Investigator Manual[1]

DIVISION OF RESEARCH

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Scope

Throughout this document “institution” refers to Texas A&M University.

What is the purpose of this manual?

This document “INVESTIGATOR MANUAL (HRP-103)” is designed to guide you through policies and procedures related to the conduct of Human Research that are specific to this institution.

General information regarding Human Research protections and relevant federal regulations and guidance is incorporated into the required human protections training. For additional information see below: “What training does my staff and I need in order to conduct Human Research?”

Definitions

Although some terms are defined in this document, a comprehensive set of definitions relevant for Human Research can be found in SOP: Definitions (HRP-001). Please refer to that SOP for additional information about terms used in this document.

What is Human Research?

An algorithm to assist with understanding whether or not an activity is Human Research, can be found in the "WORKSHEET: Human Research Determination (HRP-310)," located in the IRB Policies & Procedures section of the IRB Web site. Use this document for guidance as to whether an activity meets either the DHHS or FDA definition of Human Research, keeping in mind that the IRB makes the ultimate determination in all cases as to whether an activity constitutes Human Research subject to IRB oversight. Additional guidance is provided in the SOP: Activities that Require IRB Review (HRP-093).

You are responsible for not conducting Human Research without prior IRB review and approval or obtaining a Not-Human Subjects or exemption determination from the IRB Office.

If you have questions about whether an activity is Human Research, contact the IRB Office who will provide assistance. A written determination will be provided when the request is submitted through the electronic system. Determinations are not issued through emails or phone calls.

What is the Human Research Protection Program?

HRP-101 - HUMAN RESEARCH PROTECTION PROGRAM PLAN describes this institution's overall plan to protect subjects in Human Research.

- The mission of the Human Research Protection Program.
- The ethical principles that the institution follows governing the conduct of Human Research.
- The applicable laws that govern Human Research.
- When the institution becomes "engaged in Human Research" and when someone is acting as an agent of the institution conducting Human Research.
- The types of Human Research that may not be conducted.
- The roles and responsibilities of individuals within the institution.

Who may be a principal investigator for human Research?

Every research study requires a Principal Investigator (PI). This person takes full responsibility for the conduct of the study including the eligibility and training of the research staff. All individuals who serve in the role of a principal investigator on funded or unfunded research must be employed by Texas A&M. Below is a list of who may and may not serve as PI.

Eligible to be a Principal Investigator	With Permission of Dean and Department Head and VPR on a Case by Case Basis	Not Eligible to be a Principal Investigator
• Full, associate, and assistant professors • Instructors • Librarians • Faculty Equivalent Research Positions	• Lecturers • Visiting faculty • Retired faculty • Senior Research Fellow • Senior Staff • Post-Doctoral Research Associate	• Adjuncts • Visiting scholars • Undergraduate students • Graduate Students • Residents • Research Assistants • Research Associates • Research Coordinators

Please note that the TAMU IRB recognizes only one Principal Investigator for each study. The Principal Investigator is ultimately responsible for the conduct of the entire study and all study team members. Additional investigators must have other titles such as Co-Investigator.

Student researchers must include an individual from the first column above (**Eligible to be a Principal Investigator**) as the Principal Investigator of their projects. Although, a student may carry-out many of the protocol related functions as a 'protocol director', the Principal Investigator retains responsibility for the overall conduct of the research.

What training do researchers need to conduct Human Research?

This section describes the training requirements imposed by the HRPP. You may have additional training imposed by other institutional policies, sponsors or funding agencies.

All members of the research team involved in the design, conduct or reporting of the research must complete training. Members of the research team who have not completed human research protections training may not take part in research that involves human subjects.

Group 1: Required Training for Investigators and Research Staff conducting Clinical Studies **** (drugs, devices, biologics, invasive procedures)		
	Course	Timeline
Initial Training	CITI Biomedical Research Basic	Prior to IRB submission of research
	*Good Clinical Practice	Prior to IRB submission of research
	**TRAINTRAQ Course #2114226: HIPAA Training for Texas A&M Faculty, Staff & Students or equivalent;	Prior to IRB submission of research
	*** TRAINTRAQ Course #2111716: Financial Conflicts of Interest in Research; External researchers may use CITI Conflicts of Interest	As required by system regulation 15.01.03

Refresher Courses	CITI Biomedical Research Refresher	Every 5 years

*When using FDA regulated test articles or as required by sponsor or funding agency.
** When accessing, recording or disclosing PHI for research purposes.
*** When required for externally funded research in accordance with SAP 15.01.03.
**** Group 1 or 3 may substitute for Group 2 when appropriate.

Group 2: Required Training for Investigators and Research Staff conducting Social & Behavioral Studies **** (Surveys, Interviews, Qualitative, Educational, Record Reviews)		
	Course	Timeline
Initial Training	CITI Social and Behavioral Research Basic	Prior to IRB submission of research
	*Good Clinical Practice	Prior to IRB submission of research
	**TRAINTRAQ Course #2114226: HIPAA Training for Texas A&M Faculty, Staff & Students or equivalent or CITI;	Prior to IRB submission of research
	*** TRAINTRAQ Course #2111716: Financial Conflicts of Interest in Research; External researchers may use CITI Conflicts of Interest	As required by system regulation 15.01.03
Refresher Courses	CITI Social and Behavioral Research Refresher	Every 5 years
	**TRAINTRAQ Course #2114226: HIPAA Training for Texas A&M Faculty, Staff & Students or equivalent or CITI;	Every 5 years or as required by institutional policy
	*** TRAINTRAQ Course #2111716: Financial Conflicts of Interest in Research; External researchers may use CITI Conflicts of Interest	As required by system regulation 15.01.03

*As required by sponsor or funding agency.
** When accessing, recording or disclosing PHI for research purposes.
*** When involved in funded research in accordance with University Rule 15.01.03.MI.
**** Group 2 or 3 may substitute for Group 1 when appropriate.

Group 4: Required Education for External Researchers with Limited Roles		
	Course	Timeline
Initial Training	CITI Group 4 Educational Requirements: History and Ethical Principles (SBE: 490) Informed Consent (SBE: 504) Privacy and Confidentially (SBE:505)	Prior to Approval of Research
Refresher Courses	CITI Group 4 Educational Requirements:	Every 5 years

External researchers (non-TAMU) with limited roles in remote areas, foreign countries or other exceptional circumstances as determined by the IRB may use Group 4 requirements.

The CITI site can be accessed at http://www.citiprogram.org/.

TAMU TrainTraq can be accessed at https://apps7.system.tamus.edu/TrainTraq/web/default.aspx

For each new submission received, the IRB Office will verify that training requirements have been met. If they have not been met, the IRB Office will notify you of the deficiency and will not process the submission until all training requirements have been met or after removing individuals who have not met requirements from your research team as appropriate.

What financial interests do researchers need to disclose conduct Human Research?

All individuals involved in the design, conduct, or reporting of research, are required to disclose financial interests in accordance with System Regulation 15.01.03 and University Rule 15.01.03. M1.

Investigators involved in human subjects research can find additional details in "SOP: Management of Financial Conflicts of Interests (HRP-055)."

What other approvals are required before initiating Human Research?

In addition to securing IRB approval for Human Research you may need to secure other institutional approvals. Below are examples where other approvals are relevant; however, this list is not all inclusive. The IRB Office may ask you to obtain other approvals not listed below on a case-by-case basis depending on the specifics of your research.

Bio-Safety approval is required when your protocol also involves activities with biohazards (blood, tissue, cell lines, recombinant DNA or RNA, select agents or toxins). Contact the Biosafety Office for additional information at ibc@tamu.edu.

Export Controls laws and regulations may apply to research where controlled information and items are provided to anyone outside of the United States or to foreign persons and entities in the United States including transactions with sanctioned countries, persons or entities. Contact the Export Controls Office for more information at exportcontrols@tamu.edu.

Animal Welfare Program/IACUC approval is required when your protocol also involves the use of animals or animal tissues and fluids. Contact the Animal Welfare Office for additional information at animalcompliance@tamu.edu.

Family Educational Rights and Privacy Act (FERPA) requirements apply to any research involving TAMU students, their information, or student records. The Office of the Registrar will be notified to verify FERPA compliance. Contact ferpa@tamu.edu for additional information.

Privacy Officer review may be required when research involves identifiable information regulated by HIPAA, GDPR or other privacy laws. For more information contact the Privacy Officer at privacy@tamu.edu.

Research Administration review may be required when the research involves external collaborators or when a data use agreement (DUA), material transfer agreement (MTA), memorandum of understanding (MOU) or other agreements is needed. Contact negotiations@tamu.edu for additional information.

Site Specific Authorizations are required when your research involves any organization or entity that is not part of Texas A&M University. This includes public schools or other educational settings, private clinics, hospitals, nursing homes, government agencies or any other outside business or field site. Written approval from the organization's authorized individual is required. In certain cases, contracts or other agreements may be required. Site Specific Authorization templates are available on the IRB website.

How do I submit new Human Research to the IRB?

- Access the URL https://iris.tamu.edu
- Log into the electronic system using your NetID or UIN/SSO login and password.
- From the 'Study Assistant' menu click 'Add a New Study'.
- Then select 'IRB Application' (Human Subjects) from the 'New Study Application' list.
- Complete each section of the online IRB Application, as needed.
- Click 'Save and Continue to the Next Section' after each page is complete.
- Upload the consent form to the 'Informed Consent' page, as applicable.
- Upload all other supporting documents to the 'Study Documents' page, as applicable.

The number of additional documents required depends upon the specifics of your research. Copies of grants or contracts are always required for funded research. Below is the list of documents often required to support your application:

- investigator or multi-site protocols
- grants or contracts
- recruitment materials,
- data collection instruments including surveys, interview scripts, questionnaires, diaries
- consents, assents and HIPAA Authorizations
- site specific authorizations,
- drug or device information
- evidence of international ethics review

After all information is entered the process is not complete until you 'Signoff and Submit' the application. All key personnel entered into the 'Additional Investigators' page must be selected for 'Sign-Off', also. Your Department Head is also required to sign-off on your application.

The "Sign-off" page includes Investigator Attestation and disclosure of financial and non-financial conflict of interests.

If you need help, contact the IRB coordinator assigned to your department. This information is posted on the IRB website at My IRB Contact – Division of Research (tamu.edu).

How do I request to rely on an External IRB?

TAMU investigators may rely upon the IRB of another organization when they receive a federal award that requires the use of a single IRB or at the request of the sponsor.

In all other cases, the HRPP reserves the right to determine on an individual study basis whether or not to accept an External IRB review. The HRPP will evaluate the external IRB and the circumstances of each request.

The TAMU investigator is required to submit a request through the IRB's electronic system to facilitate the administrative evaluation of the external IRB project. Complete the truncated application and attach all protocols, consent documents and other requested supplements. Ensure your scope of work is clearly described the application.

