual Compliance Plan, which is required by the Texas A&M University System Ethics and Compliance Office. The annual plan is facilitated by the WTAMU Compliance Officer and submitted to the WTAMU President and CEO for final review and signature before being submitted to the Texas A&M University System Ethics and Compliance Officer. Quarterly updates are required as part of the annual WTAMU Compliance Plan, as well as an annual mitigation report. The AREHS Director will facilitate the completion of the HRPP

component of the WTAMU Compliance Plan and the associated quarterly and mitigation reports, and will review the associated documents with the IRB Chair and IO before submission to the WTAMU Compliance Officer. If at any time substantive or concerning issues or trends are identified, the AREHS Director will report those issues or trends to the IRB Chair and IO for resolution and support.

3 Education & Training

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

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

Orientation

New IRB members, including alternate members, will meet with the IRB Chair or the AREHS Director or staff for an orientation session. At the session, IRB processes, regulations, and resources will be reviewed. New members will be provided with information to allow access to:

- The Belmont Report;
- WTAMU HRPP SOPs;
- Federal regulations relevant to the IRB;
- Tools used by IRB reviewers (checklists etc.);
- IRB Meeting Schedule; and
- Contact Information for AREHS Office.

Initial Education

IRB members and HRPP and IRB staff must complete the required modules in the CITI Course in the Protection of Human Research Subjects.

New members are required to complete orientation and the Initial Education Requirement before they may serve as Primary Reviewer.

Continuing Education

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

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

- In-service training at IRB meetings;

- Training workshops;
- Webinars; and
- Email distribution of articles, announcements, presentations, and other materials relevant to human subject protections.

IRB members and AREHS staff are also required to complete CITI basic or refresher training every three (3) years or other training determined to be equivalent by the AREHS Director in collaboration with the IRB Chair and IO.

3.2 Training / Ongoing Education of Investigators and Research Team

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

3.2.1 Initial Education

Investigators and their associated research staff who interact or intervene with subjects, or who use subject's identifiable information for the purposes of research, must complete WTAMU's required CITI Courses. Information detailing on WTAMU's CITI training requirements is available on the IRB web site.

Evidence of current training for each member of the research team must be accessible to AREHS staff for every new study application and applications to add study personnel. New study applications and additions of study personnel will not be moved forward for IRB review without evidence of training.

3.2.2 Continuing Education

All individuals engaged in research involving human subjects must complete the required CITI training modules and quizzes with a minimum passing score as indicated on the CITI course description. Courses may be repeated as necessary to achieve the required passing score. Refresher courses are required as outlined in the course description.

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

In addition to the basic requirements described above, WTAMU will periodically provide training on topics relevant to human subject protections, regulations, policies and standards, and IRB submission processes and requirements. Training may be provided via in-service, workshops, webinars or through the distribution of articles, presentations, and other materials. Investigators and staff may request training or offer training suggestions by contacting the IRB Office.

4 West Texas A&M University Institutional Review Board

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

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

4.1 IRB Authority

The IRB derives its authority from the federal regulations which is noted in WTAMU procedure, as cited in Section 1.8. Under the federal regulations, IRBs have the authority:

1. To approve, require modifications to secure approval, or disapprove human subjects research activities, including exempt research activities under 45 CFR 46.104 for which limited IRB review is a condition of exemption (under 45 CFR 46.104(d)(2)(iii), (d)(3)(i)(C), and (d)(7), and (8));
2. To require that informed consent is obtained and documented in accordance with regulatory and policy requirements unless the criteria for the waiver or alteration of such requirements has been satisfied and approved by the IRB. The IRB may require that information, in addition to that specifically mentioned in the regulations, be given to the subjects when in the IRB's judgment the information would meaningfully add to the protection of the rights and welfare of subjects;
3. For research subject to the 2018 Common Rule: To conduct continuing review of research requiring review by the convened IRB at intervals appropriate to the degree of risk of the research, but not less than once per year, except as described in Section 10.5. When research is subject to other regulations (e.g., pre-2018 Common Rule, FDA, DOJ) or requirements (e.g., grant or contract terms), the IRB will conduct continuing review of research at intervals appropriate to the degree of risk of the research, but not less than once per year;
4. To suspend or terminate approval of research not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to participants;
5. To observe, or have a third party observe, the consent process; and

6. To observe, or have a third party observe, the conduct of the research.

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

Research that has been reviewed and approved by the IRB may be subject to review and disapproval by officials of WTAMU. However, those officials may NOT approve research if it has not been approved or has been disapproved by the IRB. Reviewing officials may strengthen requirements and/or conditions, or add other modifications before approval, or may require approval by an additional committee, office, or person. Previously approved research proposals and/or consent forms must be re-approved by the IRB before initiating any changes or modifications that result from such additional organizational reviews.

4.2 Roles and Responsibilities

4.2.1 Chair of the IRB

The IO appoints a Chair of the IRB to serve for renewable, 3-year terms. Any change in appointment, including reappointment or removal, requires written notification.

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

The IRB Chair is responsible for conducting IRB meetings and expedited reviews and may serve as signatory for correspondence generated by the IRB in addition to the Vice President of Research and Compliance/IO.

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

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

The IRB Chair advises the IO and the AREHS Director about IRB member performance.

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

4.2.2 IRB Members

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

- Completing member education and training, both initial and on-going (See Section3.1);
- Maintaining the confidentiality of IRB deliberations and research reviewed by the IRB;
- Conducting and documenting reviews in a timely fashion;
- Attending IRB meetings as scheduled;
- Recusing self from reviewing or voting on research when s/he has a conflict of interest (See Section 21.2);
- Participating in subcommittees of the IRB if requested and available;
- Conducting themselves in a professional and collegial manner;
- Members should attend all meetings for which they are scheduled. If a member is unable to attend a scheduled meeting, they should inform the IRB Chair. If a member's availability changes and they are no longer able to regularly attend IRB meetings or will be absent for an extended period of time, they should inform the IRB Chair. The Chair will assess the situation, including the availability of the alternate when applicable, and make recommendations to the IO to ensure the IRB is able to meet quorum requirements and has the necessary expertise to review the research which regularly comes before it.
- The performance of IRB members will be reviewed periodically by the IRB Chair. Feedback from this evaluation will be provided to IRB members. Members who are not acting in accordance with the IRB's mission, not following policies and procedures, have an undue number of absences, or otherwise not fulfilling the responsibilities of membership, may be removed by the IO or his/her designee.

4.2.3 Alternate members

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

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

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

4.2.4 Subcommittees of the IRB

The IRB Chair may appoint one or more other IRB members to a subcommittee of the IRB to review issues and to make recommendations to the IRB (e.g., to supplement the IRB's review of research proposals or to review of reports of potential unanticipated problems or noncompliance). The size and composition of the subcommittee shall depend on the scope of duties delegated by the IRB Chair. Any such subcommittee cannot approve research or issue determinations that require review by the convened IRB.

4.3 Composition of the IRB Membership

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

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

- The IRB includes at least one member who is not otherwise affiliated with the organization and who is not part of the immediate family of a person who is affiliated with the organization.
- The IRB Chair is a voting member of the IRB.

At the discretion of the IO and IRB Chair, AREHS staff may be appointed as IRB members or alternates.

Individuals from WTAMU Office of Sponsored Programs, Business Development Office, or Technology Transfer Office may not serve as members of the IRB or carry out day-to-day operations of the IRB. Individuals from these offices may provide information to the IRB and attend IRB meetings when invited as guests.

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

4.3.1 Appointment of Members to the IRB

When the need for a new IRB member or alternate is identified, the IRB Chair and/or the AREHS Director informs the Vice President of Research and Compliance/IO and seeks out qualified candidates. Department Chairs and others may forward recommendations to the IO, IRB Chair, or AREHS Director.

The final decision in selecting a new member is made by the Vice President of Research and Compliance/IO, in consultation with the IRB Chair and AREHS Director.

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

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

4.4 Liability Coverage for IRB Members

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

4.5 Use of Consultants

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

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

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

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

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

4.6 Reporting and Investigation of Allegations of Undue Influence

If an IRB Chair, member, or staff person feels that the IRB has been unduly influenced by any party, they shall make a confidential report to the AREHS director, IRB Chair or Vice President of Research and Compliance/IO. The Vice President of Research and Compliance/IO will ensure that a thorough investigation is conducted and, if the allegation is determined valid, that corrective action is taken to prevent additional occurrences. In the event that the allegation is regarding the IO, the matter will be referred to the CEO, WTAMU President, for investigation and any necessary action.

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

5 Collaborative Research and IRB Reliance

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

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

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

The AREHS Office utilizes a checklist to ensure that reliance agreements and any accompanying materials address all requirements and are consistent with WTAMU's standards. To support compliance, WTAMU will make every effort to ensure as much consistency as possible across reliance agreements.

Requests for the WTAMU to either rely upon an external IRB or to serve as the IRB of record for an external organization or investigator should be submitted as early as possible in the grant/contract process by contacting the AREHS Office. Note that NIH, for instance, requires that participating organizations indicate their willingness to participate in the reliance agreement at the time of proposal submission (See section 5.3.1, below).

5.1 West Texas A&M University Serving as Reviewing IRB

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

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

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

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

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

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

5.2 External IRB Review of WTAMU Research

All non-exempt human subject research (or exempt research for which limited IRB review takes place pursuant to 45 CFR §46.104(d)(2)(iii), (d)(3)(i)(C), or (d)(7)or (8)) that WTAMU is engaged in must be reviewed and approved by the WTAMU IRB or an external IRB that WTAMU has agreed to rely upon prior to the initiation of the research. See Section 1.7 for information regarding engagement.

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

The AREHS Office, in collaboration with the IRB Chair and Vice President of Research and Compliance/IO, evaluates the following factors and others, as appropriate, when considering a request to rely upon an external IRB:

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

When reliance on a non-accredited IRB is proposed, the evaluation may also take into consideration one or more of the following based upon the risks of the research, the research activities that WTAMU will be involved in, and WTAMU's familiarity with the IRB:

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

The external IRBs that serve as the IRB of record for WTAMU research have the same authority as the WTAMU IRB and all determinations and requirements of the external IRBs are equally binding. Investigators must be familiar with and comply with the external IRB's policies and procedures and any additional requirements or procedures outlined in the IRB reliance

agreement or companion materials (e.g., reliance SOPs). WTAMU will support compliance with the terms of reliance agreements by providing investigators with information relevant to their responsibilities, such as a copy or summary of the agreement, an information sheet, or reliance SOPs.

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

5.2.1 Registration of Studies Reviewed by External IRBs

Investigators must register studies that will be reviewed by an external IRB by submitting basic information about the research to the AREHS office by submitting a copy of the proposed protocol and consent document(s), when applicable]. The AREHS Office will review the information and verify that required training, COI review, and any other applicable approvals or requirements have been completed, and determine the need for relaying local context information to the reviewing IRB in accordance with the reliance agreement. The AREHS office will notify the investigators once the proposed research has been cleared for submission to the external IRB. Once approved by the external IRB, investigators must submit a copy of the approval notice and any approved consent document(s) to the AREHS office. If the protocol was modified during the external IRB review process, the approved version of the protocol should be provided as well.

5.2.2 Post-Approval Requirements

Investigators approved through external IRB review must still report local unanticipated problems, complaints, and any noncompliance to the WTAMU AREHS office or WTAMU IRB Chair in addition to reporting to the external IRB. Copies of the report submitted to the external IRB are generally acceptable, but additional information may be requested on an as-needed basis. Investigators must also submit copies of continuing review reports, updated protocols, updated consent forms, study closures, and the corresponding IRB approval or acknowledgment.

Changes in PI and the addition of other research team members must be submitted to the AREHS office prior to the new PI or research team member assuming any study responsibilities. The AREHS office must verify required training, COI review, and any other applicable requirements.

Notices about and reports from external monitors, auditors, or inspectors must be provided to the AREHS Office as described in Section 2.1 of this manual.

Any of the following issues must be reported immediately (ASAP, once aware) to the WTAMU AREHS office, by phone or email:

- Any negative actions by a government oversight office;

- Any litigation, arbitration, or settlements initiated related to human research protections; and/or
- Any press coverage (including but not limited to radio, TV, newspaper, online publications) of a negative nature regarding WTAMU's HRPP.

Upon receipt of any information related to the above, the AREHS office will immediately contact the IRB Chair and VP of Research and Compliance/IO.

Investigators are reminded that other WTAMU reporting requirements, such as to Texas A&M University System (TAMUS), compliance, privacy, and risk management, remain applicable in addition to HRPP reporting requirements.

5.3 NIH Single IRB (sIRB) for Multi-Site Research

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

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

5.3.1 Selection and Designation of a sIRB

WTAMU's investigators submitting applications for NIH-funded multi-site research must describe the sIRB plan in the funding proposal (grant application or contract proposal), and, if applicable, may request direct cost funding to cover additional costs related to the requirements of the NIH policy. The sIRB can be the IRB at one of the participating sites or an independent, fee-based IRB. When the sIRB is named in the proposal, the IRB must have agreed to take on this responsibility in advance. Requests for WTAMU's IRB to serve as the sIRB should be directed to the AREHS office. The AREHS Director will consult with others within the organization as needed and make a recommendation to the IO for consideration. Requests for WTAMU to rely upon an external IRB as the sIRB should be submitted as early in the process as possible by contacting the AREHS Office.

5.3.2 Reliance Agreements for sIRB Studies

A Reliance Agreement (or "Authorization Agreement") between the sIRB and the participating sites is required. The Reliance Agreement documents the respective authorities, roles, responsibilities, and communication between an organization providing the ethical review and a participating organization relying on a reviewing IRB.

Reliance Agreements should describe the responsibilities of all parties and how communication between parties will occur, for example, notifications of the outcome of regulatory review and management of federally-mandated reports such as reports of unanticipated problems, serious or continuing noncompliance, and suspensions or terminations of IRB approval. When IRB certification requirements apply (e.g., for NIH Genomic Data Sharing), the agreement or written procedures should indicate who is responsible for meeting the certification requirements.

The agreement or written procedures should also specify points of contact and contact information for the sIRB and relying institution(s).

The institution that is awarded the funding for the research is responsible for maintaining all agreements and for ensuring that adequate and appropriate communication channels between the sIRB and participating sites are in place. Participating sites are responsible for maintaining copies of the site agreement in accordance with the terms of their FWA.

5.3.3 Responsibilities

The sIRB will be responsible for compliance with the regulatory requirements for IRBs specified in the federal regulations (i.e., 45 CFR 46 and other applicable regulations) and for any other responsibilities outlined in the reliance agreement and/or procedures. Participating sites (relying institutions) are responsible for providing relevant, local context information to the sIRB, ensuring that the research is conducted in accordance with applicable regulations and the determinations and requirements of the sIRB, and for other responsibilities, as outlined in the reliance agreement and/or procedures.

When an external IRB serves as the sIRB for a study WTAMU is engaged in, investigators must register the study with WTAMU prior to submission to the external IRB following the procedures outlined in Section 5.2. Post-approval requirements are summarized in Section 5.2.2.

Research reviewed by external IRBs remains subject to review, approval, and oversight by WTAMU and must adhere to all applicable policies, procedures, and requirements, including those of the WTAMU HRPP.

6 Research Previously Approved by another IRB

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

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

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

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

7 Documentation and Records

WTAMU prepares and maintains adequate documentation of the IRB's activities. All records are accessible for inspection and copying by authorized representatives of the federal Office of Human Research Protections (OHRP), sponsors, and other authorized entities at reasonable times and in a reasonable manner.

7.1 IRB Records

IRB records include, but are not limited to:

1. Written operating procedures;
2. IRB membership rosters;
3. IRB member files including documentation of appointments, experience, education/training, and expertise;
4. IRB correspondence including reports to regulatory agencies;
5. IRB Study Files (See Section 7.2);
6. Documentation of exemptions including exemptions related to emergency uses;
7. Convened IRB meeting minutes;
8. Documentation of review by an external IRB, when appropriate;
9. Documentation of IRB reliance and cooperative review agreements;
    a. For nonexempt research involving human subjects covered by the Common Rule (or exempt research for which limited IRB review takes place as described in Section 9) that takes place at an institution in which IRB over sight is conducted

by an IRB that is not operated by the institution, the institution and the organization operating the IRB shall document the institution's reliance on the IRB for oversight of the research and the responsibilities that each entity will undertake to ensure compliance with the requirements of this procedure (e.g., in a written agreement between the institution and the IRB, by implementation of an institution-wide policy directive providing the allocation of responsibilities between the institution and an IRB that is not affiliated with the institution, or as set forth in a research protocol);

10. Documentation of independent or external investigator agreements;
11. Federal Wide Assurances;
12. Federal IRB Registrations; and
13. Documentation of complaints and any related findings and/or resolution.

7.2 IRB Study Files

The IRB maintains a separate file for each study (paper or electronic versions under a unique identification number assigned by the AREHS Office or the electronic system. As applicable, study files include, but are not limited to the following:

1. The initial application and all associated documents and materials;
2. Modification requests and all associated documents and materials;
3. Continuing review/progress reports and all associated documents and materials including the rationale for conducting continuing review of research that otherwise would not require continuing review as described in Section 10.5;
4. Closure reports and all associated documents and materials;
5. Reports submitted after study approval including reports of significant new findings, data and safety monitoring reports, protocol violation reports, complaints, noncompliance, and reports of injuries to subjects and unanticipated problems involving risks to subjects or others;
6. IRB-approved consent, parental permission, and assent forms;
7. DHHS-approved sample consent form and protocol;
8. IRB reviewer forms and checklists (when expedited review procedures are used);
9. Documentation of scientific or scholarly review (if available);
10. Documentation of the type of IRB review. For exempt determinations and expedited review, this will include the category under which the review is allowed;
11. For expedited review, documentation of any findings and determinations required by the regulations and study-specific findings supporting those determinations, including, but not limited to, waiver or alteration of consent, waiver of documentation of consent,

research involving pregnant women, fetuses, and neonates, research involving prisoners, and research involving children. For research reviewed by the convened board, these findings and determinations are recorded in the minutes;

12. For expedited review, documentation of the risk determination and period of approval (when continuing review is required). For research reviewed by the convened board, these determinations are recorded in the minutes;
13. For expedited review, the rationale for an expedited reviewer's determination under 45 CFR 46.110(b)(1)(i) that research appearing on the expedited review list described in 45 CFR 46.110(a) is more than minimal risk.
14. Documentation of all IRB review actions;
15. Notification of expiration of IRB approval to their investigator;
16. Notification of suspension or termination of research;
17. Letters to investigator informing them of IRB review outcomes;
18. IRB correspondence to and from investigators related to the study;
19. All other IRB correspondence related to the research;
20. Reports of unanticipated problems involving risk to subjects or others; and
21. Any statements of significant new findings provided to subjects.

7.3 The IRB Minutes

Draft minutes of IRB meeting proceedings are written and generally available for review by the next regularly scheduled IRB meeting. Once reviewed and accepted by the members, a copy is sent to the IO and, then, to the TAMUS research compliance office. Changes may not be made to finalized minutes without re-review by the IRB to verify accuracy.

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

1. Attendance:
    a. Full names of members or alternates present;
    b. Each member's (or alternate's) representative capacity (e.g., scientist, non-scientist, unaffiliated, member who represents the general perspective of research subjects);
    c. Names of members or alternate members who are participating through videoconference or teleconference and documentation that those attending remotely received all pertinent material prior to the meeting and were able to actively and equally participate in all discussions;
    d. Names of alternates attending in lieu of specified (named) absent members. (Alternates may substitute for specific absent members or categories of members only as designated on the official IRB membership roster);

e. Names of any consultants present; and

f. The names of non-members and guests in attendance, such as AREHS staff, investigators, and study coordinators.

Note: The minutes will indicate, by name, those members who enter or leave the meeting. The vote on each action will reflect the numbers of members present for the vote on that item.

2. The presence of a quorum throughout the meeting, including the presence of one member whose primary concern is in a non-scientific area;
3. When both a member and an alternate are present, the minutes will reflect if and when the alternate substituted for the member. Generally, the member votes, but an alternate may substitute when appropriate (e.g., the member has a conflict of interest, the alternate has needed expertise, etc.);
4. Business items discussed and any education provided;
5. Actions taken, including separate deliberations, actions, and votes for each submission undergoing review by the convened IRB;
6. Vote counts on these actions (Total number voting; Number voting for; Number voting against; Number abstaining; Number of those recused). When a member is recused due to conflict of interest, the name of the member and reason for the recusal will be noted;
7. Basis or justification for actions disapproving or requiring changes in research;
8. Summary of controverted issues and their resolution;
9. Approval period for initial and continuing reviews, when applicable, including identification of research that warrants review more often than annually and the basis for that determination;
10. The rationale for requiring continuing review of research that otherwise would not require continuing review as described in Section 10.5;
11. Risk determination for initial and continuing reviews, and modifications when the modification alters the prior risk determination;
12. Justification for deletion or substantive modification of information concerning risks or alternative procedures contained in the DHHS-approved sample consent document;
13. Study-specific findings supporting that the research meets each of the required criteria when approving a consent procedure that does not include or that alters some or all of the required elements of informed consent, or when waiving the requirement to obtain informed consent altogether;
14. Study-specific findings supporting that the research meets each of the required criteria when the requirements for documentation of consent are waived;

15. Study-specific findings supporting that the research meets each of the criteria for approval for vulnerable populations under any applicable Subparts;
16. Determinations related to conflicts of interest and acceptance or modification of conflict management plans;
17. Identification of any research for which there is need for verification from sources other than the investigator that no material changes are made in the research;
18. Review and determinations related to interim reports (e.g., unanticipated problems or safety reports, serious or continuing noncompliance, suspensions or terminations, etc.);
19. A list of research approved under expedited review procedures including limited IRB reviews conducted using expedited procedures, since the time of the last such report;
20. An indication that, when an IRB member or alternate has a conflicting interest (see Section 21.2) with the research under review, the IRB member or alternate was not present during the final deliberations or voting; and
21. Key information provided by consultants will be documented in the minutes or in a report provided by the consultant.

7.4 IRB Membership Roster

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

1. Name;
2. Earned degrees;
3. Employment or other relationship between each member and the organization (i.e., affiliated or non-affiliated). To be categorized as non-affiliated, neither the member nor an immediate family member of the member may be affiliated with WTAMU;
4. Status as scientist or non-scientist. Members whose training, background, and occupation would incline them to view scientific activities from the standpoint of someone within a behavioral or biomedical research discipline are considered a scientist for the purposes of the roster. Members whose training, background, and occupation would incline them to view research activities from a standpoint outside of any biomedical or behavioral scientific discipline are considered a non-scientist. Physicians, nurses, and pharmacists are considered scientists;
5. Indications of experience sufficient to describe each member's chief anticipated contributions to IRB deliberations;
6. Representative capacities of each IRB member; including which IRB member(s) is a prisoner representative, and which IRB members are knowledgeable about or experienced in working with children, pregnant women, adults with impaired decision-

making capacity, and other subjects vulnerable to coercion or undue influence commonly involved in WTAMU research;

7. Role on the IRB (Chair, member, etc.);
8. Voting status; and
9. For alternate members, the primary member or class of members for whom the member could substitute.

The AREHS Office must keep the IRB membership list current. Changes in IRB membership are reported to OHRP in the federal IRB registration within ninety (90) days of the change.

7.5 Documentation of Exemptions

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

7.6 Documentation of Expedited Reviews

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

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

7.7 Access to IRB Records

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

Ordinarily, access to IRB records is limited to the IO, AREHS Director, and assigned staff, IRB members, authorized organizational officials, and officials of federal and state regulatory agencies (e.g., OHRP). Research investigators are provided reasonable access to files related to their research.

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

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

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

7.8 Record Retention

WTAMU, as a member of the Texas A&M University System, has a retention process and periods established in procedure 61.99.01.W0.01.

In order to comply with the requirements of OHRP and FDA, IRB records are maintained for at least three (3) years after completion of the research. If the records contain Private Health Information (PHI), HIPAA regulations require that records are retained for a minimum of six (6) years. If the IRB records do not contain PHI but investigator records do contain PHI, the investigator is required to retain records for at least six (6) years.

IRB records for research cancelled without participant enrollment will be retained for at least three (3) years after closure.

IRB minutes are retained until all of the studies that were reviewed at that meeting have been completed for at least three (3) years.

After the noted times, IRB records may be shredded or otherwise securely destroyed as according to TAMUS procedures.

8 "Human Subjects" and "Research" Determinations

The responsibility for initial determination whether an activity constitutes "human subjects research" rests with the individual with primary responsibility for the activity. This individual should make this determination based on the definitions of "research" and "human subjects" as provided in Section 1.3. Consultation with the AREHS Office or IRB Chair is encouraged, as well as reviewing the WTAMU IRB website.

Because the analysis can be complex, individuals with any questions regarding the applicability of these definitions to their activities are urged to request a determination that an activity does or does not involve human subject research. Contact the AREHS office for these requests.

Note: With the implementation of the revised Common Rule, the requirement of the Newborn Screening Saves Lives Reauthorization Act of 2014 that federally-funded "research on newborn dried blood spots shall be considered research carried out on human subjects" is eliminated. Whether such research involves human subjects shall now be considered using the same standards as are used for other research involving human biospecimens (e.g., whether the identity of subjects may be readily ascertained, whether the specimens are coded and who has access to the key, whether the research involves the evaluation of the safety or effectiveness of an FDA-regulated device, etc.).

Under the Common Rule, information is considered identifiable, and thus involving human subjects, when the identity of the subject is or may readily be ascertained by the investigator or associated with the information. It should be noted that this definition differs significantly from previous standards. Investigators **may not** self-determine that research involving the use of **coded** private information or specimens does not involve "human subjects". Such determinations may only be made by the IRB using the process described above. The only exception to this policy is when the research is not subject to FDA regulations and the coded private information or specimens are to be obtained from an WTAMU IRB approved repository and the rules of that repository forbid the release of identifiable information, the key or code that would enable re-identification, or the release of sufficient information that investigators could readily ascertain the identity of subjects.

Investigators whose research involves drugs, medical devices or biologics may request a determination as to whether FDA regulations apply through the same process as submitting a request for Human Subjects Research Determination. (See Section 24.5 for a detailed discussion of FDA regulations)

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

Determinations as to whether or not an activity constitutes human subject research will be made by the AREHS Director, IRB Chair, or IRB committee member review, according to the definitions in Section 1.3, applicable federal regulations, and federal guidance. A determination letter will be issued to document the determination. Investigators conducting research under the auspices of WTAMU **may not** rely upon determinations made by other organizations or through the use of electronic (or other) determination tools.

9 Exempt Determinations

All research using human subjects must be approved by WTAMU. Although certain categories of human subject research are exempt from IRB oversight, at WTAMU, the determination of exempt status is made by the research PI and documented on the exemption claim form. The

claim for exemption is reviewed by the IRB and either confirmed or rejected. Additionally, Exemptions 2, 3, 7, and 8 may require limited IRB review. WTAMU may choose to accept an exempt determination made by an external IRB; WTAMU will consider such requests on a case-by-case basis.

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

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

9.1 Limitations on Exemptions

The following limitations on exemptions apply to all research:

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

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

9.2 Categories of Exempt Research

With the above-referenced limitations and any other limitations or restrictions due to applicable law, regulation, agency policy, or TAMUS policies and regulations or WTAMU rules and procedures research activities not regulated by the FDA (See Section 24.5 for FDA Exemptions) and any other limitations or restrictions due to applicable law, regulation, agency policy, or TAMUS policies and regulations or WTAMU rules and procedures in which the only involvement of human subjects are determined to be in one or more of the following categories are exempt from IRB approval:

1. Research, conducted in established or commonly accepted educational settings that specifically involves normal educational practices that are not likely to adversely impact students' opportunity to learn required educational content or the assessment of educators who provide instruction. This includes most research on regular and special education instructional strategies, and research on the effectiveness of or the

comparison among instructional techniques, curricula, or classroom management methods.

2. Research that only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior (including visual or auditory recording) if at least one of the following criteria is met:

    i. The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;
    ii. Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or
    i. The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a **limited IRB review** to make the determination required by .111(a)(7): *When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data*.

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

    A. The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;
    B. Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or
    C. The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a **limited IRB review** to make the determination required by .111(a)(7): *When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data*.

4. For the purpose of this provision, benign behavioral interventions are brief in duration, harmless, painless, not physically invasive, not likely to have a significant

adverse lasting impact on the subjects, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing. Provided all such criteria are met, examples of such benign behavioral interventions would include having the subjects play an online game, having them solve puzzles under various noise conditions, or having them decide how to allocate a nominal amount of received cash between themselves and someone else.

(iii) If the research involves deceiving the subjects regarding the nature or purposes of the research, this exemption is not applicable unless the subject authorizes the deception through a prospective agreement to participate in research in circumstances in which the subject is informed that he or she will be unaware of or misled regarding the nature or purposes of the research.