Know that a reliance agreement between the institutions involved is required.

The TAMU HRPP must acknowledge the request to use an external IRB prior to the conduct of any research activities by TAMU personnel regardless of any External IRB approval. Texas A&M University remains responsible for the oversight of the conduct of the research. External IRB studies are subject to TAMU post approval monitoring activities.

How do I request that the TAMU IRB serve as the IRB of record for my collaborative or multi-site research study?

Consult your designated HRPP/IRB coordinator, first. The HRPP will determine whether or not there are adequate resources to perform the functions of a single IRB related to your study.

If the TAMU IRB accepts the role of a single IRB for your study, complete the regular IRB application and attach all applicable documents. After the primary study has received TAMU IRB approval, performance sites can be added. Each site must provide local context requirements and demonstrate that all personnel are adequately trained and qualified for their designated roles. A reliance agreement between each institution and the TAMU IRB is required.

The lead PI for a multi-site study must be ready to accept additional responsibilities for overall study compliance and study-wide communications. Plans for use of a single IRB on a funded study should be thought out and budgeted during proposal. Central IRBs may be suggested as an alternative to using the TAMU IRB when single IRB is required for multi-site research.

How do I write an Investigator Protocol?

The IRB website has specific protocol templates for you to select depending upon the type of research you are proposing, social and behavioral, biomedical or retrospective data or specimen review.

Use the template as a starting point for drafting a new investigator protocol and reference the instructions in italic text for the information the IRB looks for when reviewing research. Here are some key points to remember when developing an Investigator Protocol:

- The italicized bullet points in the protocol templates serve as guidance to investigators when developing an Investigator Protocol for submission to the IRB. All italicized comments are meant to be deleted prior to submission.
- When writing an Investigator Protocol, always keep an electronic copy. You will need to modify this copy when making changes to the Investigator Protocol.
- Note that, depending on the nature of your research, certain sections of the template may not be applicable to your Investigator Protocol. Indicate this as appropriate.
- You may not involve any individuals who are members of the following populations as subjects in your research unless you indicate this in your inclusion criteria as the inclusion of subjects in these populations has regulatory implications.
    - Adults unable to provide legally effective consent
    - Individuals who are not yet adults (infants, children, teenagers)
    - Pregnant women
    - Prisoners
- If you are conducting community-based participatory research, you may contact the IRB Office for information about:
    - Research studies using a community-based participatory research design
    - Use of community advisory boards
    - Use of participant advocates
    - Partnerships with community-based organizations

How do I create consent or assent documents?

Use the Consent/Assent document templates posted on the IRB website to create consent/assent documents. Each different template contains information that is *generally* relevant for each type of research in each of these categories, social and behavioral, biomedical or simple survey research. You may ultimately need to edit sections to fit the type of research proposed.

Note that although you may edit the forms to fit your research all consent documents must contain all of the required elements of informed consent and all appropriate additional elements in accordance with regulations and policies. Review the “Long Form of Consent Documentation” section in the IRB’s WORKSHEET: Criteria for Approval (HRP-314) to ensure that these elements are addressed. Choose the appropriate signature block page or pages from the three different signature block templates: (1) adults capable of providing consent; (2) adults unable to provide consent; (3) assent of children. Delete the signature blocks that are not applicable to your research.

We recommend that you note the version of your consent document in the lower left corner to ensure that you use the most recent version approved by the IRB. The IRB Office will also watermark consent documents in the lower right corner with IRB approval dates. **You may only use the latest stamped**

version of the consent approved by the IRB. Once a new version of the consent is approved, all other versions become invalid and may not be used.

Do I need to obtain informed consent in order to screen, recruit, or determine the eligibility of prospective subjects?

The 2018 Common Rule allows an IRB to 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.

The research protocol should include information about how potential subjects will be identified and recruited in order for the IRB to be able to determine whether informed consent for these activities is required.

Note that accessing medical records or any other records subject to HIPPA regulations to determine a prospective subject's eligibility for a study will require a HIPAA authorization or a waiver when appropriate.

What are the different regulatory classifications that research activities may fall under?

The HRPP/IRB will review your submission with the goal of classifying it in the least restrictive category permissible. Activities may fall under one of the following four regulatory classifications:

- Not "Human Research": Activities must meet the institutional definition of "Human Research" to fall under IRB oversight. Activities that do not meet this definition of "Human Research" are not subject to IRB oversight or review. See SOP: Activities that require IRB Review (HRP-093) for additional guidance. Contact the IRB Office in cases activity is Human Research.

  If you have questions about whether an activity is Human Research, contact the IRB Office who will provide assistance. A written determination will be provided when the request is submitted through the electronic system. Determinations cannot be issued through emails or phone calls. Please note that a 'Not Human Research Determination" is not an IRB approval.

- Exempt: Certain categories of minimal risk Human Research may be exempt from regulation but require IRB review. It is the responsibility of the HRPP, not the investigator, to determine

whether Human Research is exempt from IRB review. Review the "WORKSHEET: Exemption (HRP-312)" for reference on the categories of research that may be exempt. Some exempt research may require Limited IRB review to determine if there are adequate provisions to protect the privacy of subjects and the confidentiality of data.

- Review Using the Expedited Procedure: Certain categories of non-exempt minimal risk Human Research may qualify for review using the expedited procedure, meaning that the project may be approved by a single designated IRB reviewer, rather than the convened board. Review the "WORKSHEET: Eligibility for Review Using the Expedited Procedure (HRP-313)" for reference on the categories of research that may be reviewed using the expedited procedure.

- Review by the Convened IRB: Non-Exempt Human Research that does not qualify for review using the expedited procedure must be reviewed by the convened IRB.

What are the decisions the IRB can make when reviewing proposed research?

The IRB may approve research, require modifications to the research to secure approval, defer research, or disapprove research:

- Approval: Made when all criteria for approval are met. See "How does the IRB decide whether to approve Human Research?" below.

- Modifications Required to Secure Approval: Made when IRB members require specific modifications to the research before approval can be finalized.

- Deferred: Made when the IRB determines that the board is unable to approve research and the IRB suggests modifications that might make the research approvable. When making this motion, the IRB describes its reasons for this decision, describes modifications that might make the research approvable, and gives the investigator an opportunity to respond to the IRB with the changes or meet with the IRB about the research.

- Disapproval: Made when the IRB determines that it is unable to approve research and the IRB cannot describe modifications that might make the research approvable. When making this motion, the IRB describes its reasons for this decision and gives the investigator an opportunity to respond to the IRB in person or in writing.

How does the IRB decide whether to approve Human Research?

The criteria for IRB approval can be found in the "WORKSHEET: Exemption (HRP-312)" for exempt Human Research and the "WORKSHEET: Criteria for Approval (HRP-314)" for non-exempt Human Research. The latter worksheet references other checklists that might be relevant. All checklists and worksheets can be found on the IRB Web site.

These checklists are used for initial review, continuing review, and review of modifications to previously approved Human Research.

You are encouraged to use the checklists to write your Investigator Protocol in a way that addresses the criteria for approval.

What will happen after IRB review?

The IRB will provide you with a written decision indicating that the IRB has approved the Human Research, requires modifications to secure approval, deferred the research or has disapproved the Human Research.

- If the IRB has approved the Human Research: The Human Research may commence once all other required TAMU compliance approvals have been met. IRB approval is usually good for a limited period of time which is noted in the IRB approval letter.

- If the IRB requires modifications to secure approval and you accept the modifications: Make the requested modifications and submit them to the IRB. If all requested modifications are made, the IRB will issue a final approval. Research cannot commence until this final approval is received. If you do not accept the required modifications, write up your response and submit it to the IRB for additional review.

- If the IRB defers the Human Research: The IRB will provide a statement of the reasons for deferral and suggestions to make the study approvable and give you an opportunity to respond in writing. In most cases if the IRB's reasons for the deferral are addressed with changes to the protocol, the Human Research can be approved.

- If the IRB disapproves the Human Research: The IRB will provide a statement of the reasons for disapproval and give you an opportunity to respond in writing.

In all cases, you have the right to address any concerns about your review to the IRB. Please contact the IRB staff to set up a meeting.

What are my obligations as an investigator after IRB approval?

1) Do not start Human Research activities until you have the final IRB approval letter.
2) Do not start Human Research activities until you have obtained all other required compliance and institutional approvals.
3) Ensure that there are adequate resources to carry out the research safely. This includes, but is not limited to, sufficient investigator time, appropriately qualified research team members, equipment, and space.

4) Ensure that Research Staff are qualified (e.g., including but not limited to appropriate training, education, expertise, credentials, protocol requirements and, when relevant, privileges) to perform procedures and duties assigned to them during the study.
5) Update the IRB application with any changes to the list of study personnel.
6) **Personally conduct or supervise the Human Research**. **Recognize that the investigator is accountable for the failures of any study team membe**r.
    a. Conduct the Human Research in accordance with the relevant current protocol as approved by the IRB, and in accordance with applicable federal regulations and local laws.
    b. When required by the IRB ensure that consent or permission is obtained in accordance with the relevant current protocol as approved by the IRB.
    c. Do not deviate or modify the research without prior IRB review and approval unless necessary to eliminate apparent immediate hazards to subjects.
    d. Protect the rights, safety, and welfare of subjects involved in the research.
7) Submit to the IRB:
    a. Proposed modifications as described in this manual. (See "How do I submit a modification?")
    b. A continuing review application or administrative check-in withing the time frame provided in the approval letter. (See "How do I submit continuing review?")
    NOTE: Any study that remains in an EXPIRED state beyond 30 days and the PI has not submitted a continuing review as required is subject to administrative closure.
    c. A study closure/completion application when the Human Research is closed. (See "How Do I Close Out a Study?")
    d. Any PI planning to leave the institution should submit a study closure or if appropriate transfer the study to another investigator. Studies that have not been transferred prior to the PI departure are subject to administrative closure.
8) Complete the Report of New Information (RNI) within five business days for any of the following items. (Reference HRP-029 for additional information).
    a) Information that indicates a new or increased risk, or a new safety issue. For example:
        i) New information (e.g., an interim analysis, safety monitoring report, publication in the literature, sponsor report, or investigator finding) that indicates an increase in the frequency or magnitude of a previously known risk or uncovers a new risk.
        ii) An investigator brochure, package insert, or device labeling is revised to indicate an increase in the frequency or magnitude of a previously known risk, or describe a new risk
        iii) Withdrawal, restriction, or modification of a marketed approval of a drug, device, or biologic used in a research protocol
        iv) Protocol deviation/violation that harmed subjects or others or that indicates subjects or others might be at increased risk of harm
        v) Complaint of a subject that indicates subjects or others might be at increased risk of harm or at risk of a new harm
        vi) Any changes significantly affecting the conduct of the research
    b) Harm experienced by a subject or other individual, which in the opinion of the investigator are **unexpected** and **probably related** to the research procedures.

i) A harm is "unexpected" when its specificity or severity are inconsistent with risk information previously reviewed and approved by the IRB in terms of nature, severity, frequency, and characteristics of the study population.

ii) A harm is "probably related" to the research procedures if in the opinion of the investigator, the research procedures more likely than not caused the harm.
NOTE: Individual Adverse Events that do not meet the criteria for Unanticipated Problems do not require submission to the IRB. Continue to report adverse events to any sponsor as required.

c) Non-compliance with the federal regulations governing human research or with the requirements or determinations of the IRB, or an allegation of such non-compliance.

d) Audit, inspection, or inquiry by a federal agency and any resulting reports (e.g. FDA Form 483.)

e) Written reports of study monitors.

f) Failure to follow the protocol due to the action or inaction of the investigator or research staff.

g) Breach of confidentiality.

h) Change to the protocol taken without prior IRB review to eliminate an apparent immediate hazard to a subject.

i) Incarceration of a subject in a study not approved by the IRB to involve prisoners.

j) Complaint of a subject that cannot be resolved by the research team.

k) Premature suspension or termination of the protocol by the sponsor, investigator, or institution.

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

9) Submit an updated disclosure of financial interests within thirty days of discovering or acquiring (e.g., through purchase, marriage, or inheritance) a new financial interest.

10) Do not accept or provide payments to professionals in exchange for referrals of potential subjects ("finder's fees.")

11) Do not accept payments designed to accelerate recruitment that were tied to the rate or timing of enrollment ("bonus payments.")

12) See additional requirements of various federal agencies in Appendix A. These represent additional requirements and do no override the baseline requirements of this section.

13) If the study is a clinical trial and supported by a federal agency that follows the Common Rule, one IRB-approved version of a consent form that has been used to enroll participants must be posted on a public federal website designated for posting such consent forms. The form must be posted after recruitment closes, and no later than 60 days after the last study visit. Please contact the study sponsor with any questions.

a. If certain information should not be made publicly available on a Federal website (e.g. confidential commercial information), the supporting Federal department or agency may permit or require redactions to the information posted. Contact the Federal department or agency supporting the clinical trial for a formal determination.
b. Contact the supporting Federal department or agency sponsor with any other questions regarding consent form posting obligations.

What are my obligations as the overall study PI for a multi-site or collaborative IRB study that requires a single IRB?

1) Coordinate with HRPP personnel to determine whether this institution's IRB can act as the single IRB for all or some institutions participating in the study or if an external IRB will assume oversight.
2) Identify all sites that will be engaged in the human research and requiring oversight by the IRB.
3) Ensure that all sites receive a request to rely on the reviewing IRB and that all institutional requirements are satisfied before a study is activated at a relying site.
4) Collaborate with the reviewing IRB to document roles and responsibilities for communicating and coordinating key information from study teams and the IRB or HRPP at relying sites.
5) Respond to questions or information requests from study teams or the IRB or HRPP staff at relying sites.
6) Provide relying site investigators with the policies of the reviewing IRB.
7) Provide relying site investigators with the IRB-approved versions of all study documents.
8) Help prepare and submit IRB applications on behalf of all sites. This includes initial review, modifications, personnel updates, reportable new information and continuing review information for all sites.
9) Establish a process for obtaining and collating information from all sites and submitting this information to the reviewing IRB. This includes site-specific variations in study conduct, such as the local consent process and language, subject identification and recruitment processes and local variations in study conduct.
10) Ensure that consent forms used by relying sites follow the consent template approved by the reviewing IRB and include required language as specified by the relying sites.
11) Provide site investigators with all determinations and communications from the reviewing IRB.
12) Submit reportable new information from relying sites to the reviewing IRB in accordance with the terms of the authorization agreement, relevant policies or communication plan.
13) Report the absence of continuing review information from relying sites if they do not provide the required information prior to submission of the continuing review materials to the reviewing IRB. Notifying the relying site of their lapse in approval and applicable corrective actions.

14) Provide study records to the relying institution, reviewing IRB or regulatory agencies upon request.

What are my obligations as investigator when relying on an external IRB?

1) Submit a request to the TAMU IRB office to rely on an external IRB prior to seeking review by an external IRB. This applies even if you have privileges at the other institution.
2) Comply with determinations and requirements of the external reviewing IRB.
3) Provide the external reviewing IRB with requested information about local requirements or local research context issues relevant to the external IRB's determination prior to IRB review.
4) Notify the external reviewing IRB when local policies that impact IRB review are updated.
5) Cooperate in the external reviewing IRB's responsibility for initial and continuing review, record keeping and reporting and providing all information requested by the external reviewing IRB in a timely manner.
6) Disclose conflicts of interest as required by the external reviewing IRB and complying with management plans that may result.
7) Promptly report to the external reviewing IRB any proposed changes to the research and not implementing those changes to the research without prior external IRB review and approval, except where necessary to eliminate apparent immediate hazards to the participants.
8) When enrolling participants, obtain, document and maintain records of consent for each participant or each participant's legally authorized representative.
9) Promptly report to the external reviewing IRB any unanticipated problems involving risks to participants or others according to the requirements specified in the reliance agreement. Also notify the TAMU IRB of the unanticipated problem.
10) Provide the external reviewing IRB with data safety monitoring reports in accordance with the external reviewing IRB's reporting policy.
11) Report non-compliance, participant complaints, protocol deviations or other events according to the requirements specified in the reliance agreement. Also, notify the TAMU IRB of any reportable events.
12) Specify the contact person and provide contact information for researchers and research staff to obtain answers to questions, express concerns, and convey suggestions regarding the use of the external reviewing IRB.

How do I submit a modification?

Log into the electronic system using your NetID or UIN/SSO login and password. Complete the Modification/Amendment form in the electronic IRB system. Update the protocol and consent

as needed and attach all applicable documents. Have the PI sign-off and submit the form. Maintain electronic copies of all information submitted to the IRB in case revisions are required.

Please note that the proposed changes cannot be implemented until IRB approval has been granted. The research may continue but only as previously approved until the proposed modifications are approved by the IRB.

How do I submit continuing review or administrative check-in?

Log into the electronic system using your NetID or UIN/SSO login and password. Complete the Continuing Review form in the electronic IRB system and attach all requested documents. Have the PI sign-off and submit the form. Maintain electronic copies of all information submitted to the IRB in case revisions are required.

If the continuing review involves modifications to previously approved research, submit those modifications as a separate request for modification following the steps in 'How do I submit a modification?'.

If the continuing review application is not received by the date requested in the approval letter, you will be restricted from submitting new Human Research applications until the continuing review or administrative check-in application has been received.

If the approval of Human Research expires all Human Research procedures related to the protocol under review must cease, including recruitment, advertisement, screening, enrollment, consent, interventions, interactions, and collection or analysis of private identifiable information. Continuing Human Research procedures is a violation of institutional policy.

NOTE: Any study that remains in an EXPIRED state beyond 30 days and the PI has not submitted a continuing review as required is subject to administrative closure.

How do I close out a study?

If the research is closed to enrollment and all research-related interventions or interactions with participants have been completed and collection of identifiable private data (as described in the IRB-approved protocol) are finished, the study may be closed with the IRB.

Alternatively, if the study was never initiated and the Investigators no longer have plans to pursue this project then the study should be closed with the IRB.

Log into the electronic system using your NetID or UIN/SSO login and password. Complete the study closure form in the electronic IRB system and attach any requested documents. Have the PI sign-off and submit the form. Maintain electronic copies of all information submitted to the IRB in case additional information is required.

Any PI planning to leave the institution should submit a study closure or if appropriate transfer the study to another investigator. Studies that have not been transferred prior to the PI departure are subject to administrative closure.

How long do I keep records?

Maintain your Human Research records, including signed and dated consent documents for at least three years after completion of the research. Maintain signed and dated HIPAA authorizations and consent documents that include HIPAA authorizations for at least six years after completion of the research.

If your Human Research is sponsored, the time-frame for keeping the records may be in the contract. Be sure to contact the sponsor before disposing of Human Research records.

What is an appropriate recruitment method?

The following methods of recruiting subjects at TAMU are generally acceptable: Advertisements, flyers, information sheets, notices, TAMU email, internet postings and/or social media. Referrals may come from outside professionals that were provided general information letters or through snowball sampling methods for minimal risk social and behavioral research. You must include a description of your recruitment methods in the application, or in the protocol, you upload into the electronic system. The IRB must approve the recruitment plan and the text of the recruitment materials.

All approved recruitment materials will be stamped electronically with the IRB ID Number and the Approval Date by the HRPP staff and available for download from the electronic system. These IRB-stamped documents must be used for recruitment.

For recruitment materials that are distributed to potential participants through electronic means for which you cannot feasibly use the stamped document, the study's IRB ID number and IRB approval date must be included in the following format: TAMU IRB#20XX-XXXX Approved: XX/XX/XXXX.

See HRP-094 – SOP - Subjects Selection Recruitment and Payments for additional information.

How do I obtain informed consent from participants?

You must describe your process for obtaining informed consent from participants in your study protocol. The process you employ for obtaining informed consent will depend on the research setting and your participant population. ***The consent process is distinct from the consent document***. When written documentation of consent is a requirement for IRB approval, a participant or their Legally Authorized Representative (LAR) must sign a consent document, but only after you have led participants through your approved consent process. See HRP-090 – SOP - Informed Consent Process for Research and sections 5, 6 and 7 of HRP-314 – WORKSHEET - Criteria for Approval for elements to include in your consent process.

Do research participants have to sign a consent document?

On all non-exempt research a participant or their Legally Authorized Representative must sign a consent document if the IRB has not waived the requirement to obtain written documentation of informed consent. Signed consent includes a signature in an electronic format.

An electronic signature means an electronic symbol or process attached to or logically associated with the record or form and executed or adopted by a person with the intent to sign the record or form. Include information about consent documentation in your study protocol. The IRB reviews the entire consent process and determines whether the process is adequate for obtaining and documenting informed consent.

The IRB may waive the requirement to obtain written documentation of informed consent if certain conditions are met:

- The research must be no more that minimal risk;
- the procedures do not normally require written consent when research is not involved;
- the subject's signature would be the only record linking the subject to the consent document; and
- principal risk would be a breach of confidentiality if signed;

See the SOP: Written Documentation of Consent (HRP-091) and CHECKLIST: Waiver of Written Documentation of Consent (HRP-411) for the criteria the IRB uses to determine whether a waiver of written documentation of consent is acceptable.

How do I document consent or assent?