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

    i. The identifiable private information or identifiable biospecimens are publicly available;
    ii. Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects;
    iii. The research involves only information collection and analysis involving the investigator's use of identifiable health information when that use is regulated under 45 CFR parts 160 and 164, subparts A and E, for the purposes of "health care operations" or "research" as those terms are defined at 45 CFR 164.501 or for "public health activities and purposes" as described under 45 CFR 164.512(b); or
    iv. The research is conducted by, or on behalf of, a Federal department or agency using government-generated or government-collected information obtained for nonresearch activities, if the research generates identifiable private information that is or will be maintained on information technology that is subject to and in compliance with section 208(b) of the E-Government Act of 2002, 44 U.S.C. 3501 note, if all of the identifiable private information collected, used, or generated as part of the activity will be maintained in systems of records subject to the Privacy Act of 1974, 5 U.S.C. 552a, and, if applicable, the information used in the research was collected subject to the Paperwork Reduction Act of 1995, 44 U.S.C. 3501 et seq.

5. Research and demonstration projects that are conducted or supported by a Federal department or agency, or otherwise subject to the approval of department or agency heads (or the approval of the heads of bureaus or other subordinate agencies that have

been delegated authority to conduct the research and demonstration projects), and that are designed to study, evaluate, improve, or otherwise examine public benefit or service programs, including procedures for obtaining benefits or services under those programs, possible changes in or alternatives to those programs or procedures, or possible changes in methods or levels of payment for benefits or services under those programs. Such projects include, but are not limited to, internal studies by Federal employees, and studies under contracts or consulting arrangements, cooperative agreements, or grants. Exempt projects also include waivers of otherwise mandatory requirements using authorities such as sections 1115 and 1115A of the Social Security Act, as amended.

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

6. ood quality evaluation and consumer acceptance studies:

   i. esome foods without additives are consumed, or
   ii. sumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

Note: Exempt categories 7 & 8 always require limited IRB review and are only available when broad consent will be (or has been) obtained.

7. Storage or maintenance for secondary research for which broad consent is required: Storage or maintenance of identifiable private information or identifiable biospecimens for potential secondary research use if an IRB conducts a limited IRB review and makes the determinations required in Section 10.3, #8.

8. for which broad consent is required: Research involving the use of identifiable private information or identifiable biospecimens for secondary research use, if the following criteria are met:

   i. nt for the storage, maintenance, and secondary research use of the identifiable private information or identifiable biospecimens was obtained in accordance with Section 18.1 and Section 18.12;

9. ormed consent or waiver of documentation of consent was obtained in accordance with Section 18.10 or Section 18.11;

iii. An IRB conducts a limited IRB review and makes the determination required by .111(a)(7): *When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data* and makes the determination that the research to be conducted is within the scope of the broad consent referenced in 8.i above; and

iv. The investigator does not include returning individual research results to subjects as part of the study plan. This provision does not prevent an investigator from abiding by any legal requirements to return individual research results.

9.3 Procedures for Exemption Determination

To request an exempt determination, investigators submit the following materials:

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

The IRB reviews all requests for exemptions and determines whether the request meets the criteria for exempt research. The reviewer's determination is documented on the Claim for Exemption form**.** If the request does not appear to meet the definition of human subject research, the reviewer evaluates the proposal as described in Section 8.

When the research requires limited IRB review or a HIPAA determination (i.e., waivers or alterations of the requirement for HIPAA authorization), the review will be conducted at a convened meeting. The review is assigned to two (2) IRB members. Any committee member may review the research and provide comments to the IRB Chair. As with all other research subject to IRB review requirements, when conducting limited IRB review the IRB has the authority to approve, require modifications in (to secure approval), or disapprove all research activities; and to suspend or terminate IRB approval. Actions of disapproval may only be made by the convened IRB.

Proposed modifications to the aspects of research subject to limited IRB review must be submitted to and approved by the IRB prior to implementation, except when necessary to eliminate apparent immediate hazards to the subject(s), in which case the change must be promptly reported to the IRB (i.e., within two (2) business days). [45 CFR 46.108(a)(3)(iii)]

Continuing review is generally not required for research determined to be exempt, even when that research is subject to limited IRB review. However, the IRB may determine that continuing review is required for a particular study subject to limited IRB review, in which case it shall

document the reasons for its determination in the IRB record and communicate the requirement to the investigator in the IRB determination letter. [45 CFR 46.109(f)(ii), 45 CFR 46.115(a)(3)]

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

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

Exempt determinations will require an annual review or include a termination date, with the maximum time allotted being three (3) years. If the investigator wants the research to extend beyond the termination date, the investigator must request another exemption determination. This process will allow the investigator and the organization the opportunity to review and update the research activity and determine whether it still qualifies for exemption.

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

10 IRB Review Process

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

- Expedited Review (Including Limited IRB Review as described in Section 9.2), or
- Review by Convened IRB

10.1 Expedited Review

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

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

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

10.1.1 Definitions

Minimal Risk. Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

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

1. The acceptability of the risk-to-benefit analysis (i.e., the change does not increase the level of risk);
2. The research design or methods (adding procedures that are not eligible for expedited review (See Section 10.1.2) would be considered more than a minor change);
3. The number of local subjects to be enrolled in the research (usually not greater than 10% of the total requested);
4. The qualifications of the research team (i.e., the change does not negatively impact the expertise available to conduct the research);
5. The facilities available to support safe conduct of the research; or
6. Any other factor which would warrant review of the proposed changes by the convened IRB.

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

10.1.2 Categories of Research Eligible for Expedited Review

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

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

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

The expedited review procedure may not be used for classified research.

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

1. Clinical studies of drugs and medical devices only when condition (a) or (b) is met;
    a. Research on drugs for which an investigational new drug application (21 CFRPart 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)
    b. Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.
2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:
    a. From healthy, non pregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an eight (8) week period and collection may not occur more frequently than two (2) times per week; or
    b. From other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an eight (8) week period and collection may not occur more frequently than two (2) times per week. (Note: Children are defined as "persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.)
3. Prospective collection of biological specimens for research purposes by noninvasive means;
    Examples: (a) hair and nail clippings in a non disfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction;
    (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gum base or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) supra- and sub gingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization; (k) vaginal swabs that do not go beyond the cervical or; rectal swabs that do not go beyond the rectum; and nasal swabs that do not go beyond the nares.
4. Collection of data through noninvasive procedures, not involving general anesthesia or sedation, routinely employed in clinical practice, excluding procedures involving x-rays

or microwaves; Where medical devices are employed, they must be cleared/approved for marketing. (Note: Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.)

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

5. Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for non research purposes (such as medical treatment or diagnosis); (NOTE: Some research in this category may be exempt from the DHHS regulations for the protection of human subjects. See Exempt Categories and 45 CFR 46 101(b)(2) and b(3). This listing refers only to research that is not exempt.)
6. Collection of data from voice, video, digital, or image recordings made for research purposes;
7. Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior); or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (NOTE: Some research in this category may be exempt from the DHHS regulations for the protection of human subjects. This listing refers only to research that is not exempt.)

Categories 8 and 9 apply only to continuing review.

8. Continuing review of research previously approved by the convened IRB as follows:
    a. Where (i) the research at WTAMU is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects (Note: "Long-term follow-up" includes research *interactions* that involve no more than minimal risk to subjects (e.g., quality of life surveys); and collection of *follow-up data* from procedures or interventions that would have been done as part of routine clinical practice to monitor a subject for disease progression or recurrence, regardless of whether the procedures or interventions are described in the research study, but not *interventions* that would not have been performed for clinical purposes, even if the research interventions involve no more than minimal risk); ***or***

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

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

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

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

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

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

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

10.1.3 Expedited Review Procedures

Under an expedited review procedure, IRB review is carried out by the IRB Chair or by one or more reviewers designated by the IRB Chair from among experienced members and alternate members of the IRB. Designated reviewers must be professionally competent (i.e., experienced with and having demonstrated the ability to apply IRB review requirements and with appropriate scientific or scholarly expertise) to conduct expedited reviews. IRB members do not participate in the review of research in which they have with a conflict of interest (See Section 21.2) but may answer questions about the research if requested.

When reviewing research under an expedited review procedure, the IRB Chair, or designated reviewer, will receive and review the same materials that would be reviewed if the research were to be reviewed by the convened IRB, and for previously approved research, will have access to the study history. The reviewer evaluates and documents whether the research qualifies for expedited review using a checklist. When a reviewer determines that research subject to the Common Rule and that does fall within the expedited categories involves **more than minimal risk**, the reviewer will document the rationale for that determination in the checklist and refer the research for review by the convened IRB. If the research otherwise does not meet the criteria for expedited review, then the reviewer will indicate that the research

requires review by the convened IRB and the submission is placed on the next available IRB meeting agenda.

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

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

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

10.1.4 Informing the IRB

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

10.2 Convened IRB Meetings

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

10.2.1 IRB Meeting Schedule

The IRB meets on a regular basis throughout the year. The schedule for the IRB may vary due to holidays, lack of quorum, or other reasons. Special meetings may be called at as needed by the IRB Chair or AREHS Director.

10.2.2 Preliminary Review

The AREHS staff will perform a preliminary review of all submissions for determination of completeness and accuracy, including an elements of consent checklist, when applicable. Only complete submissions will be placed on the IRB agenda for review. The investigator will be informed by e-mail of missing materials and any recommended changes. If an investigator is submitting for the first time or is not well-versed in submission procedures, consultations can be arranged with AREHS staff.

10.2.3 IRB Review

When full board review is determined or sought, the IRB Chair establishes a time and place for the meeting based upon availability. The protocol is made available to the entire committee for review prior to the convened meeting. The committee then discusses the protocol with the PI and moves into closed session for determinations.

When the IRB is presented with a research study which may be outside of the knowledge base or representative capacity of the IRB members, an outside consultant will be sought (See Section 10.3.1). Research studies for which appropriate expertise cannot be obtained for a given meeting will be deferred to another meeting when appropriate expertise is available.

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

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

10.2.4 Materials received by the IRB

All required materials need to be submitted to the IRB prior to the convened meeting or by the published deadline for inclusion on the IRB agenda. The meeting agenda will be prepared by AREHS staff in consultation as needed with the IRB Chair. All IRB members receive the IRB agenda, prior meeting minutes, applicable business items, and research submission materials before the scheduled meeting to allow sufficient time for review.

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

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

Additionally, for HHS-supported multicenter clinical trials, the IRB should receive and review a copy of the HHS-approved sample consent form(s) and the complete HHS-approved protocol, if they exist.

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

Primary reviewers will review the protocol using a reviewer checklist which serve as a guide for the review and a tool for summarizing recommendations prior to board discussion.

10.2.5 Quorum

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

The IRB Chair, with the assistance of the AREHS staff, will confirm that quorum is present before calling the meeting to order. The IRB Chair, with the assistance of the AREHS staff, will be responsible to ensure that the IRB meeting remains appropriately convened. If a quorum is not maintained, either by losing a majority of the members, or losing all non-scientific members or another required member, the IRB may not take votes until quorum is restored. When IRB members leave the meeting room, AREHS Staff will document the time of departure and notify the IRB Chair if a quorum is not present. A quorum worksheet may be used by the AREHS Staff and/or IRB Chair to monitor quorum and to temporarily document attendance and quorum until the minutes are prepared and finalized.

In addition to the required attendance of at least one scientific member and at least one "non-scientist" member, it is generally expected that at least one unaffiliated member, and one member who represents the general perspective of participants (one individual can serve in both capacities) will be present at all IRB meetings. The IRB may, on occasion, meet without this representation; however, this should be the exception (i.e., no more than 50% of meetings).

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

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

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

10.2.6 Meeting Procedures

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

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

The IRB reviews submissions for initial and continuing review, requests for modifications to previously approved research, and other business items, as applicable (e.g., potentially serious noncompliance). IRB members assists the IRB Chair in the evaluation of the regulatory criteria for approval or other required determinations using checklist(s) as a guide.

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

AREHS staff are responsible for taking minutes at each IRB meeting.

10.2.7 Guests

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

The AREHS Director and AREHS staff regularly attend IRB meetings and may participate in the IRB discussion and deliberations, but may not vote unless attending as a member or alternate.

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

10.3 Criteria for IRB Approval of Research

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

1. Risks to subjects are minimized: (i) by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and (ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.
2. Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

3. Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving subjects vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons.
4. Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by the Federal Regulations [45 CFR 46.116/21 CFR 50].
5. Informed consent will be appropriately documented, in accordance with, and to the extent required by the Federal Regulations [45 CFR 46.117/21 CFR50].
6. When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.
7. When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.
8. For purposes of conducting the limited IRB review required by 45 CFR 46.104(d)(7), the IRB need not make the determinations at paragraphs (1) through (7) of this section, and shall make the following determinations:
    a. Broad consent for storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens is obtained in accordance with the requirements in Section 18.1 and Section18.12;
    b. Broad consent is appropriately documented or waiver of documentation is appropriate, in accordance with 45 CFR 46.117; and
    c. If there is a change made for research purposes in the way the identifiable private information or identifiable biospecimens are stored or maintained, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, economically or educationally disadvantaged persons or individuals with impair decision-making ability, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

10.3.1 Risk/Benefit Assessment

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

- Judge whether the anticipated benefit, either of new knowledge or of improved health or other direct benefit for the research subjects, justifies asking any person to undertake the risks; and

- Disapprove research (at a convened meeting only) in which the risks are judged unreasonable in relation to the anticipated benefits.

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

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

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

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

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

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

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

10.3.1.1 Scientific or Scholarly Review

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

- The research uses procedures consistent with sound research design; and

- The research design is sound enough to yield the expected knowledge.

In making this determination, the IRB may draw on its own knowledge and expertise, or the IRB may draw on the knowledge and expertise of others, such as reviews by a funding agency, a scientific review committee, or departmental review. When scientific or scholarly review is conducted by a WTAMU individual or entity external to the IRB, documentation of the outcome and details of that review must be provided to the IRB for review and consideration.

10.3.2 Equitable Selection of Subjects

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

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

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

10.3.2.1 Recruitment of Subjects

The investigator will provide the IRB with a plan for recruitment of potential subjects. All recruiting materials will be included in the IRB application, including advertisements, flyers, scripts, information sheets and brochures. The IRB should ensure that the recruitment plan and materials appropriately protect the rights and welfare of the prospective subjects (e.g., do not present undue influence). See Section 10.4.7 for a discussion of IRB review of advertisements and Section 10.4.9 for a discussion of IRB review of payments.

10.3.3 Informed Consent

The IRB will ensure that informed consent will be sought from each prospective subject or the subject's legally authorized representative (LAR), in accordance with, and to the extent required by 45 CFR 46.116 and 21 CFR 50.20. In addition, the IRB will ensure that informed consent will be appropriately documented, in accordance with, and to the extent required by 45 CFR 46.117

and 21 CFR 50.27. The IRB will ensure, as part of its review, that the information in the consent document and process is consistent with the research plan, and, when applicable, will refer the HIPAA authorization for further review. See Section 18 for a detailed discussion on informed consent.

10.3.4 Data and Safety Monitoring

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

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

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

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

Data and Safety Monitoring plans should specify:

- The entity or person(s) who will perform the monitoring, and the independence or affiliation that the entity or person(s) has with the sponsor or investigator;
- The safety information that will be collected and monitored, including serious adverse events and unanticipated problems;
- The frequency or periodicity of review of safety data;

- The procedures for analysis and interpretation of the data;
- The procedures for review of scientific literature and data from other sources that may inform the safety or conduct of the study;
- The conditions that trigger a suspension or termination of the research (i.e., stopping rules), when appropriate; and
- The procedures for reporting findings to the IRB, including a summary description of what information, or the types of information, that will be provided.

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

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

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

10.3.5 Privacy and Confidentiality

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

10.3.5.1 Definitions

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

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

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

Sensitive Information. Data or information, on any storage media or in any form or format, which requires protection due to the risk of harm that could result from inadvertent or deliberate disclosure, unauthorized access, misuse, alteration, or loss or destruction of the

information (e.g., could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subject's financial standing, employability, or reputation).

Identifiable Biospecimens. Tissues, blood, body fluids and other specimens for which the identity of the person from whom the specimens were collected can readily be ascertained by the investigator or is associated with the biospecimens.

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

10.3.5.2 Privacy

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

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

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

10.3.5.3 Confidentiality

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

The IRB assesses whether there are adequate provisions to protect data confidentiality by evaluating the methods used to obtain, record, share, and store information about individuals who may be recruited to participate in studies and about subjects. The investigator will provide the IRB with a plan regarding the procedures to be taken to protect the confidentiality of research data and sensitive information. The investigator will provide information regarding

information security procedures and plans to address the protection of paper documents, other physical media (e.g., audio or videotapes), and electronic data, and information regarding the use, maintenance, storage, and transmission of information. The IRB will review the information received from the investigator and determine whether the confidentiality of research data is sufficiently protected. In some cases, the IRB may also require that a Certificate of Confidentiality is obtained to protect data from compelled disclosure (See Section 24.7).

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

10.3.6 Vulnerable Populations

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

For an extensive discussion about the IRB's review process for specific populations of vulnerable subjects, please refer to Section 19.

10.4 Additional Considerations

10.4.1 Determination of Risk Level

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

10.4.2 Period of Approval

At the time of initial review and at continuing review, the IRB will make a determination regarding the period of approval. All studies will be reviewed by the IRB at intervals appropriate to the degree of risk but no less than once per year. For research subject to the 2018 Common Rule (revised Common Rule), the IRB will conduct continuing review of research requiring review by the convened IRB at intervals appropriate to the degree of risk of the research, but not less than once per year, except as described in Section 10.5;

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

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

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

The approval date and approval expiration date are clearly noted on IRB determination letters and must be strictly adhered to. Investigators should allow sufficient time for development and review of continuing review submissions. As a courtesy, the AREHS Office sends reminders to the investigator sixty (60) and thirty (30) days prior to the study's expiration date, notifying him or her that the study is due for a continuing review or when approval has expired.

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

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

10.4.3 Review More Often Than Annually

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

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

In specifying an approval period of less than one year, the IRB may define the period with either a time interval or a maximum number of enrolled subjects. If a maximum number of subjects is used to define the approval period, it is understood that the approval period in no case can exceed one year unless the study does not require continuing review. If an approval period of less than one year is specified by the IRB for research that is subject to continuing review, the reason for more frequent review must be documented in the minutes or a reviewer checklist.

Independent Verification That No Material Changes Have Occurred

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

In support of this requirement, the WTAMU IRB requires the submission of Other Reportable Information (See Section 16) including reports from external monitors, auditors, or inspectors (See Section 2.1).

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

1. The nature, probability, and magnitude of anticipated risks to subjects;
2. The degree of uncertainty regarding the risks involved;

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

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

If any material changes have occurred without IRB review and approval, the IRB will decide the corrective action to be taken.

10.4.4 Consent Monitoring

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

Such monitoring may be particularly warranted for:

1. High risk studies;
2. Studies that involve particularly complicated procedures or interventions;
3. Studies where recruitment will occur in situations or circumstances that may negatively impact the consent process (e.g., the Emergency Room);
4. Studies involving highly vulnerable populations (e.g., ICU patients, children who are wards);
5. Studies involving study staff with minimal experience in administering consent to potential study participants; or

6. Other situations when the IRB has concerns that consent process may not be/is not being conducted appropriately (e.g., prior investigator noncompliance, etc.).

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

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

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

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

10.4.5 Investigator Qualifications

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

10.4.6 Significant New Findings

During the course of research, significant new knowledge or findings about the research, the test article, and/or the condition under study may develop. The investigator must report any significant new findings to the IRB and the IRB will review them and evaluate the impact on the subjects' rights and welfare. When the new knowledge or findings may affect the risks or benefits to subjects or subjects' willingness to continue in the research, the IRB may require that the investigator contact subjects to inform them of the new information. The IRB will communicate this requirement to the investigator. If the study is still enrolling subjects, the consent document should be updated. The IRB may require that the currently enrolled subjects be re-consented or otherwise provided with the new information. When appropriate, the IRB may also require that former subjects be provided with the new information (e.g., late emerging safety information).

10.4.7 Conflicts of Interest (COI)

The IRB research application solicits information about investigator and research staff COI disclosure and whether any conflict management plans are in place. As part of its review process, the IRB will make a final determination as to whether any COI is adequately addressed and protects the human subjects in the research. Likewise, when there is an institutional COI, the IRB has final authority to determine whether the conflict and the management plan, if any, allow the study to be approved. (See Section 21 for a more detailed discussion of COI).

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

10.4.8 Advertisements and Recruitment Materials

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

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

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

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

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

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

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

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

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

Directory listings of research such as ClinicalTrials.Gov are not considered advertisements and therefore do not require IRB review and approval if the listing is limited to the following basic trial information: title, purpose of the study, summary description of the research, basic eligibility criteria, study site location(s), and how to contact the study site for further information.

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

10.4.9 Payments and Reimbursement

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

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

Investigators who wish to pay research subjects must include in their application to the IRB the amount and schedule of all payments and the justification or basis for payment. Such justification should substantiate that proposed payments are reasonable and commensurate

with the expected contributions of the subject and do not constitute (or appear to constitute) undue pressure on the potential subject to volunteer for the research study.

When research involves multiple visits or interactions, payment should be prorated and not be contingent upon the participant completing the entire study. The IRB does not allow the entire payment to be contingent upon completion of the entire study. Further, any amount paid as bonus for completion of the entire study should not be so great that it could unduly induce subjects to remain in the study when they otherwise would have withdrawn.

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

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

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

10.4.10 Non-Monetary Gifts and Incentives

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

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

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

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

10.4.11 State and Local Laws

The IRB considers and adheres to all applicable state and local laws in the jurisdictions where the research is taking place. The HRPP and IRB rely on TAMUS General Counsel for the interpretation and application of Texas law and the laws of any other jurisdiction where

research is conducted as they apply to human subjects research. The IRB will ensure that consent forms are consistent with applicable state and local laws.

10.5 Continuing Review

For research subject to the 2018 Common Rule (the revised Common Rule), the IRB will conduct continuing review of ongoing research requiring review by the convened IRB at intervals that are appropriate to the level of risk of the research, but not less than once per year, except as described below. The date by which continuing review must occur will be recorded in the paper-based protocol file and on initial and continuing review approval letters.

Unless an IRB determines otherwise, continuing review of research subject to the 2018 Common Rule (the revised Common Rule) is not required in the following circumstances:

- Research eligible for expedited review in accordance with 45 CFR46.110;
- Research reviewed by the IRB in accordance with the limited IRB review described in Section 9.2;
- Research that has progressed to the point that it involves only one or both of the following, which are part of the IRB-approved study:
    - Data analysis, including analysis of identifiable private information or identifiable biospecimens, or
    - Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care.

The WTAMU IRB may determine that continuing review is required for any research protocol that falls within the above criteria. For example, the IRB may determine that continuing review is required when:

1. Required by other applicable regulations (e.g., FDA);
2. Required by the terms of a grant, contract, or other agreement;
3. The research involves topics, procedures, or data that may be considered sensitive or controversial;
4. The research involves particularly vulnerable subjects or circumstances that increase subjects' vulnerability;
5. An investigator has minimal experience in research or the research type, topic, or procedures; and/or
6. An investigator has a history of noncompliance.

When the WTAMU IRB determines that continuing review is required for such research, it will document the rationale in the IRB record and communicate the requirement to the investigator in the IRB determination letter.

There is no exception to the requirement for continuing review in FDA regulations. The IRB will conduct continuing review of ongoing FDA-regulated research, and any research where it is

required by applicable regulations, policy, or other requirements (e.g., as a condition of funding or contractually), at intervals that are appropriate to the level of risk of the research, but not less than once per year, as long as the research remains active. The date by which continuing review must occur will be recorded in the paper-based protocol file and on initial and continuing review approval letters.

10.5.1 Continuing Review Process

As a courtesy to investigators, the AREHS office staff will send out reminder notices to investigators 60 and 30 days in advance of the expiration date; however, it is the investigator's responsibility to ensure that the continuing review of ongoing research is approved prior to the expiration date. By federal regulation, no extension to that date can be granted.

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

1. The initial study application form updated with any changes (this serves as the project summary);
2. The Continuing Review Application (this serves as the progress report);
3. The current consent document and the most recent signed consent document (with the subject name and any other identifiers blacked-out);
4. The most recent report from the DSMB or DMC (if applicable);
5. For multi-site studies, the most recent progress report from other sites;
6. Any proposed modifications to the research including any changes to materials;
7. Any previously un-submitted publications or presentations resulting from the research;
8. Any previously un-submitted reports identified while completing the Continuing Review Application; and
9. CITI training certificates for each member of the research team (unless training is verified some other way).

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

In the case of expedited review, the reviewer may request that the AREHS office staff provide them with any additional materials required for their review.

10.5.2 IRB Considerations for Continuing Review

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

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

10.5.3 Convened Board Review

In conducting continuing review of research not eligible for expedited review, IRB members are provided all of the materials listed in Section 10.2.4 and are responsible for reviewing, at a minimum, the Continuing Review Application, the current IRB-approved consent form(s) (when applicable), and any proposed modifications to the research or consent form(s). The complete IRB file and relevant IRB meeting minutes are available to IRB members upon request.

The IRB Chair is responsible for reviewing the complete materials submitted for continuing review and completing a reviewer checklist to facilitate the review and discussion at the meeting. At the meeting, the IRB Chair leads the IRB through the discussion of the submission and the regulatory criteria for approval.

10.5.4 Expedited Review

In conducting continuing review under expedited procedures, the IRB Chair or designated reviewer(s) receive all of the previously noted materials. The reviewer(s) complete the continuing review checklist to determine whether the research meets the criteria allowing continuing review using the expedited procedure, and if so, whether the research continues to meet the regulatory criteria for approval. If the research subject to the 2018 Common rule (the revised Common Rule) no longer requires continuing review (See Section 10.5) and the IRB reviewer determines that continuing review is required, the reviewer shall document the rationale in the checklist.

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

- Data analysis, including analysis of identifiable private information or identifiable biospecimens; and/or
- Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care; and
- In limited circumstances described by expedited review categories (8) and (9) (see Expedited Review Categories in Section 10.1.2), it is also possible that research activities that previously qualified for expedited review, have changed or will change, such that expedited continuing review would no longer be permitted.

10.5.5 Possible IRB Actions after Continuing Review

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

If an IRB member conducting expedited review believes that continuation of the research should be disapproved, they will refer the proposed modification to the convened board for review. If the proposed changes raise significant concerns on the part of the IRB, the IRB may vote to suspend or terminate the research (See Section 12 for a detailed discussion of suspensions and terminations).

If a research study receives Conditions Required for Approval at the time of the continuing review, the IRB will specify whether any conditions need to be satisfied before an investigator can continue particular research activities related to those conditions or requirements that must be adhered to until the conditions of approval have been satisfied. For example, if at the time of continuing review, the IRB requires the investigator to change the research protocol to include a specific new procedure for screening prospective subjects, the IRB could approve the research with the following condition: "*Research activities involving currently enrolled subjects may continue, but no new subjects may be enrolled until a designated IRB member reviews a revised protocol and verifies that the protocol includes the new screening procedure"*. Additionally, the IRB may specify a time period, such as 1, 2, or 3 months, for the condition(s) to be satisfied as long as the activity with conditions is not begun or restarted until final approval is granted.

10.5.6 Lapses in Continuing Review

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

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

In the event that study approval does expire, the AREHS office staff sends a notification to the investigator noting the expiration of approval and instructions that all research activities must stop. If the investigator fails to respond to the notification, and does not submit continuing review materials or a closure report within three (3) business days, the AREHS staff will refer

the matter to the IRB Chair to evaluate for possible administrative closure or noncompliance (See Section 14).

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

10.5.6.1 Management of Enrolled Subjects during Lapse

While enrollment of new subjects cannot occur after the expiration of IRB approval, the IRB recognizes that temporarily continuing participation of already enrolled subjects may be necessary or appropriate, for example, when the research interventions hold out the prospect of direct benefit to the subjects, or when withholding those interventions or safety monitoring procedures would place subjects at increased risk. In these instances, the investigator must, at the earliest opportunity, contact the AREHS office and submit a request to continue those research activities that are in the best interests of subjects. Such a request should specifically list the research activities that should continue, provide justification, and indicate whether the request applies to all or only certain subjects. The IRB Chair or designee will review the request and provide a determination regarding what activities, if any, may continue during the lapse. Such a determination may include a time limit or other conditions or restrictions. If the IRB decides that already enrolled subjects should continue to receive the interventions that were being administered to subjects under the research project, data collection (especially safety information) should also continue for such subjects.

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

10.6 Modification of an Approved Protocol

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

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

10.6.1 Procedures

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

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

10.6.2 Convened Board Review of Modifications

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

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

The IRB Chair is responsible for reviewing the complete materials submitted for a modification and completing a reviewer checklist to facilitate the review and discussion at the meeting. At the meeting, the IRB Chair leads the IRB through the discussion of the submission and the regulatory criteria for approval.

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

10.6.3 Expedited review of Modifications

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

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

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

10.6.4 Possible IRB Actions after Modification Review

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

If an IRB member conducting expedited review believes that the proposed modifications should be disapproved, they will refer the proposed modification to the convened board for review. If the proposed changes raise significant concerns on the part of the IRB, the IRB may vote to suspend or terminate the research (See Section 12 for a detailed discussion of suspensions and terminations).

10.6.5 Protocol Exceptions

Protocol exceptions are circumstances in which the investigator wishes to deviate from eligibility criteria or one or more of the specific procedures called for in a research plan. Unlike modifications that apply to all subsequent subjects in the research, a protocol/research plan exception only applies to a specific subject or group of subjects.

Exceptions are planned, and the investigator gets approval from the IRB ahead of time. For sponsored research, prior approval from the sponsor is generally required. Depending on the nature of the exception, an expedited review may be possible. For an exception to be approved under expedited review, the research as a whole must be eligible for expedited review, or, for convened board research, the proposed exceptions must not increase risk or decrease benefit,

negatively impact the risk/benefit analysis, negatively affect the participant's rights, safety, or welfare, or negatively affect the integrity of the resultant data.

Procedures for exceptions are the same as for a Protocol Modification. The investigator must submit a Closeout/Amendment/Continuation Form along with any new or revised materials, and documentation of sponsor approval, if applicable.

The only time a protocol/Research Plan exception would not require prior sponsor or IRB approval is when the exception is necessary to avoid an apparent immediate hazard to the subject(s). In such cases, the exception must be submitted to the IRB as soon as possible.

10.7 Closure of Research Studies

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

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

For multi-center research, the study may be closed once all research activities (as above) are complete at WTAMU and any sites for which the IRB is serving as the "IRB of record". If the investigator is serving as the lead investigator or the site is the coordinating center, the study must remain open as long as the lead investigator or coordinating center is still receiving, studying, using, or analyzing identifiable private information from other sites (even if local interventions, interactions, observations, and data gathering is complete).

Investigators may submit study closures to the IRB on a Closeout/Amendment/Continuation Form. With closure submissions, the investigator must provide a summary of the research activity and any findings available at that time.

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

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

11 IRB Actions, Failure to Respond, Appeals

11.1 IRB Actions

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

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

Conditions Required for Approval *(provisional approval, conditional approval, approval with contingencies; or modifications required)*

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

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

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

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

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

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

approves research with conditions, the original expedited reviewer (and/or other qualified individual(s)) will receive the response materials.

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

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

A documentation folder is maintained in Bb on every proposal submitted. Official communications of all IRB actions are uploaded to the folder, i.e., conditional approval, requests from IRB for revisions, revisions submitted by the PI, and approval letters. All official letters from the IRB are dated and signed and all documentation is accessible by all IRB members at all times.

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

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

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

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

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

provided by the investigator) and, if appropriate, will provide certification of IRB approval in principal. Any approvals in principle will note that IRB approval must be obtained before any activities involving human subjects may commence.

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

11.2 Failure to Respond

Upon review of a research study, the IRB may require changes or request certain information from an investigator. Failure to respond to IRB required changes or requests for information within thirty (30) days (or less if the IRB determines that the information must be submitted earlier to ensure protection of the research subjects) may result in suspension or termination of IRB approval for the study. For studies that have not yet been approved, the study submission may be administratively withdrawn. At its discretion, the IRB may grant an extension beyond thirty (30) days if the investigator contacts the IRB Chair or the AREHS office prior to the deadline and presents sufficient cause for delay.

11.3 Reporting IRB Actions

All IRB actions are communicated to the investigator, and/or designated contact person for the research study, via email within ten (10) working days, whenever possible, of the review. For IRB actions of conditions required for approval or deferral, the notification will include a listing of the conditions or requirements that must be satisfied or responded to. For a disapproval, suspension, or termination, the notification will include the basis for the action and will offer the investigator an opportunity to respond in person or in writing.

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

11.4 Appeal of IRB Decisions

When the IRB suspends, terminates, or disapproves research, the IRB letter communicating the decision will include the basis for the action and will offer the investigator the opportunity to respond in person or in writing. Additionally, whenever an investigator disagrees with an IRB requirement or decision, or believes that providing the IRB with additional information may result in a different outcome, they may request that the IRB reconsider its decision by submitting a memo and other supportive materials. The investigator may be invited to attend

the IRB meeting to discuss the request and provide information, but will be asked to leave prior to the IRB's final deliberations and vote.

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

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

12 Suspensions, Terminations, and Investigator Holds

12.1 Suspension/Termination

IRB approval may be suspended or terminated if research is not being conducted in accordance with IRB or regulatory requirements or has been associated with unexpected problems or serious harm to subjects. (See Section 13 for a discussion of unanticipated problems and Section 14 for a discussion of noncompliance.) The IRB's authority to suspend or terminate research applies to all research subject to IRB approval, including exempt research with limited IRB review and research for which continuing review is no longer required.

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

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

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

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

Suspensions of IRB approval must be reported promptly to the IO, sponsors including federal department or agency heads, and federal oversight agencies as applicable. See Section 16 for a detailed discussion of reporting requirements.

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

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

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

Terminations of IRB approval must be reported promptly to the IO, sponsors including federal department or agency heads, and federal oversight agencies as applicable. See Section 16 for a detailed discussion of reporting requirements.

12.2 Investigator Hold

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

12.2.1 Procedures

Investigators must submit a memo and any supporting materials via letter and an amendment form to inform the IRB of the hold. The memo and materials should include:

1. A statement that the investigator is voluntarily placing a study on hold;
    a. The reason(s) for the hold;
    b. A description of the research activities that will be stopped;
    c. Proposed actions to be taken to protect current participants; and

d. Any actions that will be taken prior to IRB approval of proposed changes in order to eliminate apparent immediate risk of harm.

2. Upon receipt, AREHS staff notify the IRB Chair or designee and place the research on the next available agenda for review;
3. For greater than minimal risk studies, the IRB Chair or designee, in consultation with the investigator, determines whether any additional procedures need to be followed to protect the rights and welfare of current participants as described in Section 12.3;
4. For greater than minimal risk studies, the IRB Chair or designee, in consultation with the investigator, determines whether and how currently enrolled subjects will be notified of the hold;
5. Investigators may request a revision of the research on hold by submitting a request for revisions to previously approved research; and/or
6. Prior to lifting the hold, the investigator must seek approval from the IRB so that the IRB may consider whether subjects are appropriately protected and if the research remains approvable.

12.3 Protection of Currently Enrolled Participants

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

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

13 Unanticipated Problems Involving Risks to Subjects or Others

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

This section provides definitions and procedures for the reporting of UAPs to the WTAMU IRB. Investigators conducting research under the oversight of an external IRB must comply with the

reporting requirements of the external IRB and the internal reporting requirements outlined in Section 16.

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

13.1 Definitions

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

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

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

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

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

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

13.2 Procedures

13.2.1 Reporting

Investigators must report the following events or issues to the IRB as soon as possible but within seven (7) working days after the investigator first learns of the event using the Closeout/Amendment/Continuation Form.

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

Examples of UAPs include:

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

13.2.2 Review Procedures

1. Upon receipt of the Closeout/Amendment/Continuation Form, the IRB staff pre- reviews the submission and, if needed, contacts the investigator for corrections or additional information.
2. The IRB Chair or designated reviewer receives and reviews the report and makes an initial determination as to whether the event represents an UAP. If needed, the IRB Chair or designee may request additional information from the investigator, sponsor, or others (including study committees, such as data monitoring committees, data safety monitoring boards, or steering committees).
3. If the reviewer determines that the problem does not meet the definition of an UAP, they will determine whether any additional actions are necessary to ensure the protection of human subjects. As warranted, the reviewer may refer the matter to the convened IRB for review.
4. If the reviewer determines that the event may be an UAP, the report will be referred for review by the convened IRB. The convened IRB will determine whether the event is a UAP and whether any additional actions, such as those outlined below, are necessary to ensure the protection of human subjects. If needed, the IRB may request additional information from the investigator, sponsor, or others (including study committees, such as data monitoring committees, data safety monitoring boards, or steering committees). The results of the review will be recorded in the IRB minutes and communicated to the investigator.
5. Based upon the circumstances, the IRB may take any of the following actions, or others, to ensure the protection of human subjects:
    a. Requiring modifications to the protocol or plan or procedures for implantation of the research (Research Plan) as described in the application and other materials submitted to the IRB;
    b. Revising the continuing review timetable;
    c. Modifying the consent process;
    d. Modifying the consent document;
    e. Providing additional information to current participants (e.g., whenever the information may relate to the subject's rights, welfare, or willingness to continue participation);
    f. Providing additional information to past participants;
    g. Requiring additional training of the investigator and/or study staff;
    h. Requiring that current subjects re-consent to participation;
    i. Monitoring the research;
    j. Monitoring consent;

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

l. Suspending IRB approval;

m. Terminating IRB approval; or

n. Other actions as appropriate given the specific circumstances.

When the IRB determines that an event is an UAP, the IRB staff will follow the procedures for reporting to regulatory agencies, sponsors, and organizational officials in Section 17. When appropriate, a preliminary report may be submitted while more information is obtained to inform the determination or actions.

14 Noncompliance

This section provides definitions and procedures for the reporting and review of known or suspected noncompliance for research under the oversight of the WTAMU IRB. Research under the oversight of an external IRB must comply with the reporting requirements of the external IRB and the internal reporting requirements outlined in Section 16.

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

14.1 Definitions

Noncompliance is defined as the failure to follow federal, state, or local regulations governing human subject research, institutional policies related to human subject research, or the requirements or determinations of the IRB. Noncompliance may be minor or sporadic or it may be serious or continuing. Noncompliance can result from action or omission. Noncompliance may be non-serious (minor) or serious, and may also be continuing (see below).

Serious Noncompliance is defined as noncompliance that, in the judgment of the convened IRB, creates an increase in risks to subjects, adversely affects the rights, welfare, or safety of subjects, or adversely affects the scientific integrity of the study. Willful violation of policies and/ or federal regulations may also constitute serious noncompliance. Examples of serious noncompliance may include, but are not limited to: conducting or continuing non-exempt human subjects research without IRB approval; lack of legally effective informed consent from research participants; failure to report or review serious adverse events, unanticipated problems, or substantive changes in research; or inappropriate oversight of the research to insure the safety of human subjects and the integrity of the research/data.

Nonserious Noncompliance is noncompliance that does not increase risk to research participants, compromise participant's rights or welfare, or affect the integrity of the research/data or the human subjects protection program. Examples of minor noncompliance may include, but are not limited to: lapses in continuing IRB approval, failure to obtain exempt determination before exempt research involving human subjects is conducted, minor changes in or deviations from an approved protocol or administrative errors.

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

IRB or institution intervenes. Examples of continuing noncompliance may include, but are not limited to: repeated failures to provide or review progress reports resulting in lapses of IRB approval, inadequate oversight of ongoing research, or failure to respond to or resolve previous allegations or findings of noncompliance.

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

14.2 Reporting

Investigators and their study staff are required to report instances of possible noncompliance to the IRB immediately upon discovery or at least within one calendar week (7 days) of a discovery. Additionally, anyone may report concerns of possible noncompliance to AREHS or the IRB. Reports may be verbally, by email, or other means. In such cases, the reporting party is responsible for making these reports in good faith, maintaining confidentiality and, unless reporting anonymously, cooperating with any subsequent fact-finding in relation to the report.

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

14.3 Review Procedures

1. Upon receipt of the Closeout/Amendment/Continuation Form, the IRB Chair pre-reviews the submission and, if needed, contacts the investigator for corrections or additional information. If the report came from someone other than the investigator verbally, by email, or by other means, came from someone other than the investigator verbally, by email, or by other means, the IRB Chair or AREHS Director will develop a written report summarizing the available information. If the information provided suggests that subjects may be at risk of harm without immediate intervention or that research misconduct may have occurred, the AREHS Director, IRB Chair, and, when appropriate, the IO, will be notified so that they can take any necessary steps to ensure the safety of subjects or investigate the matter.
2. The IRB Chair or designated reviewer receives and reviews the report and makes an initial determination as to whether the event represents noncompliance, and, if so, if the noncompliance may be serious or continuing. If needed, the reviewer may request additional information from the investigator or others. When circumstances warrant, the AREHS Director or IRB Manager may bypass this step and assign the report for convened board review.
3. If the reviewer determines that the event or issue is not noncompliance, or is noncompliance but not serious or continuing, they will review any proposed corrective and preventative action plans and determine if the plan is acceptable as proposed or if modifications to the plan or additional actions are required. As warranted, the reviewer may refer the matter to the convened IRB for review. The results of the review will be recorded in the electronic system and communicated to the investigator.
4. If the reviewer determines that the event or issue may be serious or continuing

noncompliance, the report will be referred for review by the convened IRB. The convened IRB will determine whether the event is serious or continuing noncompliance. The IRB will review any proposed corrective and preventative action plans and determine if the plan is acceptable as proposed or if modifications to the plan or additional actions, such as those outline below, are necessary to ensure the protection of human subjects. If needed, the IRB may request additional information from the investigator or others. The results of the review will be recorded in the IRB minutes and communicated to the investigator.

5. When the IRB determines that an event is serious or continuing noncompliance, the IRB may take any of the following actions, or others, to ensure the protection of human subjects:
    - **a.** Requiring modifications to the protocol or research plan;
    - **b.** Revising the continuing review timetable;
    - **c.** Modifying the consent process;
    - **d.** Modifying the consent document;
    - **e.** Providing additional information to current participants (e.g., whenever the information may relate to the subject's willingness to continue participation);
    - **f.** Providing additional information to past participants;
    - **g.** Requiring additional training of the investigator and/or study staff;
    - **h.** Requiring that current subjects re-consent to participation;
    - **i.** Monitoring the research;
    - **j.** Monitoring consent;
    - **k.** Reporting or referral to appropriate parties (e.g., the IO, Compliance, Risk Management, Privacy);
    - **l.** Suspending IRB approval;
    - **m.** Terminating IRB approval; and/or
    - **n.** Other actions as appropriate given the specific circumstances.
6. When the IRB determines that an event is serious or continuing noncompliance, the IRB staff will follow the procedures for reporting to regulatory agencies, sponsors, and organizational officials in Section 17. When appropriate, a preliminary report may be submitted while more information is obtained to inform the determination or actions.
7. Investigators may request that the IRB reconsider its determination by following the procedures in Section 11.4.

15 Complaints

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

Investigators conducting research under the auspices of WTAMU must report complaints to the WTAMU IRB regardless of who serves as the IRB of record. Investigators conducting research under the oversight of an external IRB must comply with the reporting requirements of the external IRB and the internal reporting requirements outlined in Section 16. Investigators conducting research under the oversight of the WTAMU IRB report complaints using the Closeout/Amendment/Continuation Form. Investigators are encouraged to contact the AREHS Director or IRB Chair when they are having difficulty resolving a complaint or concern, and whenever circumstances warrant (e.g., immediate attention is needed).

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

1. Document the complaint or allegation. When appropriate, the staff may request that the subject submit the complaint in writing.
2. Reassure the subject that the HRPP/IRB will take all necessary measures to inquire into the circumstances and to address the issue.
3. Provide written confirmation of receipt of the complaint to the subject, if the subject is willing to provide contact information.
4. Convey the information to the IRB of record in a timely manner.
5. When appropriate, contact the investigator for additional information or to assist with resolution.
6. When appropriate, contact other resources (e.g., Research Compliance, Risk Management, Privacy) to assist with information-gathering or resolution.

For research under the oversight of the internal IRB, the IRB Chair or designee will consider the complaint or concern and take any reasonable steps necessary to investigate and/or resolve the issue, if appropriate, prior to review and consideration by the IRB. A report will be provided to the IRB at the next available meeting if the research is subject to convened IRB review, or provided to the designated expedited reviewer if the research is eligible for expedited review.

When reviewing complaints, the IRB will consider whether the complaint was the result of, or related to, an UAP or noncompliance, and, if so, will follow the relevant procedures. The IRB IRB Chair or designated expedited reviewer may refer any complaint for review by the convened IRB. The IRB minutes, or reviewer comments for expedited reviews, will reflect the action(s) taken and, if necessary, notice to the appropriate officials and/or agencies.

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

16 Other Reportable Information

When research is under the oversight of the WTAMU IRB, in addition to UAPs, noncompliance, and complaints, any change to the research implemented without IRB approval and any information that may impact the rights, safety, or welfare of subjects or inform the IRB's oversight of the research must be reported to the IRB within one calendar week (7 days) of discovery using the Closeout/Amendment/Continuation Form, as applicable. Investigators conducting research under the oversight of an external IRB must comply with the reporting requirements of the external IRB and the internal reporting requirements.

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

1. Changes made to the research without prior IRB approval to eliminate apparent immediate hazards to the subject(s);
2. Unanticipated Problems Involving Risks to Subjects or Others (UP, UAP, UPIRTSO) -any event that was unexpected, related or possibly related to the research and increases risks to subjects or others. The event must meet all three criteria to be reported immediately. Events not meeting all three criteria should be summarized/reported at the time of continuing review;
3. Monitoring, audit, and inspection reports in accordance with Section 2.1 of this manual;
4. Notice of:
    a. Any litigation, arbitration, or settlements initiated related to human research protections.
    b. Any press coverage (including but not limited to radio, TV, newspaper, online publications) of a negative nature regarding human subjects research conducted at or by WTAMU or WTAMU's program for the protection of human research participants.

    NOTE: The above events must be reported to the HRPP/IRB office by phone or email **as soon as anyone becomes aware**, with the formal submission within the seven (7)-day timeline as noted above.
5. Sponsor or coordinating center reports;
6. Data Safety Monitoring reports, including reports from DSMBs, DMCs, and others;
7. Enrollment or inclusion of vulnerable populations not previously approved by the IRB for the study (e.g., prisoner, pregnant woman, neonate, child, adult with impaired decision-making capacity);
8. When an existing subject becomes a member of a vulnerable population not previously approved by the IRB for inclusion in the study (e.g., incarceration, pregnancy, or change in decision-making capacity of an already enrolled subject);
9. Holds, suspensions, or terminations of a study, in part or in full, by an investigator, sponsor, or others;

10. Changes that impact the ability of the PI to conduct or supervise the study, temporarily or permanently;
11. Changes that impact the qualifications of investigators or research staff members such as actions taken by regulatory authorities, licensing boards, or credentialing committees; and/or
12. New information that may impact the rights, welfare, or willingness of subjects to continue in the research.

16.1 Review Procedures

1. Upon receipt of the report, the IRB staff pre-reviews the submission and, if needed, contacts the investigator for corrections or additional information. If the information provided suggests that subjects may be at risk of harm without immediate intervention or that research misconduct may have occurred, the HRPP/IRB Director, IRB Chair, and, when appropriate, the IO and/or Research Integrity Officer, will be notified so that they can take any necessary steps to ensure the safety of subjects or investigate the matter.
2. The IRB Chair or designated reviewer receives and reviews the report and, if the report may represent an UAP or noncompliance, reviews the report as described in Section 13 or 14. When circumstances warrant, the HRPP/IRB Director may bypass this step and assign the report for convened board review.
3. If the reviewer determines that the event or issue is not noncompliance or an UAP, they will review the event or issue, any proposed corrective and preventative action plans, and determine if any additional actions are needed to ensure the protection of human subjects. As warranted, the reviewer may refer the matter to the convened IRB for review. The results of the review will be communicated to the investigator.

17 Reporting to Federal Agencies, Departments, and Organizational Officials

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

17.1 Procedures

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

- Determines that an event may be considered an unanticipated problem involving risks to participants or others;

- Determines that noncompliance was serious or continuing; and/or
- Suspends or terminates approval of research.

The AREHS Director is responsible for preparing reports or letters which includes the following information: *(Note: this list is compiled from the reporting instructions listed on the websites of the OHRP and FDA).*

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

The IRB Chair and the IO review the letter and recommend modifications as needed. The IO is the signatory.

The AREHS Director or designee sends a copy of the report to:

- The IRB Chair;
- The IO; and
- Federal departments or agencies, as follows:
  --OHRP, if the study is subject to DHHS regulations or subject to a DHHS FWA.
  --If the study is conducted or supported by a Common Rule agency other than DHHS, the report is sent to OHRP or the head of the federal agency, as required by the agency, or
  --If the study is conducted or supported by a federal agency that has not adopted the Common Rule, and reporting is required, the report is sent to the party identified by the agency, and
  --FDA, if the study is subject to FDA regulations.
- Sponsor, if the study is sponsored;
- Investigator;

- Others as deemed appropriate by the IO.

Reports are not submitted to federal departments or agencies such as OHRP or FDA unless the research is subject to federal regulations or another mandate that necessitates such reporting. Note: Reporting to a regulatory agency is not required if the event occurred at a site that was not subject to the direct oversight of the organization, and the agency has been notified of the event by another party (e.g., sponsor).

OHRP and FDA expect timely reporting. Thirty (30) days is generally acceptable, or sooner for serious issues. A preliminary report may be submitted if additional time is needed.

The AREHS Director ensures that all steps of this policy are completed within thirty (30) working days of the determination. For more serious actions, the Director will expedite reporting. If additional time is needed to gather facts or determine corrective actions, a preliminary report will be submitted within thirty (30) days, to be followed by a final report as described above.

18 Obtaining Informed Consent from Research Subjects

The requirement to obtain the legally effective informed consent of individuals before involving them in research is one of the central protections provided for by the federal regulations and WTAMU HRPP. Investigators are required to obtain legally effective informed consent from a subject or the subject's LAR (See Section 18.3) unless the requirement has been waived by the IRB. When informed consent is required, it must be sought prospectively, and properly documented.

No investigator conducting research under the auspices of WTAMU may involve a human being as a subject in research without obtaining the legally effective informed consent of the subject or the subject's legally authorized representative (LAR) (See Section 18.3) unless a waiver of consent has been approved by the IRB of record. Except as provided in Sections 18.10, 18.11, and 18.12 of these procedures, informed consent must be documented using a written consent form approved by the IRB.

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

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

Informed consent is more than just a signature on a form. It is a process of information exchange to include reading, discussing, receiving answers to any questions, and signing the consent document. The informed consent process is the critical communication link between the prospective human subject and an investigator, beginning with the initial approach by an investigator and continuing through the completion of the research study. Investigators must

have received the appropriate training and be knowledgeable about the study procedures, potential risks, anticipated benefits, and alternatives in order that they may appropriately describe the research and answer questions. The exchange of information between the investigator and study participant can occur via one or more of the following modes of communication, among others; face to face dialogue; mail; electronic interface, telephone, or fax; however, obtaining informed consent must allow for a dialogue so that the potential subject has the opportunity to ask questions and receive responses. Investigators must obtain consent prior to entering a subject into a study, gathering data about a subject, and/or conducting any procedures required by the research plan, unless consent is waived by the IRB. See Section 18.10.1 for an exclusion for certain screening and recruitment activities.

If someone other than the investigator conducts the interview and obtains consent, the investigator needs to formally delegate this responsibility, and the person so delegated must have received appropriate training to perform this activity. The person so delegated must be knowledgeable about the research to be conducted and the consenting process, and must have the expertise be able to answer questions about the study including those regarding risks, procedures, and alternatives. The WTAMU IRB application solicits information regarding who will obtain consent; proposed changes to the personnel authorized to obtain consent must be submitted to the WTAMU IRB for approval.

Sample or draft consent documents may be developed by a sponsor or network. However, the IRB of record is the final authority on the content of the consent documents that are presented to prospective subjects.

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

18.1 General Requirements

Except as provided elsewhere in these Standard Operating Procedures:

1. Before involving a human subject in research, an investigator shall obtain the legally effective informed consent of the subject or the subject's LAR;
2. An investigator shall seek informed consent only under circumstances that provide the prospective subject or the LAR sufficient opportunity to discuss and consider whether or not to participate and that minimize the possibility of coercion or undue influence;
3. The information that is given to the subject or the LAR shall be in language understandable to the subject or the LAR;
4. The prospective subject or the LAR must be provided with the information that a reasonable person would want to have in order to make an informed decision about whether to participate, and an opportunity to discuss that information.
5. Except for broad consent (See Section 18.12):

a. Informed consent must begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject or LAR in understanding the reasons why one might or might not want to participate in the research. This part of the informed consent must be organized and presented in a way that facilitates comprehension;

b. Informed consent as a whole must present information in sufficient detail relating to the research, and must be organized and presented in a way that does not merely provide lists of isolated facts, but rather facilitates the prospective subject's or LAR's understanding of the reasons why one might or might not want to participate;

6. No informed consent may include any exculpatory language through which the subject or the LAR is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence.

18.2 Additional Requirements

Informed consent must be obtained under the following circumstances:

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

18.3 Legally Authorized Representative (LAR)

LAR means an individual recognized by state law and institutional policy as acceptable for providing consent in the nonresearch context on behalf of the prospective subject to the subject's participation in the procedure(s) involved in the research.

Who may serve as LAR is determined by state law. Texas law does not specifically address informed consent by LARs of incapacitated persons for participation in clinical research. Thus, the applicable guidelines for determining the most appropriate LAR for research are based upon the guidelines that apply in the clinical setting.

For legally incompetent adults who are unable to make medical decisions, a legal representative (court appointed guardian) or durable power of attorney for health care must provide informed consent for non-emergent medical treatment. The legal guardian must be authorized by the court to make decisions regarding the types of activities, procedures, or treatments called for in the research to serve as LAR.

When the WTAMU IRB serves as the IRB of record for external sites and the use of LARs is proposed, information regarding relevant state law and local policy will be sought (local context information) and applied.

LARs should be well informed regarding their roles and responsibilities when asked to provide surrogate consent. In addition to the consent information, LARs should be informed that their obligation is to try to determine what the potential subject would do if able to provide consent, or if the potential subject's wishes cannot be determined, what they think is in the person's best interest.

Investigators must describe the intended use of LARs in their submission to the IRB. The IRB determines whether the use of LARs is appropriate for a given research study.

Further discussion and procedures for assessment of capacity and inclusion of adults with impaired decision-making capacity in research are described in Section 19.7.

18.4 Basic Elements of Informed Consent

Note: This section does not apply for broad consent obtained as described in Section 18.12.

Informed consent must begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject or LAR in understanding the reason why one might or might not want to participate in the research.

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

1. A statement that the **study involves research**, an explanation of the **purposes** of the research and the **expected duration** of the subject's participation, a description of the **procedures** to be followed, and identification of any **procedures which are experimental**;
2. A description of any reasonably foreseeable **risks or discomforts** to the subject;
3. A description of any **benefits** to the subject or to others which may reasonably be expected from the research;
4. A disclosure of appropriate **alternative procedures** or courses of treatment, if any, that might be advantageous to the subject;

5. A statement describing the extent, if any, to which **confidentiality** of records identifying the subject must be maintained;
6. **For research involving more than minimal risk**, an explanation as to whether any compensation **and** an explanation as to whether any medical treatments are available if injury occurs **and**, if so, what they consist of, or where further information may be obtained;
7. An **explanation of whom to contact** for answers to pertinent questions about the research **and** research subjects' rights, **and** whom to contact in the event ofa research-related injury to the subject;
8. Contact information for the research team for questions, concerns, or complaints;
9. Contact information for someone independent of the research team for problems, concerns, questions, or input;
10. A statement that participation is **voluntary**, refusal to participate will involve **no penalty or loss of benefits** to which the subject is otherwise entitled, and the subject **may discontinue participation** at any time without penalty or loss of benefits to which the subject is otherwise entitled;
11. One of the following statements about any research that involves the **collection of identifiable private information or identifiable biospecimens**:
    a. A statement that **identifiers might be removed** from the identifiable private information or identifiable biospecimens **and that**, after such removal, the information or biospecimens **could be used** for future research studies or distributed to another investigator for future research studies **without additional informed consent** from the subject or the legally authorized representative, if this might be a possibility; or
    b. A statement that the subject's information or biospecimens collected as part of the research, even if identifiers are removed, **will not be used or distributed** for future research studies.
12. For **FDA-regulated studies**, a statement that notes the possibility that the Food and Drug Administration may inspect the records;
13. For **applicable NIH-funded and/or FDA-regulated clinical trials,** the following statement must be included verbatim (See NIH registration & dissemination policy):
    "A description of this clinical trial will be available on 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."

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

Note: This section does not apply for broad consent obtained as described in Section 18.12.

1. A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable;
2. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;
3. Any additional costs to the subject that may result from participation in the research;
4. When applicable, the amount and schedule of all payments;
5. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;
6. A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject;
7. The approximate number of subjects involved in the study;
8. A statement that the subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit;
9. A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions; and/or
10. For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen).

18.6 WTAMU Requirements

In addition to the federal elements of consent described above, WTAMU has defined specific additional information that must be included in consent documents when applicable to the research (e.g., 1099 language). A list of these requirements is provided on the IRB's website for investigator and reviewer reference.

18.7 Subject Withdrawal or Termination

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

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

request that the investigator or study sponsor will destroy the subject's data or that the investigator or study sponsor will exclude the subject's data from any analysis.

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

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

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

18.8 Documentation of Informed Consent

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

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

The consent form may be either of the following:

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

   or

2. A short form written consent document stating that the elements of informed consent have been presented orally to the subject or the subject's LAR and that the key information required by Section 18.1 #5.a was presented first to the subject, before other information, if any, was provided. When this method is used:
    a. The oral presentation and the short form written document should be in a language understandable to the subject; and
    b. There must be a witness to the oral presentation; and
    c. The IRB must approve a written summary of what is to be said to the subject (the approved full consent document may serve as this summary);and
    d. The short form document is signed by the subject; and
    e. The witness must sign both the short form and a copy of the summary; and
    f. The person actually obtaining consent must sign a copy of the summary; and
    g. A copy of the summary must be given to the subject or representative, in addition to a copy of the short form.