Use the signature block pages approved by the IRB. There are three different signature pages. Please select the one appropriate for your research: adults capable of providing consent, adults unable to provide consent and for parents to sign when enrolling their child in research. Complete all items, including dates and optional elements. See the SOP: Written Documentation of Consent (HRP-091)

Any plans to document consent using an electronic format must be clearly described in your study protocol. Provide a copy of any web-based or electronic signature page to the IRB for approval.

You must also keep a copy of each signed consent document with your study records and provide a copy of the consent document to the participant or their LAR.

How do I obtain a waiver or alteration of informed consent?

The IRB may waive the requirement for you to obtain informed consent from participants or to alter the consent process if certain conditions are met:

- the research is not FDA regulated;

- the research does not involve non-viable neonates or newborn dried blood spots;
- the research is no more than minimal risk; the research will not adversely affect the rights and welfare of participants;
- the research could practicably not be carried out without the waiver; and
- when appropriate the subject will be provided with pertinent information after participation;

See CHECKLIST: Waiver or Alteration of Consent Process (HRP-410) for the criteria the IRB uses to determine whether a waiver or alteration is acceptable. Include information in your protocol that will help the IRB make a determination. You must obtain informed consent prior to interacting or intervening with participants or using participants' private identifiable information for research purposes if the IRB has not waived or altered the consent process.

What is an Unanticipated Problem?

Unanticipated problems, in general, include any incident, experience, or outcome that meets **all** of the following criteria:

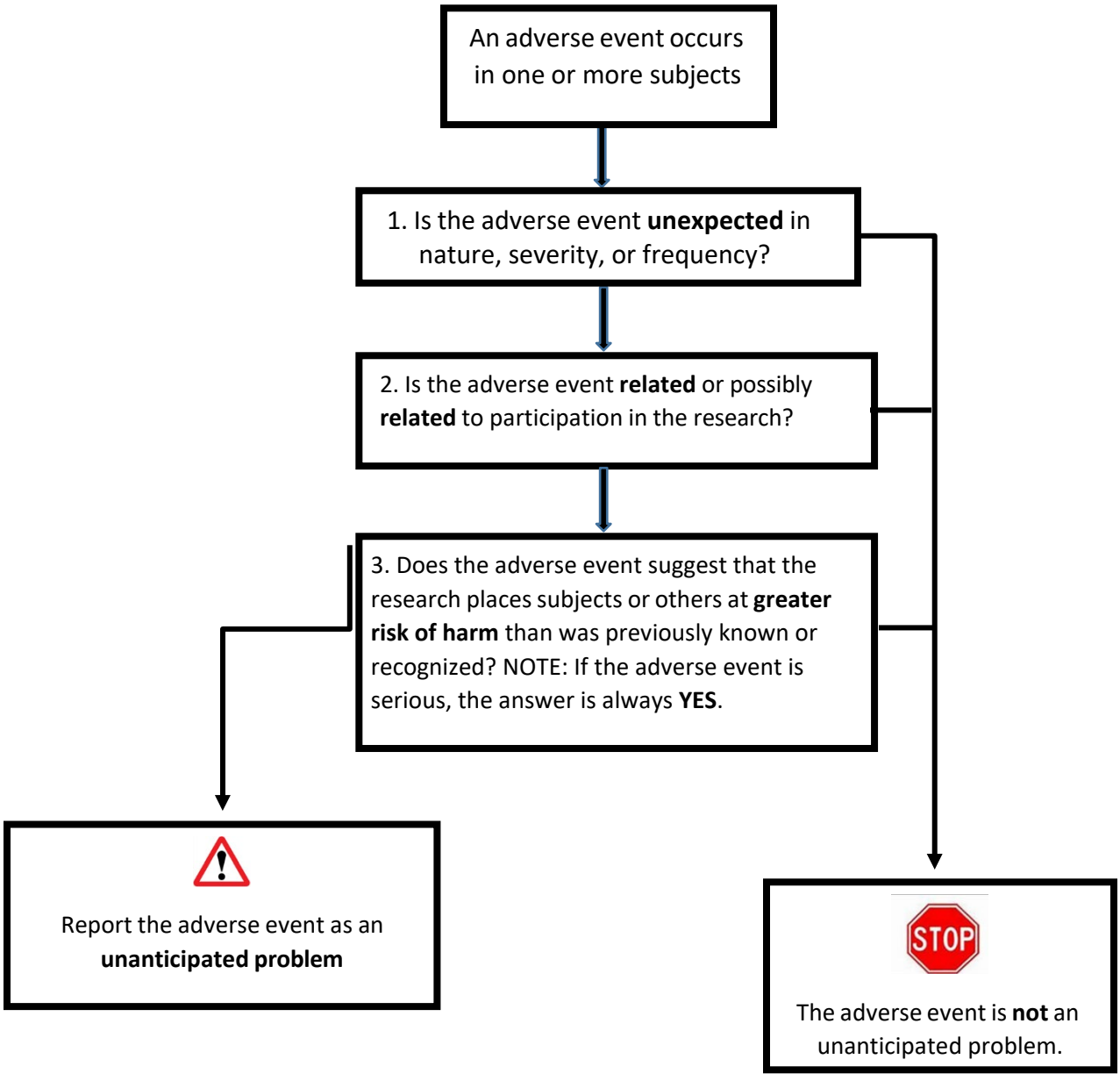
1. unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;
2. is related or possibly related to the research (this means that it is more likely than not, the incident, experience, or outcome was caused by the procedures involved in the research); and
3. suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

There are other types of incidents, experiences, and outcomes that occur during the conduct of human subjects research that represent unanticipated problems but are not considered adverse events. For example, some unanticipated problems involve social or economic harm instead of the physical or psychological harm associated with adverse events. In other cases, unanticipated problems place subjects or others at increased *risk* of harm, but no harm occurs.

See flow chart below.

Unanticipated Problem Flow Chart

Ask all three questions



Should I obtain a Certificate of Confidentiality for my research?

Certificates of Confidentiality (CoC) protect the privacy of research participants by prohibiting disclosure of identifiable, sensitive research information to anyone not connected to the research except when the participant consents or in a few other specific situations. The CoC will protect information from forced or compelled disclosure, e.g., to oppose a subpoena.

Sensitive information includes but is not limited to information relating to sexual attitudes, preferences, or practices; the use of alcohol, drugs, or other addictive products, illegal conduct; or information if released, might be damaging to an individual's financial standing, employability, or reputation within the community or might lead to social stigmatization or discrimination; information pertaining to an individual's psychological well-being or mental health; and genetic information or tissue samples.

Investigators and institutions have responsibilities associated with the CoC, including: 1) informing participants about the CoC, 2) not releasing participants identifiable, sensitive information except under limited circumstances, 3) upholding the CoC protections, and 4) informing investigators and institutions receiving a copy of protected information about the CoC protections.

Since 2017, NIH-funded research meeting specific criteria are automatically deemed to have a Certificate of Confidentiality.

Eligibility for an NIH-issued CoC may depend on the type of funding that is supporting the research. Issuance of a CoC for research that is not funded by NIH is at the discretion of NIH.

More information on obtaining a CoC can be found at: Certificates of Confidentiality (CoC) | grants.nih.gov

What additional requirements apply to International Research?

International research conducted by the Texas A&M University investigators falls under the university's purview and guidelines. Local cultural and religious norms should be considered as well as adherence to ethical standards and safeguards to protect the rights and welfare of the participants in foreign countries.

Research projects conducted outside of the United States are to be reviewed and approved by the foreign country's equivalent of an IRB, as applicable. When there is no equivalent board or group, investigators are expected to consult local experts or community leaders about the research and obtain their cooperation and support. Any cultural norms that differ from the university's guidelines and policies should be identified in the study application. All international approvals must be in writing.

If any non-English subjects are going to be recruited, please complete a Certificate of Translation form verifying accurate translation of applicable study documents. (See next section).

The Office of Human Research Protections (OHRP) publishes the International Compilation of Human Research Standards | HHS.gov. The compilation is a listing of over 1000 standards on human subjects protections in 131 countries. OHRP also provides the Listing of Social-Behavioral Research Standards | HHS.gov which is a summary of 27 social-behavioral research standards from around the world.

Note: Please be aware of any Export Control laws that apply to your project involving a foreign country. Contact the Export Controls Office at exportcontrols@tamu.edu for additional information.

When is a Certificate of Translation Required for Consents or other Study Documents written in another Language?

The IRB may approve enrollment of participants unable to speak English provided that you have the resources to communicate effectively with the participants during recruitment, while obtaining consent, and for the duration of the research. Describe your resources and enrollment plans in detail in the IRB application.

If you expect to enroll more than one non-English speaking subject in the United States or in a foreign country, you are expected to translate the approved English version of the consent into the appropriate language.

A Certificate of Translation from a qualified interpreter is required to verify that the translation of the consent, survey or other documents are accurate. Those who translate the material are to provide a brief description of their qualifications, skills or experience for serving in the role and sign the certificate of translation form. Please see the translation certificate template on the HRPP website: http://rcb.tamu.edu/humansubjects/forms/templates

A professional translation service is required when the translated materials are for use in a clinical trial or other study that is greater than minimal risk. To reduce translation costs when using a professional translation service, it is recommended that you first obtain your IRB approval of the English-Language consent document. After you receive approval, have the consent document translated and submit to the IRB as an amendment to the study.

How do I obtain Institutional Certification for submission of genomic data to an NIH-designated data repository?

You may be required to submit genomic data to an NIH-designated data repository as a condition of your federal award. In those cases, the Institutional Official or designee must certify that your genomic data sharing plan is acceptable. The IRB Office verifies for the Institutional Official or designee that your genomic data sharing plan meets the criteria for submission to an NIH-designated data repository. The IRB staff will notify you when the verification process is complete. Contact the IRB staff for additional instructions on how to submit that plan for verification.

How do I conduct research using genetic information?

The Genetic Information Nondiscrimination Act of 2008 (GINA) prohibits discrimination in health coverage and employment based on genetic information. If you conduct research using genetic information, you are responsible for becoming familiar with the provisions of the law, both to implement measures to protect that information from inappropriate disclosures and to inform potential research participants about their rights under the law.

Your consent document should contain the recommended GINA language. The Biomedical Template Consent Document (HRP-592)" has sample language for you to include for participants. Additional information is available at: Genetic Information Nondiscrimination Act Guidance (2009) | HHS.gov

Does my funded project qualify for a 'Delayed Onset Determination'?

There are some limited circumstances described by federal regulations (45 CFR 46.118) in which IRB approval or exempt status is not required before an award is made by the sponsoring agency, because definitive plans for human subjects involvement cannot be described in the grant application. This is referred to as **delayed onset human research.**

In the case of delayed onset human research, the principal investigator must submit an application to the IRB through the electronic system stating that the plans for human subjects are not fully developed and will occur during a future period of time. The explanation should contain as much detail as possible and indicate the portions of the grant that confirm the need for development of activities prior to the involvement of human subjects. Examples of developmental activities that are appropriate for a delayed onset determination include:

- Procedures or questionnaires under development or other novel research instruments;
- Completion of animal studies;
- Purification of compounds;
- Development of a device, assay or diagnostic test

Delayed Onset Human Research status is not a type of IRB approval.