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

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

18.9 Special Consent Circumstances

18.9.1 Enrollment of persons with Limited English Proficiency

1. **Expected enrollment**: In some studies, the investigator may be able to anticipate enrollment of persons who do not speak or read, or have limited proficiency in, oral or written English. When the target subject population includes such persons or the investigator or the IRB otherwise anticipates that consent will be conducted in a language other than English, the IRB requires a translated consent document and other subject materials, as applicable. Generally, translated consent forms should not be prepared until the final approved version of the English-language version is available.
   To ensure that translated documents are accurate, the IRB may choose to require a certified translation, to have an independent back-translation, or to have a review of the translated documents by an IRB member or other person who is fluent in the language.

2. **Unexpected enrollment:** If a person who does not speak or read, or has limited proficiency in, English unexpectedly presents for possible enrollment, an IRB-approved translated version of the written consent may not be available for use. Investigators should carefully consider the ethical and legal ramifications of enrolling subjects when a language barrier exists. If the subject does not clearly understand the information presented during the consent process or in subsequent discussions, his/her consent may not be informed or legally effective.
   If an investigator decides to enroll a subject into a study for which there is not an extant IRB-approved consent document in the prospective subject's language, the investigator must receive IRB approval to follow the procedures for a "short form" written consent in as described in Section 18.8.
3. **Use of interpreters in the consent process:** Unless the person obtaining consent is fluent in the prospective subject's language, an interpreter will be necessary to facilitate the consent discussion. Preferably someone who is independent of the subject (i.e., not a family member) should assist in presenting information and obtaining consent. Whenever possible, interpreters should be provided copies of the translated consent, or short form and the IRB-approved consent script (typically the English-language version of the consent document), well before (24-to-48 hours, if possible) the consent discussion with the subject. The interpreter may not serve as the witness. The person obtaining consent must document that the "short form" process was used in the subject's research record, including the name of the interpreter.

18.9.2 Braille consent

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

18.9.3 Consenting in American Sign Language (ASL)

For deaf subjects who are fluent in ASL, the IRB may approve a consent process using ASL and the IRB-approved written consent form. When this process is approved, the individual authorized to consent prospective subjects must use a certified interpreter fluent in ASL to conduct the consent process and the documentation of the consent process must conform to the requirements set forth in Section 18.8.

18.9.4 Oral Consent

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

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

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

18.9.5 Physically-Challenged Subjects

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

18.10 Waiver or Alteration of Informed Consent

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

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

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

Likewise, an IRB may approve a consent procedure that omits some, or alters some or all, of the basic and additional elements of informed consent (an "alteration") (See Sections 18.4 and 18.5), provided that the IRB finds and documents that the below criteria are satisfied. An IRB

may not omit or alter any of the general requirements for informed consent (See Section 18.1). If a broad consent procedure is used, an IRB **may not** omit or alter any of the required elements of broad consent (See Section 18.12).

1. The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine:
    a. Public benefit or service programs;
    b. Procedures for obtaining benefits or services under those programs;
    c. Possible changes in or alternatives to those programs or procedures; or
    d. Possible changes in methods or levels of payment for benefits or services under those programs; and,
2. The research could not practicably be carried out without the waiver or alteration.

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

18.10.1 Screening, recruiting, or determining eligibility

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

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

18.11 Waiver of Documentation of Informed Consent

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

1. The only record linking the subject and the research would be the consent document and the principal risk would be potential harm from a breach of confidentiality (e.g., domestic violence research where the primary risk is discovery by the abuser). Subjects must be asked whether they want documentation linking them with the research, and their wishes must govern.
   This option **does not** apply to FDA-regulated research.

OR

2. The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context. Procedures such as non-sensitive surveys, questionnaires and interviews

generally do not require written consent when conducted by non-investigators (e.g., marketing surveys, telemarketing).

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

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

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

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

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

18.12 Elements of broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens

(Note: The general requirements for informed consent described in sections 18.1 also apply to broad consent and cannot be waived or altered.)

Informed consent must begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject or LAR in understanding the reason why one might or might not want to participate in the research.

Broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens (collected for either research studies other than the proposed research or non-research purposes) is permitted as an alternative to the informed consent requirements in Sections 18.4 and 18.5. If the subject or the legally authorized representative is asked to provide broad consent, the following shall be provided to each subject or the subject's legally authorized representative:

1. The following required information from Sections 18.4 and 18.5;
   a. A description of any reasonably foreseeable **risks or discomforts** to the subject;
   b. A description of any **benefits** to the subject or to others which may reasonably be expected from the research;
   c. A statement describing the extent, if any, to which **confidentiality** of records identifying the subject must be maintained;

d. A statement that participation is **voluntary**, refusal to participate will involve **no penalty or loss of benefits** to which the subject is otherwise entitled, and the subject **may discontinue participation** at any time **without penalty or loss of benefits** to which the subject is otherwise entitled;

e. For research involving biospecimens, a statement that the subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit;

f. For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen);

2. A general description of the types of research that may be conducted with the identifiable private information or identifiable biospecimens. This description must include sufficient information such that a reasonable person would expect that the broad consent would permit the types of research conducted;

3. A description of the identifiable private information or identifiable biospecimens that might be used in research, whether sharing of identifiable private information or identifiable biospecimens might occur, and the types of institutions or researchers that might conduct research with the identifiable private information or identifiable biospecimens;

4. A description of the period of time that the identifiable private information or identifiable biospecimens may be stored and maintained (which period of time could be indefinite), and a description of the period of time that the identifiable private information or identifiable biospecimens may be used for research purposes (which period of time could be indefinite);

5. Unless the subject or LAR will be provided details about specific research studies, a statement that they will not be informed of the details of any specific research studies that might be conducted using the subject's identifiable private information or identifiable biospecimens, including the purposes of the research, and that they might have chosen not to consent to some of those specific research studies;

6. Unless it is known that clinically relevant research results, including individual research results, will be disclosed to the subject in all circumstances, a statement that such results may not be disclosed to the subject; and

7. An explanation of whom to contact for answers to questions about the subject's rights and about storage and use of the subject's identifiable private information or identifiable biospecimens, and whom to contact in the event of a research-related harm.

Investigators must include information regarding the circumstances under which broad consent will be obtained, the proposal for tracking of responses, and the proposed consent form(s) (or oral script if a waiver of documentation of consent is sought) and any other consent materials

(e.g., information sheet, audiovisual materials, etc.) in their submission to the IRB. The WTAMU IRB will review the information provided with the aid of a checklist to ensure that all requirements are satisfied. The outcome of the IRB's review will be communicated to the investigator in writing following the procedures described elsewhere in this manual.

When investigators propose research involving the use of identifiable private information and/or identifiable biospecimens research for which broad consent was obtained, the investigators must include documentation of the IRB approval for the storage or maintenance of the information or specimens and a copy of the consent form and/or other materials. The WTAMU IRB will review the information provided with the aid of a checklist to ensure that all requirements are satisfied. The outcome of the IRB's review will be communicated to the investigator in writing following the procedures described elsewhere in this manual.

18.13 Posting of Clinical Trial Consent Forms

For each applicable 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 ((Clinicaltrials.gov/ or a docket folder on Regulations.gov (Docket ID: HHS-OPHS-2018-0021)).

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.

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

19 Vulnerable Subjects in Research

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

19.1 Definitions

Children. Children are persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted [45 CFR 46.402(a)].

According to Texas State Law, minors are persons under the age of eighteen. The general rule is that a person may sign legally-binding agreements and consent for his or her own medical care at the age of eighteen. Therefore, WTAMU IRB defines children as persons who are under eighteen years of age. Certain statutes and case law, however, provide minors with "majority" status in some circumstances, giving them the right to consent to their own medical care. Texas law enumerates certain categories of individuals who, although under the age of 18, have the right to make medical decisions on their own behalf, such as minors who are married, widowed or divorced, minors who are parents, etc. Texas law also permits minors to seek care for drug addiction, sexually transmitted diseases, emotional disorders, or abortion or mental health treatment without parental permission. Because Texas law does not specifically address consent of children with majority status to research, the WTAMU IRB will review issues of consent related to enrollment of these children in research on a case-by-case basis and in conjunction with TAMUS OGC.

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

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

In Texas, a “Guardian” of a child means a court-appointed person with the duty and authority to act in the best interests of the minor, subject to residual parental rights and responsibilities, to make important decisions in matters having a permanent effect on the life and development of the minor and to be concerned with his or her general welfare.

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

Fetus. A fetus means the product of conception from implantation until delivery [45 CFR 46.202(c)].

Dead fetus. A fetus that exhibits neither heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, nor pulsation of the umbilical cord [45 CFR 46.202(a)].

Delivery. Delivery means complete separation of the fetus from the woman by expulsion or extraction or any other means [45 CFR 46.202(b)].

Neonate. A neonate is a newborn [45 CFR 46.202(d)].

Viable. As it pertains to the neonate, viable means being able, after delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration [45 CFR 46.202(h)]. If a neonate is viable, then, for the purposes of participation in research, the neonate is considered a child and the rules regarding participation of children in research apply.

Nonviable neonate. A nonviable neonate means a neonate after delivery that, although living, is not viable [45 CFR 46.202(e)].

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

Prisoner. Prisoner means any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures that provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing [45 CFR 303(c)].

19.2 Involvement of Vulnerable Populations in Research

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

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

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

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

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

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

19.3 Procedures

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

Initial Review of Research Proposal:

1. The investigator identifies the potential to enroll vulnerable subjects in the proposed research at initial review and provides the justification for their inclusion in the study;
2. The investigator describes safeguards to protect the subject's rights and welfare in the research proposal;
3. IRB staff, in collaboration with the IRB Chair as needed, ensure that the IRB has the relevant expertise with the vulnerable population, and, if necessary, arrange for consultation. When the research involves no more that minimal risk and is eligible for expedited review, the designated reviewer may determine the need for additional expertise to ensure the protection of the vulnerable population(s);
4. The IRB evaluates the proposed inclusion of vulnerable population(s) in the research and the safeguards proposed by the investigator, taking into consideration the following factors, as applicable to the research:
    a. Whether inclusion of vulnerable populations is ethically and scientifically appropriate;
    b. Whether the proposed plans, including the settings and circumstances, for the identification and recruitment of subjects, and for obtaining consent or parental permission, ensure equitable selection of subjects and promote voluntariness;
    c. Whether the proposed research confers any direct benefit, whether the benefit is available outside of the research, and whether access to the benefit may unduly influence participation by vulnerable populations;
    d. Whether any costs or plans for subject reimbursement or compensation, may exclude or unduly influence participation by vulnerable populations;
    e. Whether the provisions for privacy and confidentiality adequately protect vulnerable populations; and
    f. Other relevant considerations as appropriate for the population(s) and the circumstances of the research.
5. When applicable, the IRB considers any costs associated with participation in the proposed research and any plans for reimbursement of expenses or provision of compensation, and the potential impact of such on the vulnerable population(s);
6. The IRB evaluates the research to determine whether the proposed plan is adequate or if additional protections are needed such as interim monitoring, review more than annually, or the use of a data and safety monitoring board, consent monitor, or research subject advocate.

Modifications to Research

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

Continuing Review

1. At continuing review, the investigator should identify the number and categories of vulnerable subjects enrolled and any problems that arose relevant to their rights and welfare. When research does not include any interaction or intervention with subjects, and such information is not gathered, this should be noted on the continuing review report;
2. IRB staff, in collaboration with the IRB Chair as needed, ensure that the IRB has the relevant expertise with the vulnerable population, and, if necessary, arrange for consultation. When the research involves no more that minimal risk and is eligible for expedited review, the designated reviewer may determine the need for additional expertise to ensure the protection of the vulnerable population(s);
3. The IRB reviews the continuing review information, and any relevant information reported to the IRB during the period of approval, and determines whether the inclusion of vulnerable populations and the plans to protect the rights and welfare of vulnerable subjects remains appropriate.

19.4 Research Involving Pregnant Women, Human Fetuses and Neonates

The following applies to all research involving pregnant women, human fetuses, and neonates reviewed by the WTAMU IRB. DHHS-specific requirements are noted in the appropriate sections.

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

19.4.1 Research Involving Pregnant Women or Fetuses

WTAMU voluntarily applies 45 CFR Subpart B to all non-exempt human subject research involving pregnant women, fetuses, and neonates.

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

1. Where scientifically appropriate, pre-clinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been

conducted and provide data for assessing potential risks to pregnant women and fetuses;

2. The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important generalizable knowledge which cannot be obtained by any other means;
3. Any risk is the least possible for achieving the objectives of the research;
4. If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, then the consent of the pregnant woman is obtained in accord with the provisions for informed consent;
5. If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accord with the provisions for informed consent, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest;
6. Each individual providing consent under paragraph 4 or 5 of this section is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;
7. For children (as defined in Section 19.1) who are pregnant, assent and permission are obtained in accord with the provisions of permission and assent in Section 19.6.2;
8. No inducements, monetary or otherwise, will be offered to terminate a pregnancy;
9. Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and
10. Individuals engaged in the research will have no part in determining the viability of a neonate.

19.4.2 Research Not Otherwise Approvable

19.4.2.1 Research Conducted or Supported by DHHS

DHHS-conducted or supported research that falls in this category must be approved by the Secretary of Health and Human Services. If the IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates; and the research is not approvable under the above provisions, then the research will be sent to OHRP for DHHS review.

19.5 Research Involving Prisoners

19.5.1 Applicability

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

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

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

19.5.2 Minimal Risk

Minimal risk, in studies involving prisoners, means the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons.

19.5.3 Composition of the IRB

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

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

19.5.4 Review of Research Involving Prisoners

Initial Review of Research Proposal

1. The prisoner representative must review research involving prisoners, focusing on the requirements outlined in Subpart C and these policies;
2. The prisoner representative must receive all review materials pertaining to the research (same as primary reviewer); and

3. The prisoner representative must be present at a convened meeting when the research involving prisoners is reviewed. If the prisoner representative is not present, research involving prisoners cannot be reviewed or approved. The prisoner representative may attend the meeting by phone, video-conference, or webinar, so long as the representative is able to participate in the meeting as if they were present in person at the meeting.
4. The IRB must be familiar with the specific conditions in the local prison(s) or jail site(s) that are pertinent to subject protections, before approving the proposal for the local site (45 CFR 46.107(a)).

Modifications to Research

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

Continuing Review

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

Expedited Review

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

19.5.5 Incarceration of Enrolled Subjects

1. If a subject becomes a prisoner while enrolled in a research study that was not reviewed according to these procedures, the investigator must promptly notify the IRB and the IRB shall:
    a. Confirm that the subject meets the definition of a prisoner;
    b. Consult with the investigator to determine if it is in the best interests of the subject to continue participation in the study, in part or in full, and if so, if there are specific study activities which are in the best interests of the subject that should continue until the IRB is able to review the research applying the standards and requirements for research involving prisoners.
2. If the subject should continue, one of two options are available:
    a. Keep the subject enrolled in the study and review the research applying the standards and requirements for research involving prisoners. If some of the requirements cannot be met or are not applicable (e.g., procedures for the selection of subjects within the prison), but it is in the best interests of the subject to remain in the study, keep the subject enrolled and, if the research is DHHS-conducted or supported, inform OHRP of the decision along with the justification; or
    b. Remove the subject from the study and keep the subject on the study intervention under an alternate mechanism such as compassionate use or off-label use.
3. If a subject is incarcerated temporarily while enrolled in a study:
    a. If the temporary incarceration has no effect on the study (i.e., there is no need for study activities involving the prisoner subject to take place during the temporary incarceration), keep the subject enrolled, or
    b. If the temporary incarceration has an effect on the study, follow the guidance outlined above.

19.5.6 Additional Duties of the IRB

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

1. The research falls into one of the following **permitted categories** [45CFR46.306(a)(2)]:
    a. Study of the possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;
    b. Study of prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;

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

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

e. The research qualifies under the HHS Secretarial waiver that applies to certain epidemiological research (68 FR 36929, June 20, 2003). The criteria for this category are that the research must have as its sole purpose (i) to describe the prevalence or incidence of a disease by identifying all cases, or (ii) to study potential risk factor associations for a disease.

2. Any possible advantages accruing to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired;
3. The risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers;
4. Procedures for the selection of subjects within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the investigator provides to the IRB justification in writing for following some other procedures, control subjects must be selected randomly from the group of available prisoners who meet the characteristics needed for that particular research proposal;
5. The information is presented in language which is understandable to the subject population;
6. Adequate assurance exists that parole boards will not take into account a prisoner's participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole; and
7. Where the IRB finds there may be a need for follow-up examination or care of subjects after the end of their participation, adequate provision has been made for such

examination or care, taking into account the varying lengths of individual prisoners' sentences, and for informing subjects of this fact.

19.5.7 Certification to DHHS

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

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

Under its authority at 45 CFR 46.115(b), OHRP requires that the institution responsible for the conduct of the proposed research also submit to OHRP a copy of the research proposal so that OHRP can determine whether the proposed research involves one of the categories of research permissible under 45 CFR 46.306(a)(2), and if so, which one.

The term "research proposal" includes:

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

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

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

19.6 Research Involving Children

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

funded research and Subpart D of 21 CFR 50, which applies to FDA-regulated research involving children.

19.6.1 Allowable Categories

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

1. **Research not involving greater than minimal risk** [45 CFR 46.404/21 CFR 50.51]. Research determined to not involve greater than minimal risk to child subjects may be approved by the IRB only if the IRB finds and documents that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians as set forth in Section 19.6.2.
2. Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subj [45 CFR 46.405/21 CFR 50.52]. Research in which the IRB finds that more than minimal risk to children is presented by an intervention or procedure that holds out the prospect of direct benefit for the individual subject, or by a monitoring procedure that is likely to contribute to the subject's well-being, may be approved by the IRB only if the IRB finds and documents that:
    a. The risk is justified by the anticipated benefit to the subjects;
    b. The relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative options; and
    c. Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians as set forth in Section 19.6.2.
3. Research involving greater than minimal risk and no prospect of direct benefit to the individual subject, but likely to yield generalizable knowledge about the subject's disorder or condition [45 CFR 46.406/21 CFR 50.53]. Research in which the IRB finds that more than minimal risk to children is presented by an intervention or procedure that does not hold out the prospect of direct benefit for the individual subject, or by a monitoring procedure which is not likely to contribute to the well-being of the subject, may be approved by the IRB only if the IRB finds and documents that:
    a. The risk represents a minor increase over minimal risk;
    b. The intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations;

c. The intervention or procedure is likely to yield generalizable knowledge about the subjects' disorder or condition which is of vital importance for the understanding or amelioration of the subjects' disorder or condition; and

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

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

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

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

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

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

        ii. The following:

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

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

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

19.6.2 Parental Permission and Assent

19.6.2.1 Parental Permission

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

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

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

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

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

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

1. The research meets the provisions for waiver in Section 18.10; or
2. For research that is not FDA-regulated, if the IRB determines that the research is designed to study conditions in children or a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children) provided that an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted, and that the waiver is not inconsistent with Federal, State, or local law. The choice of an appropriate mechanism would depend upon the nature and purpose of the activities described in the protocol/research plan, the risk and anticipated benefit to the research subjects, and the child's age, maturity, status, and condition.

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

~~19.6~~22 Assent from Children

The IRB is responsible for determining that adequate provisions are made for soliciting the assent of the children, when in the judgment of the IRB the children are capable of providing assent. This judgment may be made for all children to be involved in the study, or for each child, as the IRB deems appropriate.

If the IRB determines that the capability of some or all of the children is so limited that they cannot reasonably be consulted or that the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research, the assent of the children is not a necessary condition for proceeding with the research. Even where the IRB determines that the subjects are capable of assenting, the IRB may still waive the assent requirement under circumstances in which consent may be waived in accordance with the applicable regulations. It is important to note that the FDA regulations do permit the IRB to waive the assent requirement if it finds and documents that:

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

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

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

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

Documentation of Assent

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

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

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

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

19.6.3 Children who are Wards

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

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

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

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

19.7 Adults with Impaired Decision-Making Capacity

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

with the development and review of research involving adults with impaired decision-making capacity.

19.7.1 Informed Consent

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

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

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

19.7.2 Decision-Making Capacity

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

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

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

Decision-making capacity is protocol and situation-specific. Thus, a person may have capacity to consent to participate in low risk research in usual circumstances, but not have the capacity

to consent to a higher risk protocol when s/he is under significant stress or faced with unfamiliar circumstances.

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

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

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

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

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

When a prospective subject is deemed to lack capacity to consent to participate in research, investigators may obtain informed consent from the individuals' surrogate or LAR (See Section 18.3). Under these circumstances, the prospective subject should still be informed about the research in a manner compatible with the subjects' likely understanding and, if possible, be

asked to assent to participate. Potential subjects who express resistance or dissent (by word, gesture, or action) to either participation or use of surrogate consent, should be excluded from the study. Some subjects may initially assent but later resist participation. Under no circumstances may an investigator or caregiver override a subject's dissent or resistance. When assent is possible for some or all subjects, the investigator should provide the IRB with an assent plan that describes when and how assent will be obtained, provisions that will be taken to promote understanding and voluntariness, how assent will be documented, and a copy of the assent form. If the investigator intends to use audio or video recordings to document assent, provisions to ensure the security of the recordings should be described to the IRB.

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

19.7.4 IRB Review

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

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

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

1. Whether the aims of the research cannot reasonably be achieved without inclusion of the population;
2. Whether the research is likely to improve the understanding of the condition, disease, or issue affecting the subject population;
3. Whether any experimental procedure or interventions have undergone pre-clinical testing or human testing on other populations and whether the data from that testing supports its use in the proposed research;

4. Whether the procedures or interventions that the subject will undergo in the research place them at increased risk and whether appropriate mechanisms are in place to minimize risks, when possible;
5. Whether the data and safety monitoring plan, including any stopping rules, is appropriate given the risks of the research and the vulnerability of the population;
6. Whether the procedures for withdrawing individual subjects from the research are appropriate;
7. Whether the recruitment procedures, consent process, and any plans for financial compensation support voluntariness and minimize the likelihood of undue influence or coercion;
8. Whether the subjects will be exposed to financial or other risks that they might not consider acceptable if they had the capacity to provide consent, and whether appropriate mechanisms have been put into place to minimize these risks;
9. Whether the procedures for determining capacity to provide consent, and for evaluating capacity on an ongoing basis, if applicable, are appropriate;
10. Whether the procedures for informing subjects who regain capacity about their involvement in the research, and for obtaining consent for on-going participation, if applicable, are appropriate;
11. Whether assent should be required when possible, and, if so, if the proposed procedures to obtain and document assent are appropriate;
12. Whether periodic re-evaluation of capacity and/or periodic re-consent should be required; and
13. Whether a research subject advocate or consent monitor should be required, for some or all subjects.

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

19.8 RESERVED

(Organizations should include additional sections describing procedures for research involving other vulnerable populations that the IRB reviews on a regular basis. For example, research involving employees, students, refugees, undocumented workers, mental health patients under involuntary holds, economically or educationally disadvantaged persons, etc.).

20 Investigator Responsibilities

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

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

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

20.1 Responsibilities

Investigators who conduct research involving human subjects must:

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

d. Adequate facilities;

e. Necessary equipment;

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

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

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

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

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

20.1.1 Record Retention

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

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

1. **OHRP** – Research records must be retained for at least three (3) years after the completion of the research.
2. **HIPAA** – Research authorizations, or documentation of waivers or alterations of authorization, must be held for a minimum of six (6) years after the authorization or waiver/alterations was last obtained or in effect, whichever is later.
3. **FDA – Drugs** (& biologics classified as drugs) - These must be held for a period of two (2) years following the date a marketing application is approved for the drug for the indication for which it is being investigated; or, if no application is to be filed or if the application is not approved for such indication, until 2 years after the investigation is discontinued and FDA is notified.
4. **FDA – Devices** (& biologics classified as devices) - These must be held for a period of two (2) years after the latter of the following two dates: The date on which the investigation is terminated or completed, or the date that the records are no longer required for purposes of supporting premarket approval application or a notice of

completion of a product development protocol.

20.2 Investigator Concerns

Investigators who have concerns regarding the conduct of research at WTAMU, WTAMU's HRPP or IRB, or the external IRBs WTAMU relies upon should convey them to the AREHS Director, the IRB Chair, or the IO. The recipient of the concern will consider the issue, and when deemed necessary, seek additional information and convene the parties involved to form a response for the investigator or make necessary procedural or policy modifications, as warranted. In addition, the IRB Chair and AREHS Director are available to address investigators' questions, concerns, and suggestions.

Anyone with concerns may also report via ethicspoint.

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

Sponsored Research

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

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

20.3 Definitions

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

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

20.4 Responsibility

Sponsor grants, contracts, and other written agreements will be reviewed for the following by Sponsored Research Services (SRS), with consultation with the IRB, as necessary:

1. When appropriate, Sponsor agreements will contain terms that address medical care for research participants with a research-related injury. (Usually only clinical trials agreements.)
2. In studies where Sponsors conduct research site monitoring visits or conduct monitoring activities remotely, the Sponsor agreements contain terms addressing the requirement

for the Sponsor to promptly report to WTAMU findings that could affect the safety of participants or influence the conduct of the study.

3. When the Sponsor has the responsibility to conduct data and safety monitoring, the Sponsor agreements contain terms that address provisions for monitoring the data to ensure the safety of participants and for providing data and safety monitoring reports to WTAMU.
4. Sponsor agreements will address plans for disseminating findings from the research and the roles that investigators and Sponsors will play in the publication or disclosure of results.
5. When participant safety could be directly affected by study results after the study has ended, the Sponsor agreements will require the Sponsor to inform the investigator or WTAMU of the results in order to consider informing participants.

21 Conflict of Interest in Research

It is WTAMU policy to preserve public trust in the integrity and quality of research by reducing actual or perceived conflict of interest in the conduct of research.

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

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

21.1 Researcher Conflicts of Interest

WTAMU follows Conflict of Interest regulation TAMUS 15.01.03 and WTAMU procedure 15.01.03.W1 to ensure that the research and educational activities are conducted in a manner free from bias resulting from conflict of interest. The WTAMU IRB will collaborate with the WTAMU COI Official to ensure that COI of investigators and research team members (investigators) are identified and managed before the IRB completes its review of any research application. The Vice President of Research and Compliance/ acts as COI Official concerning the WTAMU Institutional Review Board.

21.1.1 Procedures

21.1.1.1 Disclosure of Researcher COI

For IRB purposes, investigator conflict review occurs at the time of new study submission, continuing review (if applicable), with the addition of a new investigator, and whenever an

investigator updates their WTAMU COI disclosure indicating a new or changed interest. AREHS staff notify the COI Official whenever a submission requiring conflict review is received. The COI Official reviews the investigators' disclosures and either notifies the AREHS staff that no investigator COI was identified or that one or more investigators has an interest that requires evaluation by the COI Official. In the event a conflict that requires disclosure or management is identified, the COI Official will provide the IRB a written summary describing the conflict and the conflict management plan (CMP). If the COI Official has not completed the review, the internal IRB will defer the research study review or prohibit participation by the researcher with a potential COI until the COI review process is completed and the results are made available to the IRB. When the research is under an external IRB, any conflicts identified as the result of COI review and any CMP are provided to the external IRB in accordance with the IRB reliance agreement.

21.1.12 Evaluation of COI

The IRB will review COIs and CMPs to determine:

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

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

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

21.1.13 Management of COI

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

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

1. Disclosure of the COI to subjects through the consent process;
2. Modification of the research plan or safety monitoring plan;
3. Monitoring of research by a third party;

4. Disqualification of the conflicted party from participation in all or a portion of the research;
5. Appointment of a non-conflicted PI;
6. Divestiture of significant financial interests; and/or
7. Severance of relationships that create actual or potential conflicts.

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

21.2 IRB Member Conflict of Interest

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

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

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

1. Involvement in the design, conduct, and reporting of the research;
2. Significant financial interests (See TAMUS regulation 15.01.03 and WTAMU procedure 15.01.03.W1 for a definition of significant financial interests related to the research being reviewed; or
3. Any other situation where an IRB member believes that another interest conflicts with his or her ability to deliberate objectively on a study.

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

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

21.3 Institutional Conflict of Interest

Pursuant to TAMUS regulation 15.01.03 and WTAMU procedure 15.01.03.W1 on Institutional Conflicts of Interest, the WTAMU COI Official may appoint a Conflict of Interest Review Committee (CIRC) to assist in the determination of whether a COI exists. As a matter of procedure, WTAMU will not participate in a human subjects' research project when it has an institutional financial interest. An exception to this policy may be made only when the COI Official determines that circumstances exist to merit an exception and a conflict management plan is adopted to maintain research integrity and serve the best interests of participants enrolled in the research. WTAMU's AREHS Office and IRBs collaborate with the COI Official to ensure that institutional COI is identified and managed before the IRB completes its review of any research application.

22 Participant Outreach

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

The following procedures describe how WTAMU fulfils that responsibility.

22.1 Evaluation

On an annual basis, WTAMU evaluates its outreach activities and makes changes when appropriate. In order to formally evaluate its outreach activities, the AREHS Director will review:

1. The specific community outreach activities being used;
2. Whether or not these community outreach activities have an evaluative component (e.g., evaluation instrument distributed to participants), and if so whether the feedback was positive, negative, or neutral and if any suggestions were made that could be used to enhance future activities;
3. The number of times the participants' website is visited;
4. Feedback provided via the feedback mechanism on the website; and
5. Feedback provided from other sources (unaffiliated IRB members, investigators, research staff, students, etc.).

The results of the review will be used to establish both the adequacy of current outreach activities and any additional resources that may be needed to meet the needs of the research community regarding participant outreach.

23 Student Research

23.1 Human Subject Research and Course Projects

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

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

23.1.1 Responsibility of the Course Instructor:

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

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

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

In making a determination of whether or not a class research project requires IRB review, the instructor is encouraged to contact the AREHS office for assistance or to submit an email describing the proposed work to AR-EHS@wtamu.edu for a determination.

23.1.2 Individual Research Projects Conducted by Students

When students conduct, or participate as a research team member, in human subjects research, other than class work as described above, they must follow the standard procedures for research described throughout this manual, as applicable to the research. As described in Section 1.9.5, students may not serve as PI on human subjects research conducted under the auspices of WTAMU but may serve as a co-investigator or member of the research team. When students of WTAMU conduct, or participate as a research team member, in research at or with another organization, they must contact the WTAMU AREHS office to determine if review by the WTAMU IRB is required, or if a reliance agreement is needed, prior to engaging in the activity. It is important to keep in mind that any human subject research activity that will ultimately contribute to part or all of a thesis, dissertation, or other type of publication or presentation must go through the IRB review process prior to enrolling subjects and collecting data. IRB review/approval cannot occur after a study has begun.

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

24 Special Topics

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

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

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

24.1 Definitions

Authorization. An individual's written permission to allow a covered entity to use or disclose specified PHI for a particular purpose. Except as otherwise permitted by the Privacy Rule, a

covered entity may not use or disclose PHI for research purposes without a valid Authorization that includes all of the required elements under the Privacy Rule.

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

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

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

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

Health Information. Health Information means any information, including genetic information, whether oral or recorded in any form or medium, that (1) is created or received by a health care provider, health plan, public health authority, employer, life insurer, school or university, or health care clearinghouse; and (2) relates to the past, present, or future physical or mental health or condition of an individual; the provision of health care to an individual; or the past, present, or future payment for the provision of health care to an individual.

Individually Identifiable Health Information. Information that is a subset of health information, including demographic information collected from an individual, and (1) is created or received by a health care provider, health plan, employer, or health care clearinghouse; and (2) relates to the past, present, or future physical or mental health or condition of an individual; the provision of health care to an individual; or the past, present, or future payment for the provision of health care to an individual; and (a) that identifies the individual; or (b) with respect to which there is a reasonable basis to believe the information can be used to identify the individual.

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

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

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

Protected Health Information. Protected Health Information (PHI) means individually identifiable health information that is transmitted by electronic media; maintained in electronic media; or transmitted or maintained in any other form or medium. PHI excludes individually identifiable health information in education records covered by the Family Educational Rights and Privacy Act (FERPA), as amended, 20 U.S.C. 1232g; in records described at 20 U.S.C. 1232g(a)(4)(B)(iv); in employment records held by a covered entity in its role as employer; and regarding a person who has been deceased for more than fifty (50) years.

Psychotherapy Notes. Psychotherapy notes means notes recorded (in any medium) by a health care provider who is a mental health professional documenting or analyzing the contents of conversation during a private counseling session or a group, joint, or family counseling session and that are separated from the rest of the individual's medical record. Psychotherapy notes excludes medication prescription and monitoring, counseling session start and stop times, the modalities and frequencies of treatment furnished, results of clinical tests, and any summary of the following items: Diagnosis, functional status, the treatment plan, symptoms, prognosis, and progress to date.

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

24.1.1 Effects of HIPAA on Research

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

24.1.1.1 Authorized Use

Except as otherwise permitted, the Privacy Rule requires that a research subject "authorize" the use or disclosure of his/her PHI to be utilized in the research. This authorization is distinct from the subject's consent to participate in research, which is required under the Common Rule and FDA regulations. Just as a valid consent under Common Rule and FDA regulations must meet certain requirements, a valid authorization must contain certain core elements (45 CFR 164.508(c)). The subject must authorize specifically what research information may be shared and who will receive the information, must acknowledge the expiration of the authorization and have the right to revoke the authorization, and must be informed that further disclosure by recipients of the information may not be covered by the federal privacy rules. The subject's right to revoke authorization is limited. The investigator and the institution may continue to use and disclose PHI that was obtained before the subject revoked authorization to the extent that the investigator or institution has acted in reliance on the authorization, such as to use or disclose PHI in order to maintain the integrity of the research (45CFR164.508(b)(5)(i)).

24.1.1.2 Waiver of Authorization

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

24.1.1.3 De-Identified PHI

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

The Privacy Rule allows a covered entity to de-identify data by removing all 18 elements that could be used to identify the individual or the individual's relatives, employers, or household members; these elements are enumerated in the Privacy Rule. The covered entity also must have no actual knowledge that the remaining information could be used alone or in combination with other information to identify the individual who is the subject of the information. Under this method, the identifiers that must be removed are the following:

1. Names;
2. All geographic subdivisions smaller than a state, including street address, city, county, precinct, ZIP Code, and their equivalent geographical codes, except for the initial three digits of a ZIP Code if, according to the current publicly available data from the Bureau of the Census:

a. The geographic unit formed by combining all ZIP Codes with the same three initial digits contains more than 20,000 people;

b. The initial three digits of a ZIP Code for all such geographic units containing 20,000 or fewer people are changed to 000.

3. All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death; and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older;
4. Telephone numbers;
5. Facsimile numbers;
6. Electronic mail addresses;
7. Social security numbers;
8. Medical record numbers;
9. Health plan beneficiary numbers;
10. Account numbers;
11. Certificate/license numbers;
12. Vehicle identifiers and serial numbers, including license plate numbers;
13. Device identifiers and serial numbers;
14. Web universal resource locators (URLs);
15. Internet protocol (IP) address numbers;
16. Biometric identifiers, including fingerprints and voiceprints;
17. Full-face photographic images and any comparable images; and/or
18. Any other unique identifying number, characteristic, or code, unless otherwise permitted by the Privacy Rule for re-identification.

Covered entities may also use statistical methods to establish de-identification instead of removing all 18 identifiers. The covered entity may obtain certification by "a person with appropriate knowledge of and experience with generally accepted statistical and scientific principles and methods for rendering information not individually identifiable" that there is a "very small" risk that the information could be used by the recipient to identify the individual who is the subject of the information, alone or in combination with other reasonably available information. The person certifying statistical de-identification must document the methods used as well as the result of the analysis that justifies the determination. A covered entity is required to keep such certification, in written or electronic format, for at least six (6) years from the date of its creation or the date when it was last in effect, whichever is later.

24.11.4 Limited Data Set

The Privacy Rule permits a covered entity, without obtaining an Authorization or documentation of a waiver or an alteration of Authorization, to use and disclose PHI included in a limited data set. A covered entity may use and disclose a limited data set for research if the disclosing covered entity and the limited data set recipient enter into a data use agreement. Because limited data sets may contain identifiable information, they are still PHI.

A limited data set is described as health information that excludes certain, listed direct identifiers (see below) but that may include city; state; ZIP Code; elements of date; and other numbers, characteristics, or codes not listed as direct identifiers. The direct identifiers listed in the Privacy Rule's limited data set provisions apply both to information about the individual and to information about the individual's relatives, employers, or household members. The following identifiers must be removed from health information if the data are to qualify as a limited data set:

1. Names;
2. Postal address information, other than town or city, state, and ZIP Code;
3. Telephone numbers;
4. Fax numbers;
5. Electronic mail addresses;
6. Social security numbers;
7. Medical record numbers;
8. Health plan beneficiary numbers;
9. Account numbers;
10. Certificate/license numbers;
11. Vehicle identifiers and serial numbers, including license plate numbers;
12. Device identifiers and serial numbers;
13. Web universal resource locators (URLs).
14. Internet protocol (IP) address numbers;
15. Biometric identifiers, including fingerprints and voiceprints; or
16. Full-face photographic images and any comparable images.

A data use agreement is the means by which covered entities obtain satisfactory assurances that the recipient of the limited data set will use or disclose the PHI in the data set only for specified purposes.

24.1.1.5 Activities Preparatory to Research

For activities involved in preparing for research, covered entities may use or disclose PHI to a researcher without an individual's Authorization, a waiver or an alteration of Authorization, or a data use agreement. However, the covered entity must obtain from a researcher representations that (1) the use or disclosure is requested solely to review PHI as necessary to prepare a research protocol or for similar purposes preparatory to research, (2) the PHI will not be removed from the covered entity in the course of review, and (3) the PHI for which use or access is requested is necessary for the research. The covered entity may permit the researcher to make these representations in written or oral form.

24.1.1.6 Research on Decedents' Protected Health Information

To use or disclose PHI of the deceased for research, covered entities are not required to obtain Authorizations from the personal representative or next of kin, a waiver or an alteration of the Authorization, or a data use agreement. However, the covered entity must obtain from the researcher who is seeking access to decedents' PHI (1) oral or written representations that the use and disclosure is sought solely for research on the PHI of decedents, (2) oral or written representations that the PHI for which use or disclosure is sought is necessary for the research purposes, and (3) documentation, at the request of the covered entity, of the death of the individuals whose PHI is sought by the researchers.

24.2 IRB Review of Medical Records Research

24.2.1 Exempt Research

Research involving medical records is exempt provided the records utilized in the research are existing and the data are recorded in such a manner that participants cannot be identified (e.g., either all 18 HIPAA specified identifiers are removed or a biostatistical consult indicated there is only a “small risk” of re-identification of a participant).

24.2.2 Non-Exempt Research

For research that is not exempt (expedited or full review required) the IRB will require documentation that the investigator is authorized by the covered entity to receive PHI under one of the above HIPAA provisions described above.

24.3 Databases, Registries, & Repositories

Databases, registries, and biospecimen repositories (all referred to as repositories throughout this section) are used to store data and/or biospecimens for future use.

There are two types of repositories:

1. Non-research repositories created and maintained for purposes that are unrelated to research. Such purposes may include diagnosis, treatment, billing, marketing, quality control, and public health surveillance; and
2. Research repositories created and maintained specifically for research purposes. Such purposes may include databases to identify prospective subjects, patient outcome information to evaluate treatment effectiveness, and tissues samples for future research. Non-research repositories that are altered to facilitate research (e.g., through the addition of data fields not necessary for the core purpose of the repository) are considered research repositories.

24.3.1 Non-research Repositories

Even though repositories were not created for research purposes, they may contain information that is of great interest to researchers. The creation (or operation) of non-research databases or repositories does not involve human subject research and does not require IRB oversight. However, IRB approval is required for the research use of identifiable private information or identifiable human specimens from non-research repositories, and, regardless of identifiability, when specimens will be used to evaluate the safety or effectiveness of a medical device. Research under the auspices of WTAMU that includes the use of coded private information or specimens, must either be submitted for IRB review or for a "Human Subjects and Research Determination" (See Section 8).

Researchers submitting an application for research using data or specimens from non-research repositories must describe the source of the data/specimens and any terms, conditions, or restrictions on use. Data/specimens cannot be used for research if the person from whom the data/specimens originated objected to its use for research. Informed consent and HIPAA authorization (when applicable) must be obtained unless the IRB determines that the criteria for a waiver are satisfied.

24.3.2 Research Repositories

Research repositories involve three distinct activities:

- Collection of data/specimens;
- Storage and management of data/specimens; and
- Distribution of data/specimens.

Collection

Informed consent (See Broad Consent, Section 18.12, when applicable) and HIPAA authorization (when applicable) must be obtained unless the IRB determines that the criteria for a waiver are satisfied.

Informed Consent information should include:

- A clear description of

- What data/specimens will be collected;
- Where the data/specimens will be stored, who will have access, and how the data/specimens will be secured;
- Whether the data/specimens will be identifiable, coded, or de-identified;
- The types of research to be conducted and any limitations or restrictions on such; and
- The conditions under which data/specimens will be released to recipient-investigators.

- A statement regarding future withdrawal of the data from the study (i.e., state whether subjects may, in the future, request that their data be destroyed or that all personal identifiers be removed from data and how to make such a request); and
- When appropriate, the plan for management of incidental findings and sharing of results.

Storage and Management

Repositories should have written policies describing:

- The conditions under which data/specimens will be accepted (e.g., inclusion criteria);
- Informed consent;
- IRB review;
- The sources of data/specimens;
- Whether data/specimens will be identifiable, coded, or de-identified and, if coded, management of the linkage key; and
- Physical and procedural mechanisms for the secure receipt, storage, and distribution of data/specimens.

Distribution

Repositories should have written policies describing:

- How data/specimens may be requested and by whom;
- Any requirements associated with a request for data/specimens (e.g., verification of IRB approval or that approval is not required);
- Any limitations or restrictions on how data/specimens may be used;
- Whether released data/specimens will be identifiable, coded, or de-identified, and, if coded, any circumstances under which recipient investigators will access to or be provided with the key or other means to re-identify; and
- Agreements with recipient investigators specifying the terms of use.

24.3.3 IRB Oversight

IRB approval is required for the establishment and operation of a research repository when the data/specimens that are accessed, received, stored, or distributed are identifiable. In general, private information or specimens are considered individually identifiable when the identities of the subjects are known to investigators/repository operators or when the data/specimens can be linked to specific individuals either directly or indirectly through coding systems.

Separate IRB approval is required for the use of data/specimens from a repository when the recipient investigator(s) know or may readily ascertain the identity of individual subjects, and, regardless of identifiability, when specimens will be used to evaluate the safety or effectiveness of a medical device. Research under the auspices of WTAMU that includes the use of coded private information or specimens, must either be submitted for IRB review or for a "Human Subjects and Research Determination" (See Section 8). The only exception to this policy is when the coded private information or specimens are to be obtained from an IRB-approved repository and the rules of that repository forbid the release of identifiable information, the release of the key to the code or other means that would allow re-identification, or the release of sufficient information that investigators could readily ascertain the identity of subjects.

24.4 Transnational Research

The WTAMU IRB reviews transnational research involving human subjects to ensure that adequate provisions are in place to protect the rights and welfare of the subjects. All policies and procedures that are applied to research conducted domestically are applied to research in international settings, as appropriate. Approval of research is permitted if *"the procedures prescribed by the foreign institution afford protections that are at least equivalent to those provided in 45 CFR 46."*

For federally conducted or supported research, approval of research for foreign institutions or sites "engaged" in research is only permitted if the foreign institution or site holds a FWA with OHRP and local IRB review and approval is obtained.

Approval of research for foreign institutions or sites "not engaged" in research is only permitted if one or more of the following circumstances exist:

1. When the foreign institution or site has an established IRB/EC, the investigator must obtain approval to conduct the research at the "not engaged" site from the site's IRB/EC or provide documentation that the site's IRB/EC has determined that approval is not necessary for the investigator to conduct the proposed research at the site;
2. When the foreign institution or site does not have an established IRB/EC, a letter of cooperation must be obtained demonstrating that the appropriate institutional or oversight officials permit the research to be conducted at the performance site; or
3. IRB approval to conduct research at the foreign institution or site is contingent upon receiving documentation of the performance site's IRB/EC determination, or letter of cooperation, as applicable.

The WTAMU IRB seeks sufficient knowledge of the local research context by requesting approval for the project from local IRBs or ethics committees (which may or may not be OHRP-registered) and/or local letters of support. The source of this information will depend on the nature of the study, on the country, and on the resources available to the investigator. Where there is a local IRB/EC, WTAMU IRB must receive and review the foreign institution or site's IRB/EC review and approval of each study prior to beginning the research at the foreign institution or site.

In settings where there are no IRBs/ECs, WTAMU IRB may require additional verification and information from people outside the particular research project who are familiar with the customs, practices, or standards of care where the research will be taking place, including other IRBs or committees with experience reviewing research in the region, other WTAMU investigators with knowledge of the region, or a consultant who is an expert on the region, prior to approval. These individuals may either provide a written review of the research protocol or attend an IRB meeting to provide the WTAMU IRB with recommendations based on his or her expertise.

24.4.1 IRB Responsibilities

In addition to the IRB review considerations discussed elsewhere in this manual, the IRB will consider the following when reviewing transnational research:

1. The qualifications of the investigator and research staff to conduct research in that country including knowledge of relevant laws, regulations, guidance and custom;
2. Whether the consent process and consent documents are appropriate for the language(s) of the subjects and the subject population, and that arrangements are made to be able to communicate with subjects throughout the study (e.g., to ask and answer questions);
3. How modifications to the research will be handled;
4. How complaints, noncompliance, protocol deviations and unanticipated problems involving risks to subjects or others are handled;
5. How post-approval monitoring will be managed;
6. Whether the investigator has obtained the appropriate host country permissions to conduct research (e.g., institutional, governmental or ministerial, IRB, local, or tribal). When appropriate, the IRB communicates and coordinates with the local institutions or ethics committees; and
7. Mechanisms for communicating with the investigators and research staff when they are conducting the research in other countries.

24.4.2 Investigator Responsibilities

The investigator conducting transnational research is responsible for:

1. Ensuring that the resources and facilities are appropriate for the nature of the research;

2. Verifying the qualifications of the investigators and research staff for conducting research in the country(ies);
3. Obtaining all appropriate host country permissions to conduct research (e.g., institutional, governmental or ministerial, IRB, local, or tribal);
4. Complying with the requirements of country law; including, when applicable, requirements for research involving investigational articles and requirements for data management and privacy such as EU GDPR;
5. Ensuring that the consent process and consent document are appropriate for the language(s) of the subjects and the subject population, and that arrangements are made to be able to communicate with subjects throughout the study (e.g., to ask and answer questions);
6. Ensuring that the following activities will occur;
    - Initial review, continuing review, and review of modifications;
    - Post-approval monitoring of the conduct of the research in accordance with the plan approved by the IRB; and
    - Handling of complaints, noncompliance and unanticipated problems involving risk to subjects or others;
    - Not relying upon an IRB or EC that does not have policies and procedures for the activities listed above;
    - Ensuring that reportable information such as complaints, noncompliance, protocol deviations and unanticipated problems involving risks to participants or other are communicated to the IRB;
    - Notifying the IRB promptly if a change in research activities alters the performance site's engagement in the research (e.g., performance site "not engaged" begins to obtain consent of research participants, etc.); and
    - Ensuring that there are mechanisms for communicating with the IRB when they are conducting the research in other countries.

24.4.3 Consent Documents

The informed consent documents must be appropriate for and in a language understandable to the proposed subjects. The IRB will review the proposed document and a back translation of the exact content contained in the foreign language informed consent document, with the credentials of the translator detailed in the IRB application or Closeout/Amendment/Continuation form. All documents, including verification of the back translation, are maintained in the IRB file.

24.4.4 Monitoring of Approved Transnational Research

The IRB is responsible for the ongoing review of international research conducted under its jurisdiction through the continuing review process in accordance with all applicable federal regulations. When the IRB and a local ethics committee are both involved in the review of research, there is a plan for coordination and communication with the local IRB/ECs.

The IRB requires documentation of regular correspondence between the WTAMU investigator and the foreign institution or site and may require verification from sources other than the WTAMU investigator that there have been no changes made to the research since its last review.

24.5 FDA-Regulated Research

24.5.1 When do FDA regulations apply?

FDA's research regulations may apply when a protocol is studying or evaluating one or more FDA-regulated products, even when the data or specimens may have been generated for other purposes (e.g., clinical care) or are anonymized. FDA research regulations generally do not apply when a marketed FDA-regulated product (such as an MRI) is being used in a manner consistent with its labeling as a tool to gather or generate data in research that is evaluating a hypothesis that is not about the product itself. Because FDA regulates such a broad range of products, from band-aids to medical apps and other software to neurostimulators, and the nuances of the regulations are complex, investigators are encouraged to consult with the IRB office in advance of any application to the IRB that involves the evaluation or off-label use of a medical or health product.

FDA regulations apply to research that involves an FDA-regulated *test article* in a *clinical investigation* involving *human subjects* as defined by the FDA regulations, and per the definitions below. For FDA-regulated research, the IRB must apply the FDA regulations at 21 CFR 50 and 21 CFR 56. If the research is conducted or supported by a Common Rule agency or department, or if compliance with the Common Rule is required by state law or the terms of an award or contract, then the Common Rule must also be applied.

The following procedures describe the review of FDA-regulated research by the WTAMU IRB.

24.5.2 Definitions

Clinical Investigation. Clinical investigation means any experiment that involves a test article and one or more human subjects, and that either is subject to the requirements for prior submission to the FDA under section 505(i) or 520(g) of the Federal Food, Drug, and Cosmetic Act ("Act"), or is not subject to the requirements for prior submission to the FDA under these sections of the Act, but the results of which are intended to be later submitted to, or held for inspection by, the FDA as part of an application for a research or marketing permit. The terms research, clinical research, clinical study, study, and clinical investigation are synonymous for purposes of FDA regulations. [21 CFR 50.3(c), 21 CFR 56.102(c)]

Experiment. Experiment means any use of a drug other than the use of an approved drug in the course of medical practice [21 CFR 312.3(b)] or any activity that evaluates the safety or effectiveness of a medical device. [21 CFR 812.2(a)]

Human Subject. For research covered by FDA regulations (21 CFR 50, 21 CFR 56), human subject means an individual who is or becomes a participant in a clinical investigation (as defined above), either as a recipient of the test article or as a control. A subject may be in normal health or may have a medical condition or disease. In the case of a medical device, a human subject/participant also includes any individual on whose tissue specimen an investigational device is used or tested. Importantly, the FDA regulations do not exclude unidentified specimens.

Investigational Drug. Investigational *or* experimental drugs are new drugs that have not yet been approved by the FDA or approved drugs that are being studied in a clinical investigation.

Investigational Device. Investigational device means a device (including a transitional device) that is the object of an investigation. Investigation, as it pertains to devices, means a clinical investigation or research involving one or more subjects to determine the safety or effectiveness of a device.

Test Article. *Test article* means any drug for human use, biological product for human use, medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the Federal Food, Drug, and Cosmetic Act, as amended (secs. 201-902, 52 Stat. 1040 *et seq.,* as amended (21 U.S.C. 321-392)) or under sections 351 and 354-360F of the Public Health Service Act [42 U.S.C. 262 and 263b-263n]. [21 CFR 50.3(j)]

Test articles covered under the FDA regulations include, but are not limited to:

1. **Human drugs** – A drug is defined as a substance recognized by an official pharmacopoeia or formulary; a substance intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease; a substance (other than food) intended to affect the structure or any function of the body; a substance intended for use as a component of a medicine but not a device or a component, part or accessory of a device. Biological products are included within this definition and are generally covered by the same laws and regulations, but differences exist regarding their manufacturing processes (chemical process versus biological process). The primary intended use of a drug product is achieved through chemical action or by being metabolized by the body.
2. **Medical Devices** - A device is "an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is: recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them; intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals; or intended to affect the structure or any function of the body of man or other animals, and which does not achieve any of its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes."

3. **Biological Products** - include a wide range of products such as vaccines, blood and blood components, allergenics, somatic cells, gene therapy, tissues, and recombinant therapeutic proteins. Biologics can be composed of sugars, proteins, or nucleic acids or complex combinations of these substances, or may be living entities such as cells and tissues. Biologics are isolated from a variety of natural sources — human, animal, or microorganism — and may be produced by biotechnology methods and other cutting-edge technologies. Gene-based and cellular biologics, for example, often are at the forefront of biomedical research, and may be used to treat a variety of medical conditions for which no other treatments are available.
4. **Dietary Supplements** – A dietary supplement is a product taken by mouth that is intended to supplement the diet and that contains one or more "dietary ingredients." The "dietary ingredients" in these products may include vitamins, minerals, herbs or other botanicals, amino acids, and other substances found in the human diet, such as enzymes. When a dietary supplement meets the definition of drug, it is regulated as such.
5. **Medical Foods** – A medical food, as defined in section 5(b) of the Orphan Drug Act(21 U.S.C. 360ee (b) (3)), is a food which is formulated to be consumed or administered enterally under the supervision of a physician and which is intended for the specific dietary management of a disease or condition for which distinctive nutritional requirements, based on recognized scientific principles, are established by medical evaluation.
6. **Mobile Medical Apps** - Mobile apps are software programs that run on smartphones and other mobile communication devices. They can also be accessories that attach to a smartphone or other mobile communication devices, or a combination of accessories and software. Mobile Medical Apps are medical devices that are (a) mobile apps, (b) meet the definition of a medical device and (c) are either an accessory to a regulated medical device or transform a mobile platform into a regulated medical device.
7. **Radioactive Drugs** – The term radioactive drug means any substance defined as a drug which exhibits spontaneous disintegration of unstable nuclei with the emission of nuclear particles or photons and includes any nonradioactive reagent kit or nuclide generator which is intended to be used in the preparation of any such substance but does not include drugs such as carbon-containing compounds or potassium-containing salts which contain trace quantities of naturally occurring radionuclides. The term "radioactive drug" includes "radioactive biological product".
8. **Radiation-Emitting Electronic Products** - a radiation-emitting electronic product as any electrically-powered product that can emit any form of radiation on the electromagnetic spectrum. These include a variety of medical and non-medical products such as mammography devices, magnetic resonance imaging (MRI) devices, laser toys, laser pointers, liquid crystal displays (LCDs), and light emitting diodes(LEDs).

24.5.3 FDA Exemptions

The following categories of clinical investigations are exempt from the requirements of FDA regulations for IRB review:

1. Emergency use of a test article, provided that such emergency use is reported to the IRB within 5 working days. Any subsequent use of the test article at the institution is subject to IRB review; [21 CFR §56.104(c)]
2. Taste and food quality evaluations and consumer acceptance studies, if wholesome foods without additives are consumed or if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural, chemical, or environmental contaminant at or below the level found to be safe, by the FDA or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture. [21 CFR§56.104(d)]

24.5.4 Procedures

1. At initial submission, the PI must indicate whether the research involves the administration or evaluation of an FDA-regulated product on the application form.
2. During the pre-review process, the AREHS Director will confirm whether FDA regulations are applicable using the FDA Determination Checklist. If FDA regulations apply, the AREHS Director will obtain any additional information needed from the investigator (e.g., justification for why an IND is not required) and indicate on the agenda or in pre- review comments that the protocol is an FDA-regulated study.
3. The IRB, or designated reviewer, will review the research in accordance with the following requirements and the same criteria it would use in considering approval of any research involving an FDA-regulated product. [21 CFR 50 and 21 CFR 56]

24.5.5 Clinical Investigations of Articles Regulated as Drugs or Devices

24.5.5.1 IND Exemptions

For drugs, an IND is not necessary if the research falls in one of the following seven (7) categories:

1. 21 CFR 312.2(b)(1): The drug being used in the research is lawfully marketed in the United States and all of the following requirements are met:
    a. The research is not intended to be reported to FDA as a well-controlled study in support of a new indication and there is no intent to use it to support any other significant change in the labeling of the drug;
    b. In the case of a prescription drug, the research is not intended to support a significant change in the advertising for the product;

c. The research does not involve a route of administration, dose, subject population, or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product;

d. The research is conducted in compliance with the requirements for IRB review and informed consent [21 CFR parts 56 and 50, respectively];

e. The research is conducted in compliance with the requirements of 21 CFR312.7 (i.e., the research is not intended to promote or commercialize the drug product); and

f. The research does not intend to invoke FDA regulations for planned emergency research [21 CFR 50.24].

Please Note: FDA has provided specific guidance for evaluating whether this exemption applies to studies of marketed drugs/biologics for the treatment of cancer.

2. 21 CFR 312.2(b)(2): For clinical investigations involving defined (blood grouping serum, reagent red blood cells, and anti-human globulin) in vitro diagnostic biological products, an IND is not necessary if a) it is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established, diagnostic product or procedure; and b) it is shipped in compliance with 21 CFR312.160.

3. 21 CFR 312.2(b)(5): A clinical investigation involving use of a placebo is exempt from the requirements of part 312 if the investigation does not otherwise require submission of an IND.

4. 21 CFR 320.31(b) and (d): Bioavailability or Bioequivalence (BA/BE) studies if all of the following conditions are met:

   a. The drug product does not contain a new chemical entity [21 CFR 314.108], is not radioactively labeled, and is not cytotoxic;

   b. The dose (single dose or total daily dose) does not exceed the dose specified in the labeling of the approved version of the drug product;

   c. The investigation is conducted in compliance with the requirements for IRB review and informed consent [21 CFR parts 56 and 50, respectively]; and

   d. The sponsor meets the requirements for retention of test article samples [21CFR 320.31(d)(1)] and safety reporting [21 CFR 320.31(d)(3)].