Delayed Onset Human Research Status is not a substitute for IRB approval.

No human subjects activities can occur until any proposed Human Subjects Research activity has been granted exempt status, or complete IRB approval. Determinations are not issued through emails, phone calls or other means outside of a valid application through the electronic system..

Activities that are prohibited under a 'Delayed Onset Determination' include but are not limited to the following:

- Advertising for possible subjects, or any other method of recruiting or soliciting interest in the research;
- Pre-screening of records to identify possible subjects;

- Pilot studies, pre-tests, focus groups or surveys involving human research, no matter how few individuals participate.

A Delayed Onset Human Research determination is not a mechanism for delaying an IRB application, nor to satisfy urgent federal agency requirements for IRB approval prior to awarding the funds, when human subjects research activities are planned and can be described sufficiently in an IRB application. The funding agency may reject a delayed onset determination if they believe the project is sufficiently developed and requires full IRB approval. The preparation of the IRB application and fulfillment of other compliance requirements almost never qualifies as "significant pre-human subjects development activities".

If the grant has not been awarded but the research team has been informed that it is likely to receive the award (e.g., Just-in-Time, JIT, notification or any other indications that that funding is likely), the research team must have the IRB application ready for submission. The application must contain complete and accurate information to determine that all the criteria for approval or an exemption are met. Refer to WORKSHEET: Criteria for Approval (HRP-314) or WORKSHEET: Exemption (HRP-312). This includes a complete copy of the grant and grant number as well as other relevant documents such as the protocol, consents, instruments, and any other data collection forms. When all requirements are satisfied, the IRB will issue an Approval of Research or an Exemption Determination letter.

Do I need IRB review for TAMU classroom-based research projects conducted by students?

TAMU recognizes that some student projects are conducted to fulfill course requirements and to teach students research methods. If these classroom activities are conducted by the students and not designed to produce new knowledge or to be generalizable or presented outside of the class, the IRB will not require review and approval. Please note that IRB templates and consent documents may not be used for research that will not be reviewed and approved by the IRB. Please contact the IRB staff if you have any questions.

There are some student research projects that will require IRB review if they involve human subjects: Doctoral dissertations; funded research; research conducted through collaborations external to TAMU, Master's theses, and honors theses. All of these must be reviewed and approved by the IRB before students may begin their research.

Research conducted by faculty, using students and/or student data, does require IRB review and approval prior to implementation. (See next section).

Do I need IRB review for TAMU classroom-based research projects conducted by faculty?

Educational activities conducted by faculty or instructors in the classroom or with students and the intent is to generalize the information outside of the classroom or publish, will require submission to the IRB for review and approval. This includes both prospective and retrospective research conducted by

faculty or instructors using student records, interviews, surveys or other student data. IRB submission for review and approval is required prior to implementation of the research activities. Please note that research involving TAMU students or their data will also require the Registrar's approval.

When is written parental permission required for research with minors in an educational setting?

If your research requires accessing information from a student's records then FERPA requires that a consent for disclosure of education records be signed and dated by the parent or eligible student. The consent should specify the records that may be disclosed, state the purpose of the disclosure, and identify the organization or other parties to whom the disclosure may be made 34 CFR § 99.30. There are other times when written consent may be required by the IRB, depending upon the research procedures and the degree of risk.

What else do I need to know when conducting research with minors in an educational setting?

The PPRA amendment under FERPA requires that schools give notification to parents and students about the administration of a survey, analysis, or evaluation of students when one or more of the following eight protected areas are involved:

1. political affiliations or beliefs of the student or the student's parent;
2. mental or psychological problems of the student or the student's family;
3. sex behavior or attitudes;
4. illegal, anti-social, self-incriminating, or demeaning behavior;
5. critical appraisals of other individuals with whom respondents have close family relationships;
6. legally recognized privileged or 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 such program).

The parent of a student has the right, upon request, to inspect a survey created by a third party before the survey is administered or distributed to the students.

The IRB will verify that the site specific authorization from the school(s) includes the required FERPA/PPRA language to ensure appropriate notice is given to the parents. Templates for Site Specific Authorizations are posted on the IRB website.

What is Community Based Participatory Research?

Community-Based Participatory Research is a *collaborative approach* to research that involves the community partners in the research design and all aspects of the research process. CBPR begins with a research topic of importance to the community and aims to improve the quality of life of community members. Simply recruiting participants from the community is not CBPR.

Do I need an FDA Investigational New Drug (IND) Application for research with drugs, biologics, dietary supplements or other products?

Research involving drugs, biologics, dietary supplements, or other test articles including investigations of conventional foods studied for use in the diagnosis, cure, mitigation, treatment or prevention of a disease will require additional regulatory oversight and involves knowledge of specific FDA regulations: Investigational New Drug Application (21 CFR Part 312).

The principal investigator must clarify for the IRB whether or not there is an FDA issued IND number for the use of a test article in human research that meets the definition of a drug as defined in the Federal Food Drug & Cosmetic Act section 201(g)(1). Appropriate documentation from the FDA, sponsor or investigator holding the IND should be included in the IRB application.

The FDA regulates a product based upon the product's ***intended*** use. Drugs are defined as articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease and articles (other than food) intended to affect the structure or any function of the body of man or animals.

If the principal intent of the investigational use of the test article is to develop information about the products safety or efficacy, the submission of an IND is required unless all the conditions for an IND Exemption set forth in 21 CFR 312.2(b) are met (See FDA guidance: Investigational New Drug Applications (INDs) — Determining Whether Human Research Studies Can Be Conducted Without an IND (fda.gov)):

- The drug product is lawfully marketed in the United States.
- The investigation 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.
- In the case of a prescription drug, the investigation is not intended to support a significant change in the advertising for the drug.
- The investigation does not involve a route of administration, dose, patient population, or other factor that significantly increases the risk (or decreases the acceptability of the risk) associated with the use of the drug product (21 CFR 312.2(b)(1)(iii)).

If a ***dietary supplement*** or ***food product*** will be used in research designed to provide information on a health claim regardless of how readily available the product is for consumer use, the IRB will require the investigator or the sponsor to contact the FDA Review Division responsible for the relevant therapeutic area of the proposed trial. In some cases, the FDA staff may request that the sponsor or investigator submit a summary of their proposed investigation in writing for FDA review before providing advice about whether or not an IND is required.

A ***biological product*** is a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein (except any chemically synthesized polypeptide), or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound). The biological product is subject to this requirement when the proposed research is for the prevention, treatment, or cure of a disease or condition of human beings.

Information on how to file an IND Application can be found on the FDA website: https://www.fda.gov/drugs/developmentapprovalprocess/howdrugsaredevelopedandapproved/approvalapplications/investigationalnewdrugindapplication/default.htm

When can research that requires and IND begin?

Although, the IND goes into effect 30 days after the FDA has received the application (unless the FDA notifies the sponsor/investigator that the investigation is subject to clinical hold) the investigator may not begin the research, including recruiting, obtaining consent, and screening participants, until written verification of the IND is provided to the IRB and a formal IRB approval letter has been issued.

Please contact the IRB office for help if you are planning to conduct human research that involves drugs, biologics, dietary supplements or other products that may require an IND. See WORKSHEET: Drugs (HRP-306).

Do I need an FDA IDE for use of an Investigational or Approved Device on Humans?

All clinical evaluations of investigational devices, (investigational use also includes clinical evaluation of certain modifications or new intended uses of legally marketed devices) unless exempt, must have an approved IDE **before** the study is initiated.

Clinical evaluation of devices that have not been cleared for marketing in the United States requires:

- an investigational plan approved by an institutional review board (IRB). If the study involves a significant risk device, the IDE must also be approved by FDA;
- informed consent from all patients;
- labeling stating that the device is for investigational use only;
- monitoring of the study and;
- required records and reports

The IDE regulations (21 CFR 812) describe three types of device studies: significant risk (SR), nonsignificant risk (NSR), and exempt studies. SR device studies must have an IDE application approved by FDA and have IRB approval before they proceed, and they must follow all of the IDE requirements. NSR device studies must follow the abbreviated IDE requirements at 21 CFR 812.2(b), including informed consent and IRB review, and do not require submission of an IDE application to FDA.

The sponsor (or investigator if acting as the sponsor) is responsible for making the initial risk determination, SR or NSR, and presenting it to the IRB. If the sponsor has determined that a device study is NSR, the IRB must review the sponsor's determination. If the IRB disagrees with the sponsor's NSR

assessment and decides the study is SR, the IRB must inform the clinical investigator and, where appropriate, the sponsor. The IRB should also document its SR/NSR determination in the IRB meeting minutes.

Based on the information provided, FDA will determine if a device study is SR, NSR, or exempt from the IDE requirements found in 21 CFR Part 812. If FDA makes the SR, NSR, or exempt determination for a study, the FDA's determination is final. Use WORKSHEET: Devices (HRP-307) and CHECKLIST: Non-Significant Risk Device (HRP-418) for additional guidance.

When should I register my research with ClinicalTrials.gov?

Studies must be registered with ClinicalTrials.gov if:

1. they involve drugs, devices, or biologics that are regulated by the Food and Drug Administration (FDA), OR
2. they are federally funded and meet the definition of a clinical trial, OR
3. there is a plan to publish the results in a medical journal AND the study meets the International Committee of Medical Journal Editors (ICMJE) definition of a clinical trial

ClinicalTrials.gov is the result of a federal law requiring that clinical trials be registered to improve public access to information about clinical research, promote public trust in research, and inform future research. In some cases, registration is also required for journal publication.

The responsible party for an applicable clinical trial (ACT) must register the trial and submit results information. The responsible party is the person who sponsors, or initiates, the trial. If this is a TAMU investigator, the term 'Sponsor-investigator' identifies this role in the record. To register a study, investigators must use the Protocol Registration and Results System (PRS) Login to ClinicalTrials.gov PRS - ClinicalTrials.gov. To get started, investigators should contact a PRS administrator by emailing irb@tamu.edu to have an account created for them.

Food and Drug Administration Registration Requirements
The Food and Drug Administration (FDA) requires registration with ClinicalTrials.gov for all applicable clinical trials (ACTs) that were initiated after 9/27/2007, or were initiated before 9/27/2007, but were ongoing as of 12/26/2007.

Applicable clinical trials generally include interventional studies (with one or more arms) of FDA-regulated drugs, biological products, or devices that meet one of the following conditions:

- The trial has one or more sites in the United States
- The trial is conducted under an FDA investigational new drug application (IND) or investigational device exemption (IDE)
- The trial involves a drug, biologic, or device that is manufactured in the United States or its territories and is exported for research

Registration is *not* required for small trials to determine the feasibility of a device or to test prototype devices where the primary outcome measure relates to feasibility, and not to health outcomes. ClinicalTrials.gov FDAAA

Office of Human Research Protections Requirements
The Office of Human Research Protection (OHRP) requires that each clinical trial conducted or supported by a Federal Department or agency, one IRB-approved informed consent form used to enroll subjects must be posted by the awardee conducting the trials on a publicly available Federal Web site (i.e. Clinicaltrials.gov) that will be established as a repository for such informed consent forms. Additionally, the informed consent form must be posted on the Federal Web site after the clinical trail is closed to recruitment, and no later than 60 days after the last study visit by any subject, as required by the protocol.

National Institutes of Health Registration Requirements
Effective January 18, 2017, National Institutes of Health (NIH) requires registration at ClinicalTrials.gov for all clinical trials (bio-medical or behavioral interventions) funded wholly or partially by NIH.

How can I use or disclose Protected Health Information (PHI) for Research and Comply with the Privacy Rule?

The Privacy Rule describes the ways in which covered entities can use or disclose PHI, including for research purposes. In general, the Rule allows covered entities to use and disclose PHI for research if authorized to do so by the subject in accordance with the Privacy Rule. In addition, in certain circumstances, the Rule permits covered entities to use and disclose PHI without Authorization for certain types of research activities. For example, PHI can be used or disclosed for research if a covered entity obtains documentation that an Institutional Review Board (IRB) or Privacy Board has waived the requirement for Authorization or allowed an alteration. The Rule also allows a covered entity to enter into a Data Use Agreement for sharing a Limited Data Set. There are also separate provisions for how PHI can be used or disclosed for activities preparatory to research and for research on decedents' information.

Please see The Texas A&M University System guidance for conducting research with PHI OGC-Guidance-on-Conducting-Research-with-PHI-OGC-7-19-2021.pdf (netdna-ssl.com) or contact the TAMU Privacy Officer at privacy@tamu.edu for more information.

How do I get additional information and answers to questions?

This document and the policies and procedures for the Human Research Protection Program are available on the HRPP Web Site at Toolkit – Division of Research (tamu.edu).

Any changes to this manual or the HRPP Standard Operating Procedures will be posted on the HRPP website.

If you have any questions, comments or concerns, please contact the:

Human Research Protection Program

155 Ireland Street, Room 228

College Station, TX 77843-1186

Mail Stop: 1186 TAMU

Phone: 979.458.4067
Email: irb@tamu.edu

Appendix A-1 ..... Additional Requirements for DHHS-Regulated Research[2]

1. When a subject decides to withdraw from a clinical trial, the investigator conducting the clinical trial should ask the subject to clarify whether the subject wishes to withdraw from all components of the trial or only from the primary interventional component of the trial. If the latter, research activities involving other components of the clinical trial, such as follow-up data collection activities, for which the subject previously gave consent may continue. The investigator should explain to the subject who wishes to withdraw the importance of obtaining follow-up safety data about the subject.

[2] http://www.hhs.gov/ohrp/policy/subjectwithdrawal.html

2. Investigators are allowed to retain and analyze already collected data relating to any subject who chooses to withdraw from a research study or whose participation is terminated by an investigator without regard to the subject's consent, provided such analysis falls within the scope of the analysis described in the IRB-approved protocol. This is the case even if that data includes identifiable private information about the subject.

3. For research not subject to regulation and review by FDA, investigators, in consultation with the funding agency, can choose to honor a research subject's request that the investigator destroy the subject's data or that the investigator exclude the subject's data from any analysis.

4. When seeking the informed consent of subjects, investigators should explain whether already collected data about the subjects will be retained and analyzed even if the subjects choose to withdraw from the research.

5. When research is covered by a certificate of confidentiality, researchers:
    a. May not disclose or provide, in any Federal, State, or local civil, criminal, administrative, legislative, or other proceeding, the name of such individual or any such information, document, or biospecimen that contains identifiable, sensitive information about the individual and that was created or compiled for purposes of the research, unless such disclosure or use is made with the consent of the individual to whom the information, document, or biospecimen pertains; or
    b. May not disclose or provide to any other person not connected with the research the name of such an individual or any information, document, or biospecimen that contains identifiable, sensitive information about such an individual and that was created or compiled for purposes of the research.
    c. May disclose information only when:
        i. Required by Federal, State, or local laws (e.g., as required by the Federal Food, Drug, and Cosmetic Act, or state laws requiring the reporting of communicable diseases to State and local health departments), excluding instances of disclosure in any Federal, State, or local civil, criminal, administrative, legislative, or other proceeding.
        ii. Necessary for the medical treatment of the individual to whom the information, document, or biospecimen pertains and made with the consent of such individual;
        iii. Made with the consent of the individual to whom the information, document, or biospecimen pertains; or
        iv. Made for the purposes of other scientific research that is in compliance with applicable Federal regulations governing the protection of human participants in research.
    d. Researchers must inform participants of the protections and limitations of certificates of confidentiality (see language in HRP-502 - TEMPLATE CONSENT DOCUMENT).
        i. For studies that were previously issued a Certificate and notified participants of the protections provided by that Certificate, NIH does not expect participants to

be notified that the protections afforded by the Certificate have changed, although IRBs may determine whether it is appropriate to inform participants.

ii. If part of the study cohort was recruited prior to issuance of the Certificate, but are no longer activity participating in the study, NIH does not expect participants consented prior to the change in authority, or prior to the issuance of a Certificate, to be notified that the protections afforded by the Certificate have changed, or that participants who were previously consented to be re-contacted to be informed of the Certificate, although the IRB may determine whether it is appropriate to inform participants.

e. Researchers conducting research covered by a certificate of confidentiality, even if the research is not federally funded, must ensure that if identifiable, sensitive information is provided to other researchers or organizations, the other researcher or organization must comply with applicable requirements when research is covered by a certificate of confidentiality.

Appendix A-2 ..... Additional Requirements for FDA-Regulated Research

1. When a subject withdraws from a study:[3]
    a. The data collected on the subject to the point of withdrawal remains part of the study database and may not be removed.
    b. An investigator may ask a subject who is withdrawing whether the subject wishes to provide continued follow-up and further data collection subsequent to their withdrawal from the interventional portion of the study. Under this circumstance, the discussion with the subject would distinguish between study-related interventions and continued

[3] http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126489.pdf

follow-up of associated clinical outcome information, such as medical course or laboratory results obtained through non-invasive chart review, and address the maintenance of privacy and confidentiality of the subject's information.

c. If a subject withdraws from the interventional portion of the study, but agrees to continued follow-up of associated clinical outcome information as described in the previous bullet, 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 informed consent form). IRB approval of informed consent documents is required.

d. If a subject withdraws from the interventional portion of a study and does not consent to continued follow-up of associated clinical outcome information, the investigator must not access for purposes related to the study the subject's medical record or other confidential records requiring the subject's consent.

e. 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.

2. For FDA-regulated research involving investigational drugs:
   a. Investigators must abide by FDA restrictions on promotion of investigational drugs:[4]
      i. An investigator, or any person acting on behalf of an investigator, must not represent in a promotional context that an investigational new drug is safe or effective for the purposes for which it is under investigation or otherwise promote the drug.
      ii. This provision is not intended to restrict the full exchange of scientific information concerning the drug, including dissemination of scientific findings in scientific or lay media. Rather, its intent is to restrict promotional claims of safety or effectiveness of the drug for a use for which it is under investigation and to preclude commercialization of the drug before it is approved for commercial distribution.
      iii. An investigator must not commercially distribute or test market an investigational new drug.
   b. Follow FDA requirements for general responsibilities of investigators[5]
      i. An investigator is responsible for ensuring that an investigation is conducted according to the signed investigator statement, the investigational plan, and applicable regulations; for protecting the rights, safety, and welfare of subjects under the investigator's care; and for the control of drugs under investigation.
      ii. An investigator must, in accordance with the provisions of 21 CFR §50, obtain the informed consent of each human subject to whom the drug is administered, except as provided in 21 CFR §50.23 or §50.24 of this chapter.
      iii. Additional specific responsibilities of clinical investigators are set forth in this part and in 21 CFR §50 and 21 CFR §56.

[4] http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.7
[5] http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.60

c. Follow FDA requirements for control of the investigational drug[6]
    i. An investigator must administer the drug only to subjects under the investigator's personal supervision or under the supervision of a sub-investigator responsible to the investigator.
    ii. The investigator must not supply the investigational drug to any person not authorized under this part to receive it.

d. Follow FDA requirements for investigator recordkeeping and record retention[7]
    i. Disposition of drug:
        1. An investigator is required to maintain adequate records of the disposition of the drug, including dates, quantity, and use by subjects.
        2. If the investigation is terminated, suspended, discontinued, or completed, the investigator must return the unused supplies of the drug to the sponsor, or otherwise provide for disposition of the unused supplies of the drug under 21 CFR §312.59.
    ii. Case histories.
        1. An investigator is required to prepare and maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual administered the investigational drug or employed as a control in the investigation.
        2. Case histories include the case report forms and supporting data including, for example, signed and dated consent forms and medical records including, for example, progress notes of the physician, the individual's hospital charts, and the nurses' notes. The case history for each individual must document that informed consent was obtained prior to participation in the study.
    iii. Record retention: An investigator must retain required records for a period of 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.

e. Follow FDA requirements for investigator reports[8]
    i. Progress reports: The investigator must furnish all reports to the sponsor of the drug who is responsible for collecting and evaluating the results obtained.
    ii. Safety reports: An investigator must promptly report to the sponsor any adverse effect that may reasonably be regarded as caused by, or probably caused by, the drug. If the adverse effect is alarming, the investigator must report the adverse effect immediately.
    iii. Final report: An investigator must provide the sponsor with an adequate report shortly after completion of the investigator's participation in the investigation.

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[6] http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.61
[7] http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.62
[8] http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.64

iv. Financial disclosure reports:
    1. The clinical investigator must provide the sponsor with sufficient accurate financial information to allow an applicant to submit complete and accurate certification or disclosure statements as required under 21 CFR §54.
    2. The clinical investigator must promptly update this information if any relevant changes occur during the course of the investigation and for 1 year following the completion of the study.

f. Follow FDA requirements for assurance of IRB review[9]
    i. An investigator must assure that an IRB that complies with the requirements set forth in 21 CFR §56 will be responsible for the initial and continuing review and approval of the proposed clinical study.
    ii. The investigator must also assure that he or she will promptly report to the IRB all changes in the research activity and all unanticipated problems involving risk to human subjects or others, and that he or she will not make any changes in the research without IRB approval, except where necessary to eliminate apparent immediate hazards to human subjects.

g. Follow FDA requirements for inspection of investigator's records and reports[10]
    i. An investigator must upon request from any properly authorized officer or employee of FDA, at reasonable times, permit such officer or employee to have access to, and copy and verify any records or reports made by the investigator pursuant to 312.62.
    ii. The investigator is not required to divulge subject names unless the records of particular individuals require a more detailed study of the cases, or unless there is reason to believe that the records do not represent actual case studies, or do not represent actual results obtained.

h. Follow FDA requirements for handling of controlled substances[11]
    i. If the investigational drug is subject to the Controlled Substances Act, the investigator must take adequate precautions, including storage of the investigational drug in a securely locked, substantially constructed cabinet, or other securely locked, substantially constructed enclosure, access to which is limited, to prevent theft or diversion of the substance into illegal channels of distribution.

3. For FDA-regulated research involving investigational devices:
    a. General responsibilities of investigators.[12]
        i. An investigator is responsible for ensuring that an investigation is conducted according to the signed agreement, the investigational plan and applicable FDA regulations, for protecting the rights, safety, and welfare of subjects under the

[9] http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.66
[10] http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.68
[11] http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.69
[12] http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=812.100

investigator's care, and for the control of devices under investigation. An investigator also is responsible for ensuring that informed consent is obtained in accordance with 21 CFR §50.

b. Specific responsibilities of investigators[13]
    i. Awaiting approval: An investigator may determine whether potential subjects would be interested in participating in an investigation, but must not request the written informed consent of any subject to participate, and must not allow any subject to participate before obtaining IRB and FDA approval.
    ii. Compliance: An investigator must conduct an investigation in accordance with the signed agreement with the sponsor, the investigational plan, and other applicable FDA regulations, and any conditions of approval imposed by an IRB or FDA.
    iii. Supervising device use: An investigator must permit an investigational device to be used only with subjects under the investigator's supervision. An investigator must not supply an investigational device to any person not authorized to receive it.
    iv. Financial disclosure:
        1. A clinical investigator must disclose to the sponsor sufficient accurate financial information to allow the applicant to submit complete and accurate certification or disclosure statements required under 21 CFR §54.
        2. The investigator must promptly update this information if any relevant changes occur during the course of the investigation and for 1 year following completion of the study.
    v. Disposing of device: Upon completion or termination of a clinical investigation or the investigator's part of an investigation, or at the sponsor's request, an investigator must return to the sponsor any remaining supply of the device or otherwise dispose of the device as the sponsor directs.

c. Maintain the following accurate, complete, and current records relating to the investigator's participation in an investigation:[14]
    i. All correspondence with another investigator, an IRB, the sponsor, a monitor, or FDA, including required reports.
    ii. Records of receipt, use or disposition of a device that relate to:
        1. The type and quantity of the device, the dates of its receipt, and the batch number or code mark.
        2. The names of all persons who received, used, or disposed of each device.
        3. Why and how many units of the device have been returned to the sponsor, repaired, or otherwise disposed of.

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[13] http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=812.110

[14] http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=812.140

iii. Records of each subject's case history and exposure to the device. Case histories include the case report forms and supporting data including, for example, signed and dated consent forms and medical records including, for example, progress notes of the physician, the individual's hospital charts, and the nurses' notes. Such records must include:
   1. Documents evidencing informed consent and, for any use of a device by the investigator without informed consent, any written concurrence of a licensed physician and a brief description of the circumstances justifying the failure to obtain informed consent.
   2. Documentation that informed consent was obtained prior to participation in the study.
   3. All relevant observations, including records concerning adverse device effects (whether anticipated or unanticipated), information and data on the condition of each subject upon entering, and during the course of, the investigation, including information about relevant previous medical history and the results of all diagnostic tests.
   4. A record of the exposure of each subject to the investigational device, including the date and time of each use, and any other therapy.

iv. The protocol, with documents showing the dates of and reasons for each deviation from the protocol.

v. Any other records that FDA requires to be maintained by regulation or by specific requirement for a category of investigations or a particular investigation.

d. Inspections[15]

i. Entry and inspection: A sponsor or an investigator who has authority to grant access must permit authorized FDA employees, at reasonable times and in a reasonable manner, to enter and inspect any establishment where devices are held (including any establishment where devices are manufactured, processed, packed, installed, used, or implanted or where records of results from use of devices are kept).

ii. Records inspection: A sponsor, IRB, or investigator, or any other person acting on behalf of such a person with respect to an investigation, must permit authorized FDA employees, at reasonable times and in a reasonable manner, to inspect and copy all records relating to an investigation.

iii. Records identifying subjects: An investigator must permit authorized FDA employees to inspect and copy records that identify subjects, upon notice that FDA has reason to suspect that adequate informed consent was not obtained, or that reports required to be submitted by the investigator to the sponsor or IRB have not been submitted or are incomplete, inaccurate, false, or misleading.

[15] http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=812.145

e. Prepare and submit the following complete, accurate, and timely reports[16]
   i. Unanticipated adverse device effects. An investigator must submit to the sponsor and to the reviewing IRB a report of any unanticipated adverse device effect occurring during an investigation as soon as possible, but in no event later than 10 working days after the investigator first learns of the effect.
   ii. Withdrawal of IRB approval. An investigator must report to the sponsor, within 5 working days, a withdrawal of approval by the reviewing IRB of the investigator's part of an investigation.
   iii. Progress. An investigator must submit progress reports on the investigation to the sponsor, the monitor, and the reviewing IRB at regular intervals, but in no event less often than yearly.
   iv. Deviations from the investigational plan:
      1. An investigator must notify the sponsor and the reviewing IRB of any deviation from the investigational plan to protect the life or physical well-being of a subject in an emergency.
      2. Such notice must be given as soon as possible, but in no event later than 5 working days after the emergency occurred.
      3. Except in such an emergency, prior approval by the sponsor is required for changes in or deviations from a plan, and if these changes or deviations may affect the scientific soundness of the plan or the rights, safety, or welfare of human subjects, FDA and IRB also is required.
   v. Informed consent. If an investigator uses a device without obtaining informed consent, the investigator must report such use to the sponsor and the reviewing IRB within 5 working days after the use occurs.
   vi. Final report. An investigator must, within 3 months after termination or completion of the investigation or the investigator's part of the investigation, submit a final report to the sponsor and the reviewing IRB.
   vii. Other. An investigator must, upon request by a reviewing IRB or FDA, provide accurate, complete, and current information about any aspect of the investigation.

Appendix A-3 ..... Additional Requirements for Clinical Trials (ICH-GCP)

1. Investigator's Qualifications and Agreements
   a. The clinical trial should be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with good clinical practice and the applicable regulatory requirements.
   b. The investigator should be qualified by education, training, and experience to assume responsibility for the proper conduct of the trial, should meet all the qualifications specified by the applicable regulatory requirements, and should provide evidence of such qualifications through up-to-date curriculum vitae and/or other relevant documentation requested by the sponsor, the IRB, and/or the regulatory authorities.

[16] http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=812.150

c. The investigator should be thoroughly familiar with the appropriate use of the investigational product, as described in the protocol, in the current Investigator's Brochure, in the product information and in other information sources provided by the sponsor.
d. The investigator should be aware of, and should comply with, GCP and the applicable regulatory requirements.
e. The investigator/institution should permit monitoring and auditing by the sponsor, and inspection by the appropriate regulatory authorities.
f. The investigator should maintain a list of appropriately qualified persons to whom the investigator has delegated significant trial-related duties.

2. Adequate Resources
    a. The investigator should be able to demonstrate (e.g., based on retrospective data) a potential for recruiting the required number of suitable subjects within the agreed recruitment period.
    b. The investigator should have sufficient time to properly conduct and complete the trial within the agreed trial period.
    c. The investigator should have available an adequate number of qualified staff and adequate facilities for the foreseen duration of the trial to conduct the trial properly and safely.
    d. The investigator should ensure that all persons assisting with the trial are adequately informed about the protocol, the investigational product, and their trial-related duties and functions.
3. Medical Care of Trial Subjects
    a. A qualified physician (or dentist, when appropriate), who is an investigator or a sub-investigator for the trial, should be responsible for all trial-related medical (or dental) decisions.
    b. During and following a subject's participation in a trial, the investigator/institution should ensure that adequate medical care is provided to a subject for any adverse events, including clinically significant laboratory values, related to the trial. The investigator/institution should inform a subject when medical care is needed for intercurrent illnesses of which the investigator becomes aware.
    c. It is recommended that the investigator inform the subject's primary physician about the subject's participation in the trial if the subject has a primary physician and if the subject agrees to the primary physician being informed.
    d. Although a subject is not obliged to give his/her reasons for withdrawing prematurely from a trial, the investigator should make a reasonable effort to ascertain the reasons, while fully respecting the subject's rights.
4. Communication with IRB
    a. Before initiating a trial, the investigator/institution should have written and dated approval opinion from the IRB for the trial protocol, written informed consent form, consent form updates, subject recruitment procedures (e.g., advertisements), and any other written information to be provided to subjects.
    b. As part of the investigator's/institution’s written application to the IRB, the investigator/institution should provide the IRB with a current copy of the Investigator's

Brochure. If the Investigator's Brochure is updated during the trial, the investigator/institution should supply a copy of the updated Investigator's Brochure to the IRB.

c. During the trial the investigator/institution should provide to the IRB all documents subject to review.

5. Compliance with Protocol
    a. The investigator/institution should conduct the trial in compliance with the protocol agreed to by the sponsor and, if required, by the regulatory authorities and which was given approval opinion by the IRB. The investigator/institution and the sponsor should sign the protocol, or an alternative contract, to confirm agreement.
    b. The investigator should not implement any deviation from, or changes of the protocol without agreement by the sponsor and prior review and documented approval opinion from the IRB of an amendment, except where necessary to eliminate an immediate hazards to trial subjects, or when the changes involves only logistical or administrative aspects of the trial (e.g., change in monitors, change of telephone numbers).
    c. The investigator, or person designated by the investigator, should document and explain any deviation from the approved protocol.
    d. The investigator may implement a deviation from, or a change of, the protocol to eliminate an immediate hazard to trial subjects without prior IRB approval opinion. As soon as possible, the implemented deviation or change, the reasons for it, and, if appropriate, the proposed protocol amendments should be submitted: a) to the IRB for review and approval opinion, b) to the sponsor for agreement and, if required, c) to the regulatory authorities.
6. Investigational Product
    a. Responsibility for investigational product accountability at the trial site rests with the investigator/institution.
    b. Where allowed/required, the investigator/institution may/should assign some or all of the investigator's/institution's duties for investigational product accountability at the trial site to an appropriate pharmacist or another appropriate individual who is under the supervision of the investigator/institution.
    c. The investigator/institution and/or a pharmacist or other appropriate individual, who is designated by the investigator/institution, should maintain records of the product's delivery to the trial site, the inventory at the site, the use by each subject, and the return to the sponsor or alternative disposition of unused product. These records should include dates, quantities, batch/serial numbers, expiration dates (if applicable), and the unique code numbers assigned to the investigational product and trial subjects. Investigators should maintain records that document adequately that the subjects were provided the doses specified by the protocol and reconcile all investigational product received from the sponsor.
    d. The investigational product should be stored as specified by the sponsor and in accordance with applicable regulatory requirements.
    e. The investigator should ensure that the investigational product are used only in accordance with the approved protocol.

f. The investigator, or a person designated by the investigator/institution, should explain the correct use of the investigational product to each subject and should check, at intervals appropriate for the trial, that each subject is following the instructions properly.
g. Randomization Procedures and Unblinding: The investigator should follow the trial's randomization procedures, if any, and should ensure that the code is broken only in accordance with the protocol. If the trial is blinded, the investigator should promptly document and explain to the sponsor any premature unblinding (e.g., accidental unblinding, unblinding due to a serious adverse event) of the investigational product.

7. Informed Consent of Trial Subjects
    a. In obtaining and documenting informed consent, the investigator should comply with the applicable regulatory requirements, and should adhere to GCP and to the ethical principles that have their origin in the Declaration of Helsinki. Prior to the beginning of the trial, the investigator should have the IRB's written approval opinion of the written informed consent form and any other written information to be provided to subjects.
    b. The written informed consent form and any other written information to be provided to subjects should be revised whenever important new information becomes available that may be relevant to the subject's consent. Any revised written informed consent form, and written information should receive the IRB's approval opinion in advance of use. The subject or the subject's legally acceptable representative should be informed in a timely manner if new information becomes available that may be relevant to the subject's willingness to continue participation in the trial. The communication of this information should be documented.
    c. Neither the investigator, nor the trial staff, should coerce or unduly influence a subject to participate or to continue to participate in a trial.
    d. None of the oral and written information concerning the trial, including the written informed consent form, should contain any language that causes the subject or the subject's legally acceptable representative to waive or to appear to waive any legal rights, or that releases or appears to release the investigator, the institution, the sponsor, or their agents from liability for negligence.
    e. The investigator, or a person designated by the investigator, should fully inform the subject or, if the subject is unable to provide informed consent, the subject's legally acceptable representative, of all pertinent aspects of the trial including the written information and the approval opinion by the IRB.
    f. The language used in the oral and written information about the trial, including the written informed consent form, should be as non-technical as practical and should be understandable to the subject or the subject's legally acceptable representative and the impartial witness, where applicable.
    g. Before informed consent may be obtained, the investigator, or a person designated by the investigator, should provide the subject or the subject's legally acceptable representative ample time and opportunity to inquire about details of the trial and to decide whether or not to participate in the trial. All questions about the trial should be answered to the satisfaction of the subject or the subject's legally acceptable representative.

h. Prior to a subject's participation in the trial, the written informed consent form should be signed and personally dated by the subject or by the subject's legally acceptable representative, and by the person who conducted the informed consent discussion.

i. If a subject is unable to read or if a legally acceptable representative is unable to read, an impartial witness should be present during the entire informed consent discussion. After the written informed consent form and any other written information to be provided to subjects, is read and explained to the subject or the subject's legally acceptable representative, and after the subject or the subject's legally acceptable representative has orally consented to the subject's participation in the trial and, if capable of doing so, has signed and personally dated the informed consent form, the witness should sign and personally date the consent form. By signing the consent form, the witness attests that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the subject or the subject's legally acceptable representative, and that informed consent was freely given by the subject or the subject's legally acceptable representative.

j. Both the informed consent discussion and the written informed consent form and any other written information to be provided to subjects should include explanations of the following:
    i. That the trial involves research.
    ii. The purpose of the trial.
    iii. The trial treatments and the probability for random assignment to each treatment.
    iv. The trial procedures to be followed, including all invasive procedures.
    v. The subject's responsibilities.
    vi. Those aspects of the trial that are experimental.
    vii. The reasonably foreseeable risks or inconveniences to the subject and, when applicable, to an embryo, fetus, or nursing infant.
    viii. The reasonably expected benefits. When there is no intended clinical benefit to the subject, the subject should be made aware of this.
    ix. The alternative procedures or courses of treatment that may be available to the subject, and their important potential benefits and risks.
    x. The compensation and/or treatment available to the subject in the event of trial related injury.
    xi. The anticipated prorated payment, if any, to the subject for participating in the trial.
    xii. The anticipated expenses, if any, to the subject for participating in the trial.
    xiii. That the subject's participation in the trial is voluntary and that the subject may refuse to participate or withdraw from the trial, at any time, without penalty or loss of benefits to which the subject is otherwise entitled.
    xiv. That the monitors, the auditors, the IRB, and the regulatory authorities will be granted direct access to the subject's original medical records for verification of clinical trial procedures and/or data, without violating the confidentiality of the subject, to the extent permitted by the applicable laws and regulations and that,

by signing a written informed consent form, the subject or the subject's legally acceptable representative is authorizing such access.

xv. That records identifying the subject will be kept confidential and, to the extent permitted by the applicable laws and/or regulations, will not be made publicly available. If the results of the trial are published, the subject's identity will remain confidential.

xvi. That the subject or the subject's legally acceptable representative will be informed in a timely manner if information becomes available that may be relevant to the subject's willingness to continue participation in the trial.

xvii. The persons to contact for further information regarding the trial and the rights of trial subjects, and whom to contact in the event of trial-related injury.

xviii. The foreseeable circumstances and/or reasons under which the subject's participation in the trial may be terminated.

xix. The expected duration of the subject's participation in the trial.

xx. The approximate number of subjects involved in the trial.

k. Prior to participation in the trial, the subject or the subject's legally acceptable representative should receive a copy of the signed and dated written informed consent form and any other written information provided to the subjects. During a subject's participation in the trial, the subject or the subject's legally acceptable representative should receive a copy of the signed and dated consent form updates and a copy of any amendments to the written information provided to subjects.

l. When a clinical trial (therapeutic or non-therapeutic) includes subjects who can only be enrolled in the trial with the consent of the subject's legally acceptable representative (e.g., minors, or patients with severe dementia), the subject should be informed about the trial to the extent compatible with the subject's understanding and, if capable, the subject should sign and personally date the written informed consent.

m. Except as described above, a non-therapeutic trial (i.e. a trial in which there is no anticipated direct clinical benefit to the subject), should be conducted in subjects who personally give consent and who sign and date the written informed consent form.

n. Non-therapeutic trials may be conducted in subjects with consent of a legally acceptable representative provided the following conditions are fulfilled: a) The objectives of the trial cannot be met by means of a trial in subjects who can give informed consent personally. b) The foreseeable risks to the subjects are low. c) The negative impact on the subject's well-being is minimized and low. d) The trial is not prohibited by law. e) The approval opinion of the IRB is expressly sought on the inclusion of such subjects, and the written approval opinion covers this aspect. Such trials, unless an exception is justified, should be conducted in patients having a disease or condition for which the investigational product is intended. Subjects in these trials should be particularly closely monitored and should be withdrawn if they appear to be unduly distressed.

o. In emergency situations, when prior consent of the subject is not possible, the consent of the subject's legally acceptable representative, if present, should be requested. When prior consent of the subject is not possible, and the subject's legally acceptable representative is not available, enrolment of the subject should require measures described in the protocol and/or elsewhere, with documented approval opinion by the

IRB, to protect the rights, safety and well-being of the subject and to ensure compliance with applicable regulatory requirements. The subject or the subject's legally acceptable representative should be informed about the trial as soon as possible and consent to continue and other consent as appropriate should be requested.

8. Records and Reports
    a. The investigator should ensure the accuracy, completeness, legibility, and timeliness of the data reported to the sponsor in the CRFs and in all required reports.
    b. Data reported on the CRF, that are derived from source documents, should be consistent with the source documents or the discrepancies should be explained.
    c. Any change or correction to a CRF should be dated, initialed, and explained (if necessary) and should not obscure the original entry (i.e. an audit trail should be maintained); this applies to both written and electronic changes or corrections. Sponsors should provide guidance to investigators and/or the investigators' designated representatives on making such corrections. Sponsors should have written procedures to assure that changes or corrections in CRFs made by sponsor's designated representatives are documented, are necessary, and are endorsed by the investigator. The investigator should retain records of the changes and corrections.
    d. The investigator/institution should maintain the trial documents as specified in Essential Documents for the Conduct of a Clinical Trial and as required by the applicable regulatory requirements. The investigator/institution should take measures to prevent accidental or premature destruction of these documents.
    e. Essential documents should be retained until at least 2 years after the last approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications in an ICH region or at least 2 years have elapsed since the formal discontinuation of clinical development of the investigational product. These documents should be retained for a longer period however if required by the applicable regulatory requirements or by an agreement with the sponsor. It is the responsibility of the sponsor to inform the investigator/institution as to when these documents no longer need to be retained.
    f. The financial aspects of the trial should be documented in an agreement between the sponsor and the investigator/institution.
    g. Upon request of the monitor, auditor, IRB, or regulatory authority, the investigator/institution should make available for direct access all requested trial-related records.
9. Progress Reports
    a. The investigator should submit written summaries of the trial status to the IRB annually, or more frequently, if requested by the IRB.
    b. The investigator should promptly provide written reports to the sponsor, the IRB and, where applicable, the institution on any changes significantly affecting the conduct of the trial, and/or increasing the risk to subjects.
10. Safety Reporting
    a. All serious adverse events (SAEs) should be reported immediately to the sponsor except for those SAEs that the protocol or other document (e.g., Investigator's Brochure) identifies as not needing immediate reporting. The immediate reports should be

followed promptly by detailed, written reports. The immediate and follow-up reports should identify subjects by unique code numbers assigned to the trial subjects rather than by the subjects' names, personal identification numbers, and/or addresses. The investigator should also comply with the applicable regulatory requirements related to the reporting of unexpected serious adverse drug reactions to the regulatory authorities and the IRB.

b. Adverse events and/or laboratory abnormalities identified in the protocol as critical to safety evaluations should be reported to the sponsor according to the reporting requirements and within the time periods specified by the sponsor in the protocol.
c. For reported deaths, the investigator should supply the sponsor and the IRB with any additional requested information (e.g., autopsy reports and terminal medical reports).
d. Premature Termination or Suspension of a Trial If the trial is prematurely terminated or suspended for any reason, the investigator/institution should promptly inform the trial subjects, should assure appropriate therapy and follow-up for the subjects, and, where required by the applicable regulatory requirements, should