5. 21 CFR 361.1: Research using a radioactive drug or biological product if all of the following conditions are met:

   a. It involves basic research not intended for immediate therapeutic, diagnostic, or similar purposes, or otherwise to determine the safety and efficacy of the product;

   b. The use in humans is approved by a Radioactive Drug Research Committee (RDRC) that is composed and approved by FDA;

c. The dose to be administered is known not to cause any clinically detectable pharmacological effect in humans; and

d. The total amount of radiation to be administered as part of the study is the smallest radiation dose practical to perform the study without jeopardizing the benefits of the study and is within specified limits.

6. FDA practices enforcement discretion for research using cold isotopes of unapproved drugs if all of the following conditions are met:

   a. The research is intended to obtain basic information regarding the metabolism (including kinetics, distribution, and localization) of a drug labeled with a cold isotope or regarding human physiology, pathophysiology, or biochemistry;

   b. The research is not intended for immediate therapeutic, diagnostic, or preventive benefit to the study subject;

   c. The dose to be administered is known not to cause any clinically detectable pharmacologic effect in humans based on clinical data from published literature or other valid human studies;

   d. The quality of the cold isotope meets relevant quality standards; and

   e. The investigation is conducted in compliance with the requirements for IRB review and informed consent. [21 CFR parts 56 and 50, respectively]

If the FDA has already determined whether an IND is required, documentation evidencing such should be provided to the IRB. The FDA's determination is final and the IRB does not have to make the determination.

When the FDA has not made a determination, the sponsor or investigator is responsible for providing the IRB with justification explaining why, in their opinion, an IND is not required and any other information that may help the IRB in evaluating the IND status of the study.

The IRB will review the information provided by the sponsor and investigator including, but not limited to: the sponsor or investigator's IND assessment, the drug labeling (for marketed drugs), reports of prior investigations of the drug (if applicable), the proposed investigational plan, subject selection criteria, and the drug accountability plan. If the study entails greater than minimal risk, a plan for Data and Safety Monitoring must be included. When the IRB determines that an IND is required, or is uncertain if an IND is needed, the IRB will require evaluation by the FDA prior to approving the study. When an IND is required or when otherwise appropriate (e.g., the IRB lacks the needed expertise), WTAMU may require review by an external IRB.

24.5.5.2 Dietary Supplements

Research involving dietary supplements may or may not fall under FDA regulations. Under the Dietary Supplement Health and Education Act (DSHEA) of 1994, a dietary supplement is not considered a drug and is not subject to the premarket approval requirements for drugs if the intended use for which it is marketed is only to affect the structure or any function of the body (i.e., not intended to be used for a therapeutic purpose). Whether a study falls under FDA

oversight is determined by the intent of the clinical investigation. If the clinical investigation is intended only to evaluate the dietary supplement's effect on the structure or function of the body, FDA research regulations do not apply. However, if the study is intended to evaluate the dietary supplement's ability to diagnose, cure, mitigate, treat, or prevent a disease, then FDA regulations do apply. Studies involving the ingestion of dietary supplements that are not subject to FDA oversight are still research, and therefore must be reviewed by the IRB.

Similarly, whether an IND is needed for a study evaluating a dietary supplement is determined by the intent of the study. If the study is intended only to evaluate the dietary supplement's effect on the structure or function of the body, an IND is not required. However, if the study is intended to evaluate the dietary supplement's ability to diagnose, cure, mitigate, treat, or prevent a disease, an IND is required under part 312.

As with any research involving a test article, the investigator must supply the IRB with sufficient information to determine that the criteria for approval are satisfied and to determine or verify whether the research requires an IND. Applications should provide detail consistent with that expected on a drug protocol and consistent with the level of risk associated or anticipated with the research. At a minimum, the research plan should provide the following information regarding the supplement: Name, Manufacturer, Formulation, Dosage, Method/Route of Administration, Mechanism of Action, Known Drug Interactions, Risk Profile, IND number (or justification for why an IND is unnecessary), documentation of approval for use in humans, documentation or certification of Quality or Purity. As with drugs and devices there should be an accountability plan for the product describing where the product will be stored and how it will be dispensed, usage tracked, and disposal or return. If the study entails greater than minimal risk, a plan for Data and Safety Monitoring must be included.

24.5.5.3 IDE Exemptions

For clinical investigations of medical devices, an IDE is not necessary if:

1. The research involves a device, other than a transitional device, in commercial distribution immediately before May 28, 1976, when used or investigated in accordance with the indications in labeling in effect at that time;
2. The research involves a device other than a transitional device, introduced into commercial distribution on or after May 28, 1976, that FDA has determined to be substantially equivalent to a device in commercial distribution immediately before May 28, 1976, and that is used or investigated in accordance with the indications in the labeling FDA reviewed under subpart E of 21 CFR 807 in determining substantial equivalence (a "510k" device);
3. The research involves a diagnostic device, if the sponsor complies with applicable requirements in 21 CFR 809.10(c) and if the testing:
    a. Is noninvasive,
    b. Does not require an invasive sampling procedure that presents significant risk,
    c. Does not by design or intention introduce energy into a subject, and

d. Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure.

4. The research involves a device undergoing consumer preference testing, testing of a modification, or testing of a combination of two or more devices in commercial distribution, if the testing is not for the purpose of determining safety or effectiveness and does not put subjects at risk;
5. The research involves a device intended solely for veterinary use;
6. The research involves a device shipped solely for research on or with laboratory animals and labeled in accordance with 21 CFR 812.5(c);
7. The research involves a custom device as defined in 21 CFR 812.3(b), unless the device is being used to determine safety or effectiveness for commercial distribution.

If the FDA has already determined a study to be IDE exempt, documentation evidencing such should be provided to the IRB. The FDA's determination is final and the IRB does not have to make the device determination.

Unless the FDA has already issued a determination, the IRB will review studies that the sponsor or investigator have put forth as IDE-exempt to determine if the study is IDE-exempt.

The sponsor or sponsor-investigator is responsible for providing the IRB with an explanation describing the basis for their initial determination of IDE-exempt and any other information that may help the IRB in evaluating the IDE status of the study.

The IRB will review the information provided by the sponsor and investigator including, but not limited to: the sponsor or investigator's IDE-exempt assessment, the description of the device, reports of prior investigations of the device (if applicable), the proposed investigational plan, subject selection criteria, and the device accountability plan. If the study entails greater than minimal risk, a plan for Data and Safety Monitoring must be included. When the IRB determines that a study is not IDE-exempt, it will inform the investigator and may require submission of additional information to support its evaluation of whether the study is Significant or Non-Significant Risk or may require evaluation by the FDA. The IRB will not finalize approval of a medical device study until the device determination is made.

24.5.4 Significant and Non-Significant Risk Device Studies

A device study is a Non-Significant Risk (NSR) Device study if it is not IDE-exempt and does not meet the definition of a Significant Risk (SR) Device study.

Under 21 CFR 812.3(m), an SR device means an investigational device that:

1. Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject;
2. Is purported or represented to be for use supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject;

3. Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or
4. Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

If the FDA has already determined a study to be SR or NSR, documentation evidencing such should be provided to the IRB. The FDA's determination is final and the IRB does not have to make the device determination.

Unless the FDA has already made a device determination for the study, the IRB will review studies that the sponsor or investigator have put forth as NSR at a convened meeting to determine if the device represents SR or NSR.

The sponsor or sponsor-investigator is responsible for providing the IRB with an explanation describing the basis for their initial determination of NSR and any other information that may help the IRB in evaluating the risk of the study (e.g., reports of prior investigations of the device).

The IRB will review the information provided by the sponsor and investigator including, but not limited to: the sponsor or investigator's NSR assessment, the description of the device, reports of prior investigations of the device (if applicable), the proposed investigational plan, subject selection criteria, and the device accountability plan. If the study entails greater than minimal risk, a plan for Data and Safety Monitoring must be included.

The NSR/SR determination made by the IRB will be based on the proposed use of the device in the investigation, not on the device alone. The IRB will consider the nature of any harms that may result from use of the device, including potential harms from additional procedures subjects would need to undergo as part of the investigation (e.g., procedures for inserting, implanting, or deploying the device). The IRB may consult with the FDA or require the sponsor or investigator to obtain a determination from the FDA. The IRB will document the SR or NSR determination and the basis for it in the meeting minutes and provide the investigator, and sponsor when applicable, with the determination in writing. When a study is determined to be SR or when otherwise appropriate (e.g., the IRB lacks the needed expertise), WTAMU may require review by an external IRB. SR device studies cannot begin until an IDE is obtained from the FDA and IRB approval is finalized.

Non-significant risk device studies do not require submission of an IDE application to the FDA but must be conducted in accordance with the abbreviated requirements of IDE regulations (21 CFR 812.2(b)). Under the abbreviated requirements, the following categories of investigations are considered to have approved applications for IDE's, unless FDA has notified a sponsor under 21 CFR 812.20(a) that FDA approval of an application is required:

1. An investigation of a device other than a significant risk device, if the device is not a banned device and the sponsor (or sponsor-investigator):
    a. Labels the device in accordance with 21 CFR812.5;

b. Obtains IRB approval of the investigation after presenting the reviewing IRB with an explanation of why the device is not a significant risk device, and maintains such approval;

c. Ensures that each investigator participating in an investigation of the device obtains from each subject under the investigator's care, informed consent under part 50 and documents it, unless the requirement is waived by the IRB;

d. Complies with the requirements of 812.46 with respect to monitoring investigations;

e. Maintains the records required under 812.140(b) (4) and (5) and makes the reports required under 812.150(b) (1) through (3) and (5) through(10);

f. Ensures that participating investigators maintain the records required by 812.140(a)(3)(i) and make the reports required under 812.150(a) (1), (2), (5), and (7);

and

g. Complies with the prohibitions in 812.7 against promotion and other practices.

24.5.6 Investigator Responsibilities

The investigator holds additional responsibilities when conducting a clinical investigation subject to FDA regulations. These responsibilities include, but are not limited to, the following:

1. The investigator is responsible for indicating on the IRB application that the proposed research is FDA-regulated and for providing relevant information regarding the test article.
2. The investigator is responsible for ensuring that a clinical investigation is conducted according to the signed investigator statement for clinical investigations of drugs (including biological products) or agreement for clinical investigations of medical devices, the investigational plan and other applicable regulations, and any requirements imposed by the FDA or IRB.
3. The investigator is responsible for personally conducting or supervising the investigation. When study-related tasks are delegated by an investigator, the investigator is responsible for providing adequate supervision of those to whom tasks are delegated. The investigator is accountable for regulatory violations resulting from failure to adequately supervise the conduct of the clinical study.
4. The investigator must maintain a list of the appropriately qualified persons to whom significant trial-related duties have been delegated. This list should also describe the delegated tasks, identify the training that individuals have received that qualifies them to perform delegated tasks (e.g., it can refer to an individual’s CV on file and/or training conducted by the investigator or sponsor), and identify the dates of involvement in the study. An investigator should maintain separate lists for each study conducted by the investigator.

5. The investigator is responsible for protecting the rights, safety, and welfare of subjects under their care during a clinical trial. This responsibility includes:
    a. Informing subjects that the test articles is being used for investigational purposes and ensuring that the requirements relating to obtaining informed consent are met;
    b. Providing or arranging for reasonable medical care for study subjects for medical problems arising during participation in the trial that are, or could be, related to the study intervention;
    c. Providing reasonable access to needed medical care, either by the investigator or by another identified, qualified individual (e.g., when the investigator is unavailable, or when specialized care is needed);
    d. Adhering to the protocol so that study subjects are not exposed to unreasonable risks; and,
    e. As appropriate, informing the subject's primary physician about the subject's participation in the trial if the subject has a primary physician and the subject agrees to the primary physician being informed.
6. The investigator is responsible for reading and understanding the information in the investigator brochure or device risk information, including the potential risks and side effects of the drug or device.
7. The investigator is responsible for maintaining adequate and accurate records in accordance with FDA regulations and to making those records available for inspection by the FDA. These records include, but are not limited to: correspondence with other investigators, the IRB, the sponsor, monitors, or the FDA; drug and device accountability records; case histories; consent forms; and documentation that consent was obtained prior to any participation in the study. Records must be obtained for a minimum of two (2) years following the date a marketing application is approved for the drug for the indication for which it is being investigated; or, if no application is to be filed or if the application is not approved for such. For clinical investigations of medical devices, required records must be maintained for a period of two (2) years after the latter of the following two dates: The date on which the investigation is terminated or completed, or the date that the records are no longer required for purposes of supporting a premarket approval application or a notice of completion of a product development protocol. Other regulations, such as HIPAA, organizational policies, or contractual agreements with sponsors may necessitate retention for a longer period of time.
8. The investigator is responsible for controlling test articles according to FDA regulations and the Controlled Substances Act, if applicable.
9. For research reviewed by the WTAMU IRB, the investigator proposing the clinical investigation will be required to provide a plan – to be evaluated by the IRB - that includes storage, security, and dispensing of the test article.

a. The investigator is responsible for investigational drug accountability that includes storage, security, dispensing, administration, return, disposition, and records of accountability. Such details will be provided in the IRB submission and reviewed by the IRB for acceptability.

b. The investigator may delegate in writing, as part of the IRB submission, the responsibility detailed in 'a' above.

c. Investigational drugs and devices must be labeled in accordance with federal and state standards.

d. All devices received for a study must be stored in a locked environment under secure control with limited access. When applicable, proper instructions on the use of the device must be provided to the subjects. A log must be kept regarding the receipt, use, and/or dispensing of the device, and the disposition of remaining devices at the conclusion of the investigation.

10. The investigator shall furnish all reports required by the sponsor of the research including adverse events, progress reports, safety reports, final reports, and financial disclosure reports.

11. The investigator will permit inspection of research records by the sponsor, sponsor representatives, HRPP and IRB representatives, the FDA, accrediting bodies, and any other agencies or individuals entitled to inspect such records under regulation, organizational policy, or contractual agreement.

24.6 Lead Investigator/Coordinating Center

When WTAMU IRB is serving as the IRB of record for a PI or site who is serving as the lead investigator or lead/coordinating center of a multi-site or collaborative research project, the PI must describe within the protocol and IRB application how the research will be overseen and how issues relevant to the protection of human subjects (e.g., IRB initial and continuing approvals, study modifications, reports of unanticipated problems, interim results, data-safety monitoring, etc.) will be coordinated and communicated among participating sites and investigators. For FDA-regulated clinical trials, the plan should address the plan for study monitoring and for the reporting and evaluation of adverse events, significant new risk information, and any other reports mandated by regulation or policy.

The lead PI or lead/coordinating center is responsible for serving as the liaison with other participating sites and investigators and for ensuring that all participating investigators obtain IRB review and approval prior to initiating the research, maintain approval, and obtain IRB approval for modifications to the research. The WTAMU IRB will evaluate whether the plan for research oversight and management of information that is relevant to the protection of human subjects is adequate.

24.7 Certificates of Confidentiality

Certificates of Confidentiality (CoC) protect research information by prohibiting certain disclosures and conditioning others upon consent from the subject. The protections and requirements of CoCs are outlined in 42 U.S.C. 241(d) and in written policies and requirements of certain Federal agencies such as NIH and CDC and are summarized below.

CoC's are obtained as follows:

- CoCs are issued automatically when research is conducted or supported by NIH and falls within the scope of the NIH policy;
- CoCs are issued automatically when research is conducted or supported by the CDC and involves the collection of identifiable, sensitive information;
- Research that is not supported by NIH or CDC may still have the protections afforded by CoCs through successful application to the NIH, FDA, HRSA, SAMHSA, or other authorized Federal agencies or departments.

Additional information about CoCs and the application process for research not covered by the NIH policy is available on the NIH CoC Website.

24.7.1 Definitions

Identifiable, sensitive information means information that is about an individual and that is gathered or used during the course of biomedical, behavioral, clinical, or other research and:

1. Through which an individual is identified; or
2. For which there is at least a very small risk, as determined by current scientific practices or statistical methods, that some combination of the information, a request for the information, and other available data sources could be used to deduce the identity of an individual.

24.7.2 Protections and Requirements

When a CoC is issued, whether automatically or under an approved application, the person(s) engaged in the research must not disclose or provide the name of a subject or any information, document, or biospecimen that contains identifiable, sensitive information about the subject and that was compiled for the purposes of the research:

1. In any Federal, State, or local civil, criminal, administrative, legislative, or other proceeding, unless the disclosure is made with the consent of the individual to whom the information, document, or biospecimen pertains; or
2. To any other person not connected with the research, unless:
    a. Required by Federal, State, or local laws (e.g., adverse event reporting to the FDA, transmissible disease reporting required under State law), but excluding proceedings as described in "1" above;

b. Necessary for the medical treatment of the subject to whom the information, document, or biospecimen pertains and made with the consent of the subject;

c. Made with the consent of the individual to whom the information, document, or biospecimens pertains; or

d. Made for the purposes of other scientific research that is in compliance with applicable Federal regulations governing the protection of human subjects in research.

Additional Protections

Identifiable, sensitive information protected under a CoC, and all copies thereof, are immune from the legal process, and shall not, without the consent of the of the individual to whom the information pertains, be admissible as evidence or used in any action, suit, or other judicial, legislative, or administrative proceeding.

Identifiable, sensitive information that has been collected under a CoC, and all copies thereof, are protected for perpetuity. If identifiable, sensitive information covered by a CoC is shared with other researchers or organizations, the researchers or organizations must be informed that the information is covered by a CoC and of their responsibility to protect the information accordingly.

Nothing in the rule (42 U.S.C. 241(d)) may be construed to limit the access of a subject to information about himself or herself collected during the research.

When consent is obtained, the consent should inform subjects that a CoC is in place and describe the protections and limitations.

24.7.3 NIH and CDC

The NIH Policy on CoCs applies to *"all biomedical, behavioral, clinical, or other research funded wholly or in part by the NIH, whether supported through grants, cooperative agreements, contracts, other transaction awards, or conducted by the NIH Intramural Research Program, that collects or uses identifiable, sensitive information"* that was commenced or ongoing on or after December 13, 2016.

The CDC requirements for CoCs apply to *"CDC supported research commenced or ongoing after December 13, 2016 and in which identifiable, sensitive information is collected, as defined by Section 301(d)."*

CoCs are automatically granted, and the requirements of such must be complied with, whenever a NIH or CDC funded activity falls within the scope of the NIH policy or CDC's requirements. Investigators and institutions are responsible for determining when research with NIH or CDC support are covered by a CoC.

NIH and CDC expand upon 42 U.S.C. 241(d) by explaining that NIH and CDC consider research in which identifiable, sensitive information is collected or used, to include:

- Human subjects research as defined in 45 CFR 46, including research determined to be exempt (except for exempt research when the information obtained is recorded in such

a manner that human subjects cannot be identified or the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects);

- Research involving the collection or use of biospecimens that are identifiable to an individual or for which there is at least a very small risk that some combination of the biospecimen, a request for the biospecimen, and other available data sources could be used to deduce the identity of an individual;
- Research that involves the generation of individual level, human genomic data from biospecimens, or the use of such data, **regardless of whether the data is recorded in such a manner that human subjects can be identified or the identity of the human subjects can readily be ascertained;** or
- Any other research that involves information about an individual for which there is at least a very small risk, as determined by current scientific practices or statistical methods, that some combination of the information, a request for the information, and other available data sources could be used to deduce the identity of an individual, as defined in subsection 301(d) of the Public Health Service Act.

24.7.4 NIH and CDC CoC Determination

At WTAMU, Sponsored Research Services staff will, in consultation with the investigator(s) (or Program or Project Director, if applicable), determine if the NIH policy or CDC requirements applies to research with NIH or CDC involvement or support. The questions outlined in the NIH policy and CDC requirements will be used to guide the analysis. When it has been determined that the NIH policy or CDC requirements do not apply, investigators (or Program or Project Directors, if applicable) are responsible for consulting with SPA whenever they are proposing changes to the NIH or CDC supported activity that may impact or change the analysis.

The NIH policy and CDC requirements include additional responsibilities and requirements for internal controls and for ensuring that recipients of identifiable, sensitive information protected by a CoC understand that they are also subject to the requirements of subsection 301(d) of the Public Health Service Act.

24.7.5 Application Procedures for non-NIH, non-CDC Research

Any person engaged in human subjects research that collects or uses identifiable, sensitive information may apply for a CoC. For most research, CoCs are obtained from NIH, an investigator may apply for a CoC through the NIH Institute or Center funding research in a scientific area similar to the project.

When a researcher is conducting a research project that is covered by the Agency for Healthcare Research and Quality (AHRQ) confidentiality statute (42 U.S.C. section 299c-3(c)), a CoC is not needed (AHRQ notice NOT-HS-18-012). While the AHRQ statute does not define "identifiable", AHRQ applies the PHS Act definition of "identifiable, sensitive information". Investigators should consult with AHRQ when they believe that data might be considered "non-

identifiable" or when otherwise uncertain whether a research project falls within the scope of the statute.

When a researcher is conducting a research project that is covered by the Department of Justice (DoJ) confidentiality statute, 28 CFR 22, and/or a NIJ Privacy Certificate, a CoC may not be needed. Investigators should consult with DoJ/NIJ to determine whether a CoC should be obtained.

If there is an Investigational New Drug Application (IND) or an Investigational Device Exemption (IDE), the sponsor can request a CoC from the FDA. When FDA funds or conducts research, a CoC is automatically issued.

CoCs may also be issued by other Federal agencies and departments, such as SAMSHA and HRSA.

For more information, see the NIH CoC Website.

24.7.6 IRB Review

Investigators are responsible for clearly representing in the IRB submission that a CoC is in place, or that an application for CoC has been submitted or is pending. When the CoC application is in process or pending, the IRB may condition final approval upon its receipt.

For studies that are already underway, investigators must submit an Closeout/Amendment/Continuation Form to the IRB, along with updated consent language (if applicable), when a CoC is applied for, or when automatically issued under the NIH policy or CDC requirements.

When reviewing research under a CoC, the WTAMU IRB will evaluate whether the research plan is consistent with the obligations to protect information and specimens under a CoC and, when consent will be obtained, whether the proposed consent language or other form of notification properly discloses the CoC and appropriately describes the associated protections and limitations. Sample consent language is available on the NIH CoC Website.

When research is not under a CoC, the IRB may require an investigator to apply for a CoC if the research includes identifiable, sensitive information and the IRB determines that a CoC is necessary to minimize risks and adequately protect subjects' privacy and the confidentiality of subjects' information or specimens.

24.8 Case Reports Requiring IRB Review

Federal regulations at 45 CFR 46.102(d) and 45 CFR 164.501 define research as a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. The WTAMU IRB does not consider the retrospective review and analysis of records for publication of a single case report or a case series involving data from two or three individuals to be research, and therefore such a report of 1-3 cases does not need to be submitted to the IRB. This is because reporting on such a small number of individuals does not involve a systematic investigation, including defining a hypothesis that is then investigated prospectively and systematically, to develop or contribute to generalizable

knowledge. WTAMU regards such limited case report preparation as an educational activity, not research, and thus it is permissible when the case report will be used internally, or in other learning environments, for educational purposes. When a larger series of individuals is being evaluated for presentation or publication, the commonalities of those individuals are typically explored and conclusions are drawn (i.e., a systematic investigation). Such a systematic investigation more closely resembles prospectively designed research and as such requires IRB review and approval. While drawing such a "bright line" to distinguish non-research from research may seem arbitrary, it serves as a guide to those who would prepare case reports. If a researcher ever does intend a report of 1-3 cases to develop or contribute to generalizable knowledge, or to otherwise constitute research, the report should be submitted to the IRB with a request for a determination whether the case report constitutes research using the procedures outlined in Section 8. As always, anyone who is unsure whether a project requires IRB review should contact the AREHS Office or IRB Chair for assistance.

Regardless of the number of cases, providers must comply with all applicable laws and WTAMU policies related to the use and release of private, identifiable information. Permission from the individuals who will be included in the report should be sought whenever possible, and journals may require such as a condition of publication.

A copy of this policy can be provided to journal editors or others who request confirmation of IRB review or waiver. If needed, the IRB office can provide a letter confirming that submission of single case reports or series of up to 3 cases is not required.

24.9 Research Involving or Generating Genetic Information

Research that generates or uses genetic information may create special risks to human subjects and their relatives. These involve medical, psychosocial, legal and economic risks, such as the possible loss of privacy, insurability, and employability, and may result in stigmatization and discrimination. Information about one's own genetic make-up may also provide information about family members.

In studies involving genetic testing or analysis of genetic information, several questions should to be addressed to ensure that potential risks are well understood and that the rights and interests of subjects and their family members are carefully considered and planned for. For example:

1. Is the testing intrinsic to the study? If not, has participation in the genetic testing component been provided as an opt-in?
2. Will test results be given? Is there an appropriate plan for return of results?
3. Does the subject or family member be provided the option to receive or not receive results? How will this decision be recorded?
4. Could the results provide information about individual disease risk? Disease risk for family members?

5. Could other clinically relevant information or incidental findings be uncovered by the study? Is there a plan for the management of such findings?
6. Will testing that could produce clinically relevant information occur in a CLIA-certified lab? If not, are there tests available that could validate or support findings?
7. Could a change in a family relationship be disclosed, such as mistaken paternity?
8. Could/will the research provide information about the origins, ancestry, or natural history of families, indigenous peoples, tribal populations, or other populations? What are the possible risks?
9. Could/will the research generate information that could place subjects or family members at risk or be stigmatizing?
10. Could/will the research generate information of other value or importance to subjects/families?
11. Do any practical limitations exist on the subject's right to withdraw from the research, withdraw data, and/or withdraw biological materials (e.g., specimens, cell lines, extracted genomic DNA)?
12. How will the information and/or biological materials be protected and who will have access?
13. What is the potential for re-identification of individual subjects (e.g., through the combination of their genetic information and/or materials with other sources of information (e.g., public records))? What measures can be taken to mitigate these risks?
14. Is a Certificate of Confidentiality (CoC) in place or should one be considered? (See Section 25.6)

Investigators should carefully consider the above and other factors relevant to their specific study when developing the protocol, consent process, and consent form. The President's Bioethics Commission, the National Academies of Sciences, Engineering, and Medicine, and others have produced reports, recommendations, and materials that investigators and the IRB may find helpful in protocol development and review, including:

- Returning Individual Research Results to Participants: Guidance for a New Research Paradigm
- Anticipate and Communicate: Ethical Management of Incidental and Secondary Findings in the Clinical, Research, and Direct-to-Consumer Contexts
- Privacy and Progress in Whole Genome Sequencing
- Genetics Research and American Indian and Alaska Native Communities
- National Human Genome Research Institute:
    - Human Subjects Research in Genomics
    - Return of Research Results
    - Data Sharing and Privacy
    - Informed Consent for Genomics Research

In addition to the ethical considerations, investigators must ensure that research involving genetic testing or use of genetic information is consistent with applicable law (e.g., GINA, HIPAA, EU GDPR, state law) and policy (e.g., NIH).

24.9.1 Genetic Information Nondiscrimination Act (GINA)

GINA generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against individuals based on their genetic information. This law protects individuals, including research subjects, in the following ways:

- Health insurance companies and health plans are generally prohibited from requesting or requiring genetic information of an individual or their family members, including genetic information generated from research;
- If health insurance companies and health plans do receive such genetic information, they may not use it to make decisions regarding coverage, rates, or preexisting conditions; and
- Employers with 15 or more employees generally may not use genetic information for hiring, firing, promotion, or other decisions regarding terms of employment.

GINA's protections do not extend to life insurance, disability insurance, or long-term care insurance.

GINA defines genetic information as information about:

- An individual's genetic tests;
- Genetic tests of an individual's family members;
- Genetic tests of any fetus of an individual or family member who is a pregnant woman, and genetic tests of any embryo legally held by an individual or family member utilizing assisted reproductive technology;
- The manifestation of a disease or disorder in an individual's family members(family history); or
- Any request for, or receipt of, genetic services or participation in clinical research that includes genetic services (genetic testing, counseling, or education) by an individual or an individual's family members.

GINA includes a "research exception" that allows health insurers and health plans who are engaged in research to request, but not require, that an individual undergo a genetic test so long as certain requirements are satisfied. Additional information on GINA and this exception are available on this OHRP website.

The WTAMU IRB will consider the protections and limitations of GINA when it assesses the risks of research generating or using genetic information and the adequacy of the measures to protect privacy and maintain confidentiality. Generally, the IRB will also require that the protections and limitations of GINA are disclosed in the consent process when applicable.

24.9.2 Genetics and State Law

Investigators must ensure that the research they conduct conforms to applicable law. When developing and conducting research involving genetic testing, genetic information in Texas, the following should be considered:

When conducting research in other jurisdictions, investigators must ensure that the research conforms to applicable law in that jurisdiction. Investigators should be prepared to provide information on relevant law and their plans to ensure compliance to the IRB of record for the study, whether it is WTAMU's IRB or another. Investigators may consult with the AREHS Director as needed.

24.10 Genomic Data Sharing

WTAMU complies with the NIH GDS Policy, which allows for "broad and responsible sharing of genomic research data", via submission of said data, into an NIH-designated data repository. The intent of NIH's policy is to speed discoveries to diagnose, treat, and prevent disease. **To ensure consistency in the protection of human subjects, WTAMU applies the NIH principles for informed consent and for a genomic data sharing plan to all research that involves or contemplates genomic data sharing.**

The NIH policy applies to grant activities requesting support from NIH for research involving the generation of large-scale human (and/or non-human) genomic data, regardless of funding level, such as:

- Research project grants (Rs);
- Program projects (Ps) and SCORs (Ss);
- Cooperative agreements for research (Us);
- Individual career development awards (Ks) that include a research component;
- S activities that include a research component; and
- All other activities that include a research component.

Also covered under this policy is research involving data derived from these activities for subsequent research. All basic and clinical research, including clinical trials, supported by NIH that involves the generation or use of large-scale genomic data fall within the scope of the policy.

The policy does not apply to:

- Institutional training grants (T32s, T34s, T35s, and TL2s);
- K12 career development awards (KL2s);
- Individual fellowships (Fs);
- Resource grants and contracts (Ss);
- Linked awards derived from previously reviewed applications (KL1, KL2, RL1, RL2, RL5, RL9, TL1, UL1);

- Facilities or coordinating centers funded through related initiatives to provide genotyping, sequencing, or other core services in support of GDS.

Because of the potential for re-identification of genomic data, Certificates of Confidentiality (CoCs) are automatically issued by the NIH for any research it supports, in part or in whole, that involves *"the generation of individual level, human genomic data from biospecimens, or the use of such data, regardless of whether the data is recorded in such a manner that human subjects can be identified or the identity of the human subjects can readily be ascertained as defined in the Federal Policy for the Protection of Human Subjects (45 CFR 46)."* Research covered by the NIH policy and/or the underlying PHS Act is protected by the CoC in perpetuity; as such any downstream recipients of such information must comply with the requirements of the PHS Act.

Investigators without NIH support who intend to submit genomic data to a NIH repository are encouraged to obtain a CoC. Investigators conducting research generating or using genomic data are encouraged to obtain a CoC when one is not already in place (e.g., for downstream use of data that was collected under a CoC.

For more information on CoCs, see Section 24.7.

24.10.1 Definitions

Genomic data: information derived from study of an organism's genome, i.e., the set of DNA (including all the genes within) in every cell that provides all of the information needed to build and maintain that organism.

Genomic Summary Results (GSR): GSR (also referred to as "aggregate genomic data" or "genomic summary statistics") are results from primary analyses of genomic research that convey information relevant to genomic associations with traits or diseases across datasets rather than associations specific to any one individual research participant (e.g., genotype counts and frequencies; allele counts and frequencies; effect size estimates and standard errors; likelihood; and p-values). **Sensitive GSR** refers to GSR where the privacy risks may be heightened for study populations (e.g., populations from isolated geographic regions or with rare traits) or the study populations may be more vulnerable to group harm (e.g., because the data includes potentially stigmatizing traits). Information regarding NIH's updated policy on the access, use, and management of GSR may be found here: https://grants.nih.gov/grants/guide/notice-files/NOT-OD-19-023.html.

Large-scale data include genome-wide association studies (GWAS), single nucleotide polymorphisms (SNP) arrays, and genome sequence, transcriptomic, epigenomic, and gene expression data. Examples of genomic research projects that are subject to the Policy and the timeline for submission and sharing of data from such projects may be found here: https://osp.od.nih.gov/wp-content/uploads/Supplemental_Info_GDS_Policy.pdf

NIH-Designated Data Repository: any data repository maintained or supported by NIH either directly or through collaboration. Examples of such repositories is available here:

https://osp.od.nih.gov/scientific-sharing/data-repositories-and-trusted-partners/. Data may be unrestricted or controlled access.

- **Unrestricted-Access ("Open Access"):** data are publicly available to anyone (e.g., The 1000 Genomes Project). Non-sensitive GSR are made available through unrestricted access.
- **Controlled-Access:** the data are available to an investigator for a specific project only after the investigators and institution certify to abide by specified terms and conditions and NIH has approved the use. Sensitive GSR are made available through controlled access.

24.10.2 Procedures

IRB Submissions and GDS

For any cell lines created or specimens to be collected, analyzed, and shared subject to the GDS Policy, the IRB expects that informed consent will be obtained from the research subject for the future research uses and broad sharing of data required under the policy, including GSR. **This is the case even if the specimens or cell lines are de-identified.** If there are compelling scientific or legal reasons that necessitate the use of genomic data from cell lines or clinical specimens that lack consent for research use and data sharing, investigators will need to provide a justification in the funding request to NIH for their use. The funding NIH institute/center will review the justification and decide whether to make an exception to the consent expectation. Exceptions from the NIH are not required if only some participants decline to consent to broad sharing, rather an exception request must be granted by NIH for research when consent for broad sharing has not or will not be sought.

Subjects asked to allow for future research uses and broad sharing of their genomic data have the ability to decline, and still remain in the research (however their data cannot be placed into a repository or otherwise broadly shared). The only exception to this is when sharing of the data is intrinsic to the study (e.g., the purpose of the study is to establish a repository for sharing biological specimens and/or data for future research).

Sample consent language for studies subject to GDS is available in the consent template, from the AREHS Office. NIH and NHGRI also provides guidance and resources to assist in the development of appropriate consent forms for research involving or generating genetic or genomic data.

Applications to the WTAMU IRB should include information about the proposed generation or use of genomic data including, as applicable:

- Whether the research will generate or use data subject to the NIH GDS policy;
- The name of the NIH data repository/database, or other repository or database, that data will be submitted to or acquired from;
- Whether the data is or should be classified as restricted access or unrestricted access;

- Whether the data is or should be classified as sensitive (e.g., studies involving populations from isolated geographic regions or with rare traits, studies that include data on potentially stigmatizing traits, etc.);
- Whether there are any data use limitations or modifiers (e.g., use limited to a specific disease, restricted to not-for-profit organizations, IRB approval requirement, etc.);
- The plan for informed consent and the proposed consent language;
- Request for Storing Data or Specimens for Future Use; and
- A copy of the genomic data sharing plan.

The IRB will review the proposal for genomic data sharing or subsequent use of such genomic data in accordance with the criteria for approval of research and the guidelines for IRBs provided by NIH.

When WTAMU is responsible for NIH Institutional Certification (see below), the IRB review will specifically address the required assurances outlined on the Extramural Institutional Certification. When appropriate, if the IRB is unable to confirm that a certification element is satisfied (e.g., because the IRB has not yet granted final approval), Provisional Institutional Certification will be provided.

Grant Applications and GDS

Investigators planning to apply to NIH for research that will generate large-scale human genomic data as defined above should contact the appropriate NIH Program/Project officials to discuss expectations and timelines for complying with this policy. Along with the grant, the following will need to be submitted:

- **Notification in a cover letter** of the intent to generate large-scale human genomic data
- **A genomic data sharing plan,** within the grant's resource sharing plan section (NIH guidance on these plans is available here: https://osp.od.nih.gov/wp-content/uploads/NIH_Guidance_Developing-GDS_Plans.pdf)
- **Institutional Certification** from the Sponsored Research Services (templates available here: https://osp.od.nih.gov/scientific-sharing/institutional-certifications/).Certification must be provided for all sites contributing samples. If more than one site is contributing samples, the primary site may submit one certification on behalf of all collaborating sites (or each site may provide their own certification if this is the site's preference). This certification assures that:
    - The data submission is consistent, as appropriate, with applicable national, tribal, and state laws and regulations as well as relevant institutional policies;
    - Any limitations on the research use of the data, as expressed in the informed consent documents, are delineated within the certification;
    - The identities of research participants will not be disclosed to the repositories;
    - An IRB and/or Privacy Board has reviewed the investigator's proposal for data submission and assures that:

    - the protocol for the collection of genomic and phenotypic data is consistent with 45 CFR 46;
    - data submission and subsequent data sharing for research purposes are consistent with the informed consent of study participants from whom the data were obtained;
    - consideration was given to the risks to individual participants and their families associated with data submitted to the repositories and subsequent sharing, including unrestricted access to GSR; and
    - the investigator's plan for de-identifying datasets is consistent with the standards outlined in the NIH Genomic Data Sharing (GDS) Policy (See section IV.C.1).
- **In situations where the sharing of human data is not possible** (i.e., the Institutional Certification criteria cannot be met), a justification is required to explain why these data cannot be shared, and an alternative data sharing plan will need to be provided. Exceptions to NIH expectations for data submission to an NIH-designated data repository will be considered on a case-by-case basis by the NIH funding Institute or Center (IC).

Investigators who wish to use controlled-access human genomic data from NIH-designated data repositories should briefly address their plans for requesting access to the data and state their intention to abide by the NIH Genomic Data User Code of Conduct in the Research Plan of the application. The code of conduct is available here: https://osp.od.nih.gov/wp-content/uploads/Genomic_Data_User_Code_of_Conduct.pdf . Access to controlled-access data is dependent on an approval process that involves the relevant NIH Data Access Committee(s). Applicants may wish to secure access to the data prior to submitting their application for NIH support. Secondary users of controlled-access data are not expected to deposit their findings into NIH-designated data repositories, unless appropriate.

Investigators who wish to use/download data NIH unrestricted-access repositories, including non-sensitive GSR, should use the data to promote scientific research or health; and should not use the data to re-identify individuals or generate information that could allow participant's identities to be readily ascertained, and, in all oral and written presentations, disclosures, or publications, acknowledge the specific dataset or accession numbers and the repository through which the data were accessed.

Procedures for submitting data into, or requesting access for data from an NIH-designated repository, are available here: https://osp.od.nih.gov/scientific-sharing/institutional-certifications/

24.11 Community Based Research

Community based research (CBR) is research that is based in a community and conducted in collaboration with members of that community. *Community* is often self-defined, but general

categories of community include geographic community, a community of individuals with a common problem or issue, or a community of individuals with a common interest or goal.

Where research is being conducted in communities, investigators are encouraged to involve members of the community in the research process, including the design and implementation of research and the dissemination of results when appropriate.

The most significant community involvement is in a subset of CBR called Community Based Participatory Research (CBPR) where there is an equal partnership between the academic investigators and members of a community, with the latter actively participating in all phases of the research process including the design and implementation of research and the dissemination of results when appropriate.

Questions to be considered as CBR studies are developed, and issues that the IRB will consider when reviewing CBR, are as follows:

- How was the community involved or consulted in defining the need for the proposed research (i.e., getting the community's agreement to conduct the research)?
- How was the community involved or consulted in generating the study research plan?
- How will the research procedures, including recruitment strategies and consent processes be assessed to ensure sensitivity and appropriateness to various communities (e.g., literacy issues, language barriers, cultural sensitivities, etc.)?
- How will the community be involved in the conduct of the proposed research?
- How will community members who participate in the implementation of the research be trained and supervised?
- How have "power" relationships between investigators and community members on the research team, and in subject recruitment strategies been considered to minimize coercion and undue influence?
- What are the risks and benefits of the research for the community as a whole?
- How will boundaries between multiple roles (e.g., investigator, counselor, peer) be maintained, i.e., what happens when the investigator/research staff is the friend, peer, service provider, doctor, nurse, social worker, educator, funder, etc.)?
- How will the research outcomes be disseminated to the community?
- Is there a partnership agreement or memorandum of understanding to be signed by the investigator and community partners that describes how they will work together?

25 Regulations from Other Federal Agencies

25.1 Department of Defense

Research conducted or supported by the Department of Defense (DoD Research) is reviewed and conducted in compliance with part 219 of title 32 CFR, part 980 of title 10 USC, applicable parts of title 21 CFR (50, 56, 312, 600, 812), DoD Instruction 3216.02, DoD Directive 3210.07, and applicable additional requirements from respective DoD component(s). Support of a study generally means the provision of funding, personnel (both military and civilian DoD employees), facilities, and any other resources.

DoD components (e.g., Army, Navy) may have additional requirements. The PI and a representative of the HRPP or IRB should contact the Human Research Protection Official (HRPO) for the DoD Component conducting or supporting the research. In most cases, protocols will also require review, approval and oversight by the DoD component HRPP. DoD review must be conducted before research involving human subjects can begin. The HRPO provides administrative review and approval to confirm the research is compliant with federal and DoD requirements.

WTAMU assures that DoD supported research complies with all relevant DoD human subjects protection requirements, including but not limited to:

1. The Belmont Report;
2. Title 32 Code of Federal Regulations Part 219 (32 CFR 219), Department of Defense Regulations, "Protection of Human Subjects" (DoD adoption of the "Common Rule");
3. Title 45 Code of Federal Regulations Part 46, (45 CFR 46) Department of Health and Human Services Regulations, "Protection of Human Subjects," Subparts B, C, and D as made applicable by DoD Directive (DoDD) 3216.02;
4. Title 21 Code of Federal Regulations 50, 56, 312, and 812, Food and Drug Administration (FDA) Regulations;
5. DoDD 3216.02, "Protection of Human Subjects and Adherence to Ethical Standards in DoD-supported Research";
6. Title 10 United States Code Section 980 (10 USC 980), "Limitation on Use of Humans as Experimental Subjects";
7. DoDD 3210.7, "Research Integrity and Misconduct";
8. DoDD 6200.2, "Use of Investigational New Drugs in Force Health Protection".

It is the responsibility of the PI to ensure compliance with DoD requirements for human subject protection. AREHS staff, IRB Chair and members will use these SOPs, DoDD 3216.02, the DoD Reviewer Checklist, and any relevant DoD component-specific instructions or materials to guide the IRB review and oversight of DoD research.

25.1.1 Key DoD Standards and Requirements

25.1.1 Minimal Risk

The definition of minimal risk based on the phrase *"ordinarily encountered in daily life or during the performance of routine physical or physiological examination or tests"* may not be interpreted to include the inherent risks certain categories of human subjects face in their everyday life. For example, the risks imposed in research involving human subjects focused on a special population should not be evaluated against the inherent risks encountered in their work environment (e.g., emergency responder, pilot, soldier in a combat zone) or having a medical condition (e.g., frequent medical tests or constant pain).

25.1.2 Education and Training

All personnel involved in the conduct of DoD research must complete initial and continuing education in the protection of human subjects as described in this manual. Personnel must also familiarize themselves with DoD's specific requirements by reviewing these SOPs, DoDD 3216.02, and any relevant materials specific to the DoD component. The DoD component may require additional education and/or certification to ensure that personnel are qualified to perform the research. The DoD component may evaluate the training policies of WTAMU to ensure the personnel are qualified to perform the research, based on the complexity and risk of the research.

25.1.3 Appointment of a Research Monitor

When DoD research involves **more than minimal risk**, the IRB **will** require and approve an independent research monitor by name. When research involves no more than minimal risk, an investigator may identify a research monitor or the IRB or IO may appoint a monitor. There may be more than one research monitor (e.g. if different skills or experience are needed). The monitor may be an ombudsman or a member of the data safety monitoring board.

The IRB must approve a written summary of the monitors' duties, authorities, and responsibilities and the IRB or a HRPP official shall communicate with research monitors to confirm their duties, authorities, and responsibilities.

The duties of the research monitor are determined on the basis of specific risks or concerns about the research. The monitor:

- May perform oversight functions (e.g. observe recruitment, enrollment procedures, and the consent process, oversee study interventions and interactions, review monitoring plans and reports of unanticipated problems involving risks to participants or others, oversee data matching, data collection and analysis);
- May discuss the research protocol with researchers, interview human subjects, and consult with others outside of the study; and/or
- The research monitor has the authority to stop a research study in progress, remove individual subjects from the study, and to take whatever steps are necessary to

protect the safety and well-being of participants until the IRB can assess the monitor's report.

- Research monitors are obligated to promptly report their observations and findings to the IRB or other designated official.

25.1.4 Additional protections for vulnerable subjects

Non-exempt research involving **pregnant women, fetuses, or neonates** as subjects must meet the requirements of Subpart B of the Common Rule, with the following modifications:

- The applicability of Subpart B is limited to non-exempt research involving:
    - Pregnant women as human subjects involved in research that is more than minimal risk and that includes interventions or invasive procedures to the woman or the fetus; or
    - Involving fetuses or neonates as subjects.
- For purposes of applying Subpart B, the phrase "biomedical knowledge" will be replaced with "generalizable knowledge."
- Fetal research must comply with the US Code Title 42, Chapter 6A, Subchapter III, Part H, 289g.

Research involving **prisoners** as subjects must meet the requirements of Subpart C of the Common Rule, with the following modifications:

- Research involving prisoners cannot be reviewed by the expedited procedure.
- When the IRB reviews research involving prisoners, at least one prisoner representative must be present for quorum. The prisoner representative may be a prisoner, an employee of the prison, or an individual not affiliated with the prison.
- In addition to the four allowable categories of research involving prisoners in Subpart C, two additional categories are allowable:
    - Epidemiological research that meets the following criteria:
        - The research describes the prevalence or incidence of a disease by identifying all cases or studies potential risk factor association for a disease;
        - The research presents no more than minimal risk;
        - The research presents no more than an inconvenience to the participant; or
        - Prisoners are not a particular focus of the research.
    - Research that would meet the criteria for exemption described at 32 CFR 219.101(b), can be conducted but must be approved by a convened IRB and meet the requirements of subpart C, DoDD 3216.02, and other applicable requirements.

- When a previously enrolled human subject becomes a prisoner and the research was not previously approved for the inclusion of prisoners:
    - The PI must promptly notify the IRB;
    - If the PI asserts to the IRB that it is in the best interest of the prisoner to continue to participate in the research while a prisoner, the IRB Chair may determine that the prisoner may continue to participate until the convened IRB can review the request to approve a change in the research protocol and until the IO and DoD Component office review the IRB's approval to change the research protocol. Otherwise, the IRB Chair will require that all research interactions and interventions with the prisoner (including obtaining identifiable private information) cease until the convened IRB can review the request to approve a change in the research protocol;
    - The convened IRB, upon receipt of notification that a previously enrolled human subject has become a prisoner, will promptly re-review the research protocol to ensure that the rights and wellbeing of the human subject, now a prisoner, are not in jeopardy. The IRB should consult with a subject matter expert having the expertise of a prisoner representative if the IRB reviewing the research protocol does not have a prisoner representative. If the prisoner can continue to consent to participate and is capable of meeting the research protocol requirements, the terms of the prisoner's confinement does not inhibit the ethical conduct of the research, and there are no other significant issues preventing the research from continuing as approved, the convened IRB may approve a change in the study to allow the prisoner to continue to participate in the research. This approval is limited to the individual prisoner-subject and does not allow recruitment of prisoners as participants;
    - This type of request for change in the research protocol cannot be reviewed and approved by expedited review. The research does not have to meet one of the six allowable DoD categories for research involving prisoners;
    - WTAMU will promptly report all decisions in this matter to the component HRPO. The HRPO must concur with the IRB decisions before the human subject can continue to participate while a prisoner.

Research involving **Children** as subjects must meet the requirements of Subpart D of the Common Rule, including that:

- The exemption for research involving survey or interview procedures or observation of public behavior, does not apply to research with children, except for research involving observations of public behavior when the investigator(s) do not participate in the activities being observed.

Research involving **Military Personnel** as subjects must meet the following requirements:

- Service members must follow their command policies regarding the requirement to obtain command permission to participate in research involving human subjects while on-duty and for approving off-duty employment or activities;
- Superiors (e.g., military and civilian supervisors, unit officers, and noncommissioned officers (NCOs)) are prohibited from influencing the decisions of their subordinates (e.g., junior enlisted personnel and equivalent civilians) regarding participation as subjects in research;
- Superiors of Service members (e.g., unit officers, senior NCOs, and equivalent civilians) in the chain of command must not be present at any human subject recruitment sessions or during the consent process in which members of units under their command are afforded the opportunity to participate as research subjects. When applicable, the superiors so excluded shall be afforded the opportunity to participate as research subjects in a separate recruitment session; and
- When research involving Service members is greater than minimal risk and recruitment occurs in a group setting, the IRB will appoint an ombudsman. The ombudsman must not be associated in any way to the research and must be present during the recruitment to monitor that the voluntary involvement or recruitment of the Service members is clearly and adequately stressed and that the information provided about the research is clear, adequate, and accurate. The ombudsman may also be the research monitor.

Research involving **DoD Civilians** as subjects must meet the following requirements:

- DoD Civilians must follow their organization's policies regarding the requirement to obtain permission to participate in research;
- Supervisors (e.g., military and civilian supervisors or anyone in the supervisory structure are prohibited from influencing the decisions of their subordinates regarding participation as subjects in research;
- Supervisors (e.g., military and civilian supervisors or anyone in the supervisory structure) must not be present at any human subject recruitment sessions or during the consent process in which DoD civilians under their supervision are afforded the opportunity to participate as human subjects. When applicable, supervisors so excluded shall be afforded the opportunity to participate as human subjects in a separate recruitment session; and
- For research involving civilians as human subjects when recruitment occurs in a group setting, the IRB will discuss appointing an ombudsman. The decision to require the appointment of an ombudsman should be based in part on the human subject population, the consent process, and the recruitment strategy.

Research involving **other vulnerable populations** must meet the following requirements:

- Investigators, IRBs, and IOs will consider the need for appropriate similar safeguards for other vulnerable populations, such as: research involving human subjects and

investigators in supervisor-subordinate relationships, human subjects with decisional or mental impairments, human subjects with a physical disability, or any other kind of human subjects in circumstances that may warrant provision of additional protections. As appropriate, qualified individuals (e.g., research monitors, ombudsmen, advocates) may be appointed to perform oversight functions or assist the human subjects.

25.1.5 Additional Consent Elements

When consent is to be obtained, the following additional elements of consent should be provided to potential subjects when applicable unless the requirement is waived by the DoD:

1. A statement that the DoD or DoD component is funding the research; and
2. A statement that representatives of the DoD are authorized to review research records.

25.1.6 Limitation of Waivers and Exceptions from Informed Consent

For DoD-funded research, if the research meets the definition of "*research involving a human being as an experimental subject*," informed consent must be obtained in advance from the experimental subject or their LAR if the subject cannot consent. If consent is to be obtained from a LAR, the IRB must determine that the research intends to benefit the individual subject.

The Assistant Secretary of Defense for Research and Engineering may waive the requirements for consent when all of the following are met:

- The research is necessarily to advance the development of a medical product for the Military Services;
- The research may directly benefit the individual experimental subject; and
- The research is conducted in compliance with all other applicable laws and regulations.

Research involving a human being as an experimental subject is an activity, for research purposes, where there is an intervention or interaction with a living individual for the primary purpose of obtaining data regarding the effect of the intervention or interaction. If the research participant does not meet the definition of "experimental subject," policies and procedure allow the IRB to waive the consent process.

For classified research, waivers of consent are prohibited.

An exception from consent in emergency medicine research is prohibited unless a waiver is obtained from the Secretary of Defense.

25.1.7 Limitations on Compensation for Human Subjects in Research

DoDD 3216.02 describes allowable and prohibited compensation for human subjects participating in DoD research and for Federal personnel such as civil servants and Service members. These provisions are intended to ensure compliance with the Dual Compensation Act and 24 U.S.C. 30. Summarized:

- Federal personnel while on duty and non-Federal personnel may be compensated for blood collections for research up to $50 for each blood collection;
- Federal personnel are prohibited from receiving pay or compensation for research during duty hours (except for blood collection as noted above);
- Non-Federal personnel may be compensated for research participation other than blood collections in a reasonable amount, as approved by the IRB according to local prevailing rates and the nature of the research;
- Federal personnel may be compensated for research if the participant is involved in the research when not on duty in the same way as human subjects who are not Federal personnel (i.e., compensated for participation in a reasonable amount as approved by the IRB according to local prevailing rates and the nature of the research). However, payment to off-duty Federal personnel for research participation other than blood draws must not be directly from a Federal source (payment from a Federal contractor or other non-Federal source is permissible).

Additional detail is available in DoDD 3216.02 or by consulting the component HRPO.

25.1.8 Reporting Requirements

The Institution must promptly (no longer than within 30 days) notify the HRPO of the following: when significant changes to the research protocol are approved by the IRB, the results of the IRB continuing review, if the IRB used to review and approve the research changes to a different IRB, when the institution is notified by any Federal department or agency or national organization that any part of its HRPP is under investigation for cause involving a DoD-supported research protocol, and all unanticipated problems involving risks to subjects or others, suspensions, terminations, and serious or continuing noncompliance regarding DoD-supported research involving human subjects.

25.1.9 Recordkeeping Requirements

Recordkeeping requirements for DOD-supported research with human subjects are longer than the Common Rule's requirement. DOD may require submitting records to DOD for archiving. Investigators should consult with the HRPO regarding record-keeping requirements for their research.

Records must be made accessible for inspection and copying by representatives of the DoD at reasonable times and in a reasonable manner as determined by the supporting DoD component. The fact that DoD may inspect records should be disclosed in the consent process.

25.1.10 Addressing and Reporting Allegations of Non-Compliance with Human Research Protections

WTAMU must report the initiation of all investigations of allegations of non-compliance and report the results of all such investigations (regardless of the findings) to the HRPO.

25.1.11 Addressing and Reporting Allegations of Research Misconduct

WTAMU will adhere to the requirements of DODD 3210.7 and the terms of any DoD award when allegations or findings of research misconduct arise.

25.1.12 Prohibition of Research with Detainees

Involvement of detainees (e.g. civilian internees, retained persons, lawful and unlawful enemy combatants) as human subjects of research is prohibited. Research involving any person captured, detained, held or otherwise under the control of DoD personnel (military and civilian, or contractor employee) is prohibited. There is an exception for treatment of detainees with an investigational drug or device (described below).

A detainee is defined as any individual captured by, or transferred to the custody or control of, DoD personnel pursuant to the law of war. This does not include persons being held solely for law enforcement purposes, except where the United States is the occupying power.

The prohibition of research involving a detainee does not apply to the use of FDA-regulated investigational new drugs or investigational devices for the purpose of diagnosis or treatment of a medical condition in a patient. Such treatment (e.g., an investigational new drug) may be offered to detainees with the detainees' informed consent when the medical products are subject to FDA regulations as investigational new drugs or investigational medical devices, and only when the same product would be offered to members of the U.S. Military Services in the same location for the same medical condition and only when consistent with established medical practice involving investigational drugs and devices. Such permitted treatment involving detainees as subjects must comply with all sections of DoDD 3216.02.

25.1.13 Classified research

Secretary of Defense approval is required (after IRB approval) for all classified non-exempt research involving human subjects. The involvement of classified information may be limited to information needed for IRB approval and oversight of the research; information needed to inform the human subjects during the consent process; and information provided by the human subjects during the course of the research.

Waivers of informed consent are prohibited.

Informed consent procedures must include:

1. Identification of the DoD as the supporting institution of the research, unless the research involves no more than minimal risk. The Secretary of Defense may grant an exception to this requirement on the grounds that providing this information could compromise intelligence sources or methods; and
2. A statement that the research involving human subjects is classified and an explanation of the impact of the classification.

The IRB will determine whether potential human subjects need access to classified information to make a valid, informed consent decision.

IRB review will be conducted using a full board review and shall include at least one non-affiliated member who is not a Federal employee. Use of an expedited review procedure is prohibited. Any IRB member who disagrees with a majority decision approving a project may appeal the decision to the Secretary of Defense.

25.1.14 Additional Requirements for DoD Research

IRB review must consider the scientific merit of the research. The IRB may rely on outside experts to provide an evaluation of scientific merit.

When conducting research with international populations, additional safeguards for research conducted with international populations the organization or researcher must have permission to conduct research in that country by certification or local ethics review. Researchers must follow all local laws, regulations, customs, and practices.

Disclosure regarding the provisions for research-related injury must follow the requirements of the DoD component.

Surveys performed on DoD personnel must be submitted, reviewed, and approved by the DoD component HRPO after the research protocol is reviewed by the IRB. When a survey crosses DoD components, additional review may be required by DoD.

When any institution relies upon another institution's IRB for DoD research, there must be a written agreement defining the responsibilities and authorities of each organization in complying with the terms of each institution's Federal assurance and DoDD 3216.02.

When conducting multi-site or collaborative research, a formal agreement between organizations is required to specify the roles and responsibilities of each party.

Civilian researchers attempting to access military subjects should seek collaboration with a military researcher familiar with service-specific requirements.

25.2 Department of Education

The U.S. Department of Education (ED) is a signatory to the Common Rule with regulations equivalent to 45 CFR 46 published under 34 CFR 97. Research conducted or supported by ED is reviewed by the WTAMU IRB in accordance with the Common Rule as described throughout this manual with the following variations and additional requirements.

ED has not adopted Subpart B (Pregnant Women, Fetuses, or Neonates) or Subpart C (Prisoners) of the Common Rule.

ED requires reporting of **alleged** (1) unanticipated problems involving risks to subjects or others; and, (2) serious or continuing noncompliance with the Common Rule or Subpart D (protection of children in research). Other mandated reports, as described in Section 17, are submitted to ED instead of OHRP when the research is funded or sponsored by ED. When applicable, WTAMU will follow the directions for incident reporting provided on ED's Protection of Human Subjects in Research website.

25.2.1 Family Educational Rights and Privacy Act (FERPA)

The Family Educational Rights and Privacy Act (FERPA) is a Federal law that protects the privacy of student education records at educational entities that receive funds from the ED. In general, schools must have written permission from the parent or eligible student to release any information from a student's education record. However, FERPA allows schools to disclose personally identifiable information from an education record of a student without consent if the disclosure is to organizations conducting studies for, or on behalf of, educational agencies or institutions to:

1. Develop, validate, or administer predictive tests;
2. Administer student aid programs; or
3. Improve instruction. [34 CFR 99.31(a)(6)]

A written agreement with the receiving organization is required, including:

1. The purpose, scope, and duration of the study(ies);
2. The information to be disclosed;
3. A requirement that the receiving organization uses the personally identifiable information from the educational records only for the purpose(s) of the study as stated in the agreement;
4. A requirement that the receiving organization conducts the study in a manner that does not permit personal identification of students and parents by anyone other than representatives of the organization with legitimate interests; and
5. A requirement that the receiving organization destroys or returns all personally identifiable information when the information is no longer needed for the purposes for which the study was conducted and that specified the time period in which the information must be returned or destroyed.

Education records may be released without consent under FERPA if all personally identifiable information has been removed including:

1. Students' names and other direct identifiers, such as students' Social Security Numbers or student numbers;
2. Indirect identifiers, such as the name of students' parents or other family members, the students' or families addresses, and personal characteristics or other information that would make the students' identities easily traceable, and dates and places of birth and mothers' maiden names;
3. Biometric records, including measurable biological or behavioral characteristics that can be used for automated recognition of an individual, including fingerprints, retina and iris patterns, voiceprints, DNA sequence, facial characteristics, and handwriting; and
4. Other information that, alone, or in combination, is linked or linkable to a student that would allow a reasonable person in the school community, who does not have personal

knowledge of the relevant circumstances, to identify to student with reasonable certainty.

At WTAMU, when FERPA applies, investigators must provide the IRB with information describing how they will ensure compliance with the rule. A letter of support or other documentation from the school supporting the conduct of the research should be provided. The IRB will review the information provided to verify compliance, including verification that permission for the use of the records will be obtained or that it is not required under an allowed use or exception.

25.2.2 Protection of Pupil Rights Amendment (PPRA)

The Protection of Pupil Rights Amendment (PPRA) affords parents of elementary and secondary students certain rights regarding the conduct of survey, collection and use of information for marketing purposes, and certain physical exams. PPRA applies to the programs and activities of a state educational agency (SEA), local educational agency (LEA), and any other recipient of ED funds. These rights transfer from parents to students when they reach the age of 18 or are an emancipated minor. This section is not intended to address PPRA as a whole, rather it addresses PPRA requirements as they most commonly relate to research.

25.2.2.1 Definitions:

Instructional Material means instructional content that is provided to a student, regardless of its format, including printed or representational materials, audio-visual materials, and materials in electronic or digital formats (such as materials accessible through the Internet). The term does not include academic tests or academic assessments.

Invasive Physical Examination means any medical examination that involves the exposure of private body parts, or any act during such examination that includes incision, insertion, or injection into the body, but does not include a hearing, vision, or scoliosis screening.

Personal Information means individually identifiable information including: (1) a student's or parent's first and last name; (2) a home or other physical address (including a street name and the name of a city or town); (3) a telephone number; or, (4) a Social Security Number.

Research or Experimentation Program or Project means any program or project in any program that is designed to explore or develop new or unproven teaching methods or techniques.

25.2.2.2 Rights under PPRA

When **research is funded by ED**, no student can be required to submit **without prior consent** to a survey that concerns one or more of the following protected areas:

1. Political affiliations or beliefs of the student or the student's parent;
2. Mental and psychological problems of the student or his or her family;
3. Sex behavior and attitudes;

4. Illegal, anti-social, self-incriminating, and demeaning behavior;
5. Critical appraisals of other individuals with whom the student has close family relationships;
6. Legally recognized privileged and analogous relationships, such as those of lawyers, physicians, and ministers;
7. Religious practices, affiliations, or beliefs of the student or student's parent; or
8. Income, other than that required by law to determine eligibility for participation in a program or for receiving financial assistance under a program.

Parents have the right to **receive notice and an opportunity to opt a student out** of:

1. Any other survey that concerns any of the above protected areas, **regardless of funding**;
2. Any non-emergency, invasive physical exam or screening required as a condition of attendance, administered by the school or its agent, that is not necessary to protect the health and safety of a student, except for hearing, vision, or scoliosis screenings, or any physical exam or screening permitted or required under state law; and
3. Activities involving collection, disclosure, or use of personal information collected from students for marketing or to sell or otherwise distribute the information to others. (This does not apply to the collection, disclosure, or use of personal information collected from students for the exclusive purpose of developing, evaluating, or providing educational products or services for, or to, students or educational institutions.)

Parents also have the **right to inspect** upon request and before administration or use:

1. Surveys that concern any of the protected areas and surveys created by third parties;
2. Instruments used to collect personal information from students for any of the above marketing, sales, or other distribution purposes;
3. Any instructional material used as part of the educational curriculum for the student; and
4. Instructional material, including teachers' manuals, films, tapes, or other supplementary instructional material, which will be used in conjunction with any research or experimentation program or project.

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At WTAMU, when PPRA applies, investigators should review the school's PPRA policies and must provide the IRB with information describing how they will ensure compliance with the rule and the school's policies. A letter of support or other documentation from the school supporting the conduct of the research and its compliance with PPRA should be provided. The IRB will review the information provided to verify compliance.

25.3 Department of Energy

The U.S. Department of Energy (DOE) is a signatory to the Common Rule with regulations equivalent to 45 CFR 46 published under 10 CFR 745. Research conducted or supported by DOE, or performed in DOE facilities, is subject to additional requirements for investigators and for reviewing IRBs. These requirements are outlined in this section.

DOE Order 443.1B Chg 1 establishes DOE-specific policy and principles for the protection of human subjects. DOE Notice 443.1 outlines requirements that must be met for classified research. DOE provides additional resources on its website that investigators and IRBs may also find helpful.

The WTAMU IRB will review DOE research in accordance with the Common Rule and applicable DOE-specific requirements.

25.3.1 Definitions

DOE expands upon the definitions provided in the Common Rule with the following additional or modified definitions:

Adverse Event. Any unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subjects participation in the research, whether or not considered related to the subject's participation in the research. A significant adverse event is an adverse event that is unexpected and substantively impacts the human subjects.

De-identified Data. A data set that has no, or limited, identifiers and for which a person with current knowledge of generally accepted scientific principles determines that the risk that the information could be used, alone or in combination with other reasonably available information, by an anticipated recipient, to identify an individual who is a subject of the information, has been reduced to the extent practicable. A graded approach must be used in balancing de-identification of the datasets and the usability of the dataset to accomplish the needed research.

Generalizable. Information/research findings that can be applied to populations or situations beyond that studied.

Personally Identifiable Information (PII). Any information collected or maintained about an individual, including but not limited to, education, financial transactions, medical history and criminal or employment history, and information that can be used to distinguish or trace an individual's identity, such as his/her name, Social Security number, date and place of birth, mother's maiden name, biometric data, and any other personal information that is linked or linkable to a specific individual.

Research. A systematic investigation, including research development, testing and evaluation, designed to contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported

under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities.

Unanticipated Problem. In general, to be classified as an unanticipated problem, any incident, experience, or outcome should meet all three of the following criteria:

1. Unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b)the characteristics of the subject population being studied;
2. Related or possibly related to participation in the research (possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
3. Likely to place subjects or others at greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

25.3.2 Human Subjects Research

DOE requires that the following activities are managed as Human Subjects Research and require IRB review:

1. Generalizable studies in human environments (e.g., occupied homes and offices, classrooms, and transit centers like subway systems and airports) that use tracer chemicals, particles, and/or other materials, such as perfluorocarbons, to characterize airflow;
2. Generalizable studies in occupied homes and/or offices that:
    a. Manipulate the environment to achieve research aims (e.g., increasing humidity and/or reducing influx of outside air through new energy-saving ventilation systems);
    b. Test new materials (e.g., sequentially changing the filter materials in the HVAC system while monitoring the effects on air quality and energy use);or
    c. Collect information on occupants' views of appliances, materials, or devices installed in their homes or their energy saving behaviors through surveys and focus groups. Some surveys may be online surveys administered through providers such as Amazon Mechanical Turk and Survey Monkey;
3. Human Terrain Mapping (HTM) – HTM is defined by DOE as research and data gathering activities primarily conducted for military or intelligence purposes to understand the "human terrain,"—the social, ethnographic, cultural, and political elements of the people among whom the U.S. Armed Forces are operating and/or in countries prone to political instability. This work includes observations, questionnaires, and interviews of groups of individuals, as well as modeling and analysis of collected data, and may become the basis for U.S. military actions in such locations. In addition to HTM, such activities are often referred to as human social culture behavior (HSCB) studies.

25.3.3 Protection of Data

Research involving human subjects must also comply with Federal and DOE-specific requirements for protecting Personally Identifiable Information (PII) as defined above.

Requirements include:

1. Keeping PII confidential;
2. Releasing PII only under a procedure approved by the responsible IRB and DOE;
3. Using PII only for purposes of the IRB-approved project; handling and marking documents containing PII as "containing PII or containing Protected Health Information (PHI)";
4. Establishing and documenting safeguards to prevent unauthorized use or disclosure of PII and PHI;
5. Protecting PII stored on removable media using encryption procedures that are compliant with Federal standards (FIPS-140-2 certified);
6. Sending removable media containing PII by express overnight service with signature and tracking capability;
7. Sending passwords to encrypted files separately from the files; and
8. Using 2-factor authentication for log-on access for remote systems.

Investigators must describe the measures that they will employ to protect the confidentiality of subject information and certify compliance with the above requirements on their IRB application. The IRB may accept the plan as described by the investigator or require changes to enhance data protections and ensure compliance with the above.

Loss or suspected loss of PII/PHI must be reported **immediately** upon discovery, (**as soon as aware of incident**), to the: (1) DOE Program Manager or the DOE funding office HSP Program Manager, or the DOE-CIRC 866-941-2472, (doecirc@doecirc.energy.gov); if the DOE Program Manager is unreachable; and (2) IRB.

25.3.4 Classified Research

When DOE research is classified, the following requirements and restrictions apply:

1. IRB Review
    a. Convened IRB review is required, even when a study would otherwise qualify for exemption;
    b. If the IRB believes that the proposed research can be thoroughly reviewed in an unclassified manner, a waiver of the requirements of this part can be requested via submission of a waiver request, using the appropriate form and signed by the IRB Chair, to the DOE HSP Program Manager;

c. In addition to the IRB membership and quorum requirements outlined elsewhere in this manual, an unaffiliated nongovernmental (i.e., not a Federal employee or a DOE contractor) voting member with appropriate security clearance must be in attendance;

d. The IRB must determine whether potential human subjects need access to classified information in order to decide whether to participate;

e. Any IRB member can appeal an approval decision to the DOE IO, Secretary of Energy, and Director of the Office of Science and Technology Policy, in that order;

f. After IRB approval, the DOE IO must review proposed projects and determine whether to brief the Secretary, approve, or disapprove the project; and

g. Annually, no later than October 15th, the IRB must submit information about classified reviews that took place during the DOE fiscal year by submitting the appropriate form to the DOE and NNSA Program Manager.

2. Informed Consent

a. Informed consent may not be waived;

b. The identity of the sponsoring Federal agency must be disclosed to subjects, unless the Sponsor requests that the information is not disclosed because doing so could compromise intelligence sources or methods, and the research involves no more than minimal risk, and the IRB determines that subjects will not be adversely affected by not disclosing the Sponsor's identity; and

c. The informed consent document must state that the project is classified and what that means for the purposes of the proposed project.

25.3.5 DOE Employees, Contractors, and Students

DOE considers DOE personnel (employees, contractors, and students) to be vulnerable to pressures to cooperate with research conducted by their managers and/or coworkers. When the WTAMU IRB reviews such research, it will consider whether the proposed plan for the recruitment, consent, and ongoing participation adequately protects vulnerable populations as described in Section 19.3. Additionally, it will consult with the DOE HSP to determine whether there are any DOE site-specific requirements that should be taken into consideration.

25.3.6 Reporting Requirements

In addition to the reporting requirements outlined throughout this manual, investigators must report the following **within 48 hours** to the IRB and the DOE (or NNSA) HSP Program Manager when conducting DOE research:

1. Any significant adverse events, unanticipated problems, and complaints about the research;

2. Any non-compliance with applicable regulations, IRB requirements, DOE HSP (or NNSA) program procedures or other requirements; and
3. Any suspension or termination of IRB approval.

Investigators must **immediately** (**as soon as aware**) report any finding of a suspected or a confirmed data breach involving PII as outlined in 28.10.3.

Reports should include a description of any corrective actions to be taken. The HSP (or NNSA) Program Manager and IRB will review the report and may accept or modify the corrective action plan and take any other actions necessary to ensure the protection of human subjects and the integrity of the research.

25.4 Department of Justice

DOJ IS NOT A SIGNATORY TO THE REVISED COMMON RULE. PER NOTICE ON NIJ'S WEBSITE, DOJ IS CONSIDERING NEXT STEPS. APPLICANTS ARE ADVISED TO MONITOR AND FOLLOW THE INSTRUCTIONS ON THIS WEBSITE.

The U.S. Department of Justice (DoJ) is a signatory to the Common Rule with regulations equivalent to 45 CFR 46 published under 28 CFR 46; however, DOJ has chosen not to adopt Subparts B, C and D. The National Institute of Justice (NIJ) serves as DoJ's research arm. Confidentiality regulations for DoJ/NIJ research are described at 28 CFR 22. Research conducted within the Federal Bureau of Prisons is subject to the requirements described at 28 CFR Part 512.

This section summarizes additional requirements for the conduct and IRB review of human subjects research conducted or supported by DoJ/NIJ (including funding through grants, subgrants, contracts, subcontracts, cooperative agreements, and interagency agreements) and human subjects research conducted in the Federal Bureau of Prisons.

25.4.1 Principal Investigator Responsibilities

In addition to complying with the Common Rule requirements outlined by DoJ at 28 CFR 46, PIs conducting research supported by DoJ/NIJ have the following responsibilities. PIs must:

1. Submit a Privacy Certificate to NIJ to document understanding of investigator's obligations under the confidentiality regulations found in 28 CFR 22. NIJ provides guidelines for the certificate on it's website;
2. Comply with the requirements of the Privacy Certificate, including the requirement to obtain separate written consent for the reporting of domestic, child, or elder abuse;
3. Inform subjects (in the confidentiality section of the consent form) that private, identifiable information will be kept confidential and will only be used for research and statistical purposes. If, due to sample size or some unique feature, the identity of the individual cannot be maintained, the subjects need to be explicitly notified. If the investigator intends to disclose any information, the subject needs to be *explicitly* informed what information would be disclosed, under what circumstances, and to

whom. The subject must be informed of any potential risks which may result from this disclosure and must explicitly provide prior written consent;

4. When applicable, disclose in the consent form that the research is funded by DoJ/NIJ;
5. Submit a copy of the IRB approval as well as supporting documentation of the IRB's institutional affiliation, assurance, etc. to the NIJ prior to initiation of any research activities that are not exempt from the requirements of 28 CFR 46; or
   Submit supporting documentation of the IRB's determination that the research qualifies for exemption under 28 CFR 46.101(b);
6. Comply with NIJ's policy for the protection of the privacy and well-being of participants in NIJ research studies through the statutory protection provided to private information under the authority of 42 U.S.C. § 3789g and the other DOJ regulations on the Confidentiality of Identifiable Research and Statistical Information found in 28 CFR 22;
7. Sign and maintain an Employee Confidentiality Statement for themselves and their research staff. A model employee confidentiality statement can be found at https://nij.ojp.gov/funding/model-employee-confidentiality-statement; and
8. Send a copy of all de-identified data, including copies of the informed consent document, data collection instruments, surveys and other relevant research materials to the National Archive of Criminal Justice Data.

25.4.2 Bureau of Prisons

Additional requirements for research conducted research within the Bureau are described at 28 CFR Part 512 and in Program Statement 1070.07. Although some research may be exempt from 28 CFR part 46 under 46.101(b)(5), as determined by the Office of Research and Evaluation (ORE) of the Bureau, no research is exempt from 28 CFR Part 512. However, ORE may determine that certain activities are not research (e.g., implementation of Bureau initiatives through a pilot project).

IRB approval must be obtained by WTAMU IRB (first) and the BOP IRB. Sufficient time must be allotted for review by both IRBs; per the information currently provided on BOP's website, BOP approval for a proposal that qualifies for expedited review typically takes twelve (12) weeks. The content that must be included in the BOP proposal are outlined in Program Statement 1070.07, all information and materials submitted to the BOP must also be submitted to the WTAMU IRB.

The following principles and requirements for research conducted within BOP are in addition to those outlined in 28 CFR 46 and will be evaluated during the IRB review.

Requirements for Approval:

1. The PI must have academic preparation or experience in the area of study;
2. The PI must assume responsibility for actions of other research team members;
3. PI's who are not employees of BOP must sign a statement of compliance;
4. The rights, health, and human dignity of subjects must be respected;

5. The project must have an adequate research design and contribute to the advancement of knowledge about corrections;
6. The research design must be compatible with both the operation of prison facilities and the protection of human subjects. Researchers must observe the rules of the institution or office where the research is conducted;
7. The project may not involve medical experimentation, cosmetic research, or pharmaceutical testing;
8. The project must minimize risk to subjects and risks to subjects must be reasonable in relation to anticipated benefits;
9. Selection of subjects within any one institution must be equitable;
10. Incentives may not be offered to inmate subjects to help persuade inmate subjects to participate. However:
    a. Soft drinks and snacks to be consumed at the test setting may be offered;
    b. Reasonable accommodations such as nominal monetary compensation (i.e., do not exceed twice the minimum wage for each hour of the subject's expected participation in the research activity) for time and effort may be offered to non-inmate subjects who are both:
        i. No longer in BOP custody; and
        ii. Participating in authorized research conducted by Bureau employees or contractors.

Informed Consent Requirements:

1. Informed consent must be sought, when applicable (See 28 CFR 512.15 and 512.16) and follow the requirements outlined in BP-S606;
2. Additional required consent elements for research conducted within the BOP:
    a. Identification of the researchers;
    b. Anticipated uses of the results of the research;
    c. A statement that participation is completely voluntary and that the participant may withdraw consent and end participation in the project at any time without penalty or prejudice (the inmate will be returned to regular assignment or activity by staff as soon as practicable);
    d. A statement regarding the confidentiality of the research information and exceptions to any guarantees of confidentiality required by federal or state law. For example, a researcher may not guarantee confidentiality when the participant indicates intent to commit future criminal conduct or harm himself or herself or someone else, or, if the participant is an inmate, indicates intent to leave the facility without authorization; and

e. A statement that participation in the research project will have no effect on the inmate participant's release date or parole eligibility.

3. Documentation of consent –

   a. Researchers (not employed by the BOP) must obtain the subject's signature on the statement of informed consent prior to initiating the research activity. The researcher may not be required to obtain the signature if the researcher can demonstrate that the only link to the subject's identity is the signed statement of informed consent or that there is significantly more risk to the subject if the statement is signed. The signed statement must be submitted to the Chairperson of the appropriate BOP IRB. See Program Statement 1070.07 for requirements that apply when consent is obtained by an employee or contractor of BOP;

   b. The original of any signed consent form must be placed in the specific research project's file at the institution where the research is conducted. A copy of any signed consent form which grants a researcher access to an Inmate's Central File must be placed in the non-disclosable portion of the Inmate Central File and a copy must be offered to the inmate.

Post-Approval Requirements:

1. Except as noted in the informed consent form, researchers may not provide identifiable research information to any person without the subject's prior written consent to release the information (e.g., identifiable research information cannot be admitted as evidence or used for any purpose in any action, suit, or other judicial, administrative, or legislative proceeding without written consent);
2. Except for computerized data records maintained at an official Department of Justice site, records that contain non-disclosable information directly traceable to a specific person may not be stored in, or introduced into, an electronic retrieval system;
3. If the researcher is conducting a study of special interest to the Office of Research and Evaluation (ORE) but the study is not a joint project involving ORE, the researcher may be asked to provide ORE with the computerized research data, not identifiable to individual participants, accompanied by detailed documentation. These arrangements must be negotiated prior to the beginning of the data collection phase of the project;
4. At least once a year, the PI must provide the Chief, Office of Research and Evaluation, with a report on the progress of the research;
5. At least 12 working days before any report of findings is to be released, the PI must distribute one copy of the report to each of the following: the Chair of the Bureau Research Review Board, the Regional Director, and the Warden of each institution that provided data or assistance. The PI must include an abstract in the report of findings;
6. Prior to submitting for publication the results of a research project conducted under this subpart, the researcher shall provide two copies of the material, for informational purposes only, to the Chief, Office of Research and Evaluation, Central Office, Bureau of Prisons;

7. In any publication of results, the PI must acknowledge the Bureau's participation in the research project; and
8. The PI must expressly disclaim approval or endorsement of the published material as an expression of the policies or views of the Bureau.

25.5 Environmental Protection Agency

The Environmental Protection Agency (EPA)) is a signatory to the Common Rule with regulations equivalent to 45 CFR 46 published under 40 CFR 26 (Subpart A). EPA has outlined additional regulations that apply to EPA research in the following subparts:

Subpart B – Prohibition of Research Conducted or Supported By EPA Involving Intentional Exposure of Human Subjects who are Children or Pregnant or Nursing Women;

Subpart C – Observational Research: Additional Protections for Pregnant Women and Fetuses Involved as Subjects in Observational Research Conducted or Supported by EPA;

Subpart D – Observational Research: Additional Protections for Children Involved as Subjects in Observational Research Conducted or Supported by EPA;

Subpart K – Basic Ethical Requirements for Third Party Human Research for Pesticides Involving Intentional Exposure of Non-Pregnant, Non-Nursing Adults;

Subpart L – Prohibition of Third Party Research Involving Intentional Exposure to a Pesticide of Human Subjects who are Children or Pregnant or Nursing Women;

Subpart M – Requirements for Submission of Information on the Ethical Conduct of Completed Human Research;

Subpart O – Administrative Actions for Noncompliance;

Subpart P – Review of Proposed and Completed Human Research;

Subpart Q – Standards for Assessing Whether to Rely on the Results of Human Research in EPA Actions.

Additional EPA requirements for human research are outlined in EPA Order 1000.17A "Policies and Procedures on Protection of Human Subjects in EPA Conducted or Supported Research".

EPA regulations and requirements for the protection of human subjects apply to research supported or conducted by the EPA **and** to research in which the intent is submission of data to the EPA.

WTAMU investigators must comply with all applicable EPA requirements in addition to other applicable regulations, policies, **and** the requirements of the IRB of record. Investigators are responsible for clearly indicating within their IRB application materials that proposed research is subject to EPA regulations and for providing information regarding compliance with EPA requirements. The WTAMU IRB will evaluate compliance with the aid of a checklist and by consulting regulations and guidance.

The information provided in this section summarizes key EPA standards and requirements.

25.5.1 EPA Definitions:

Intentional Exposure - Research involving intentional exposure of a human subject means a study of a substance in which the exposure to the substance experienced by a human subject participating in the study would not have occurred but for the human subject's participation in the study.

Observational Research - Observational research means any human research that does not meet the definition of research involving intentional exposure of a human subject.

Observational Human Exposure Studies. As defined in Scientific and Ethical Approaches for Observational Exposure Studies (SEAOES), observational human exposure studies are studies that involve the collection of environmental samples, data, and information from study participants in their everyday environments as they go about their normal activities. They involve neither the deliberate exposure of participants nor the control of environmental conditions in a way that impacts the participants' naturally occurring exposures.

Pesticide - Pesticide means any substance or mixture of substances meeting the definition in 7 U.S.C. 136(u) (Federal Insecticide, Fungicide, and Rodenticide Act, section 2(u)).

Substance – A substance includes any chemical, biological organism, or physical property tracked or regulated by the EPA or identified in an environmental statute. The Substance Registry Services (SRS) is the EPA's central system for information about substances tracked or regulated by EPA.

Assent - Assent means a child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.

Child – A child is a person who has not attained the age of 18.

Guardian - Guardian means an individual who is authorized under applicable State, Tribal, or local law to consent on behalf of a child to general medical care.

Parent - Parent means a child's biological or adoptive parent.

Permission - Permission means the agreement of parent(s) or guardian to the participation of their child or ward in research.

25.5.2 EPA Human Subjects Research Review Official (HSRRO) Approval

All human subjects research conducted or supported by EPA must either be approved or be acknowledged as exempt research by the EPA Human Subjects Research Review Official (HSRRO) before any work involving human subjects research can begin. Preliminary review by the HSRRO can be requested for any research project, contract, grant application, cooperative agreement, cooperative research and development agreement (CRADA), interagency agreement or any formal agreement involving EPA support of such studies. However, preliminary review is not required for any project, and if provided does not substitute for approval following IRB review.

To obtain approval or a concurrence of exemption by the HSRRO, researchers must submit the IRB-approved research package or documentation of exemption, including evidence of IRB approval and any correspondence between the IRB and the researchers. Researchers must also provide evidence of a Federalwide Assurance (FWA) on file with the U.S. Department of Health and Human Services (HHS) or other agency that their institution or organization will comply with regulatory provisions in the Common Rule.

25.5.3 PI Reporting Requirements

After research is approved, PIs are responsible for notifying EPA and the HSRRO (and HSO where applicable) of IRB suspension or termination of the research, of Unanticipated Problems Involving Risk to Subjects or Others that the IRB deems reportable, and any event that is significant enough to result in the removal of a subject from the study. In addition, for grantees of EPA, the PI must notify his/her Project Officer promptly, according to the terms specified by the IRB of record for the project.

25.5.4 Intentional Exposure

EPA outlines requirements and restrictions applicable to research involving intentional exposure to substances or pesticides in the following subparts:

Subpart B **prohibits** research involving intentional exposure (see definition above) of pregnant women, nursing women, or children.

Subpart L **explicitly extends the prohibition** to include intentional exposure of pregnant women, nursing women, or children to a **pesticide**.

Subpart K describes the requirements for third-party research involving intentional exposure of non-nursing, non-pregnant adults to substances and pesticides.

Among other provisions, Subpart K requires that:

1. Informed consent is obtained from subjects (there is no provision for LARs or for waiver or alteration of consent);
2. Informed consent must be documented using a written consent form or short form method (there is no provision for waiver of documentation of consent);
3. If the research involves intentional exposure to a pesticide, the prospective subject must be informed of the identity of the pesticide and the nature of its pesticidal function (as an element of consent); and
4. The proposed research must be submitted to the EPA for approval after approval by the IRB(s). The submission requirements are outlined in §26.1125.

25.5.5 Observational Research

EPA outlines requirements and restrictions applicable to observational research involving in the following subparts:

Subpart C describes the rules that apply to observational research conducted or supported by EPA that involves pregnant women (and thus their fetuses). In summary, such research is subject to the Common Rule Subpart B requirements stipulated at 45 CFR 46.203 (Duties of IRBs), 45 CFR 46.204 (Research Involving Pregnant Women or Fetuses), and 45 CFR 46.206 (Research Involving, After Delivery, the Placenta, the Dead Fetus, or Fetal Material).

Subpart D describes the rules that apply to observational research conducted or supported by EPA that involves children. In summary, the subpart stipulates that IRBs may only approve (and that EPA will only fund or conduct) research that satisfies all applicable conditions outlined in the subpart, including that:

1. EPA will conduct or fund observational research in which the IRB finds that **no greater than minimal risk** to children is presented, **only** if the IRB finds that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth in §26.406.
2. EPA **will not** conduct or fund observational research that **involves an intervention or procedure that involves greater than minimal risk** to children **unless** the IRB finds and documents that:
    a. The intervention or procedure holds out the prospect of direct benefit to the individual subject or is likely to contribute to the subject's well-being;
    b. The risk is justified by the anticipated benefit to the subjects;
    c. The relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches; and
    d. Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians, as set forth in§26.406.
3. §46.406 describes the requirements for permission from parents (or guardians) and for assent from children. The EPA requirements are consistent with the requirements outlined in §46.408 of 45 CFR 46. For each of the allowable categories (above) of observational research involving children, the IRB may determine that the permission of one parent is sufficient.

25.5.6 Observational Human Exposure Studies

All human observational exposure studies conducted or supported by EPA will adhere to the principles set forth in SEAOES. SEAOES addresses six major topic areas:

- Identifying elements to be considered in study conceptualization;
- Ensuring protection of vulnerable groups;
- Addressing privacy and other concerns related to observational human exposure studies;
- Creating an appropriate relationship between the participant and investigator;
- Building and maintaining appropriate community and stakeholder relationships; and

- Designing and implementing strategies for effective communication.

25.5.7 Other EPA Regulations

Subpart M describes the requirement for submission of information about the ethical review and conduct of research whenever a report containing the results of the research is submitted to the EPA for consideration for consideration in connection with actions that may be performed by EPA.

Subpart O describes the actions that EPA may take when they find that an IRB, institution, or investigator are not compliant with EPA's requirements.

Subpart P describes the requirements and procedures for EPA's and EPA's Human Studies Review Board review of proposed and completed human research under §26.1125 and §26.1701.

Subpart Q describes the standards EPA applies in deciding whether to rely upon the results of research involving intentional exposure to substances or pesticides in EPA actions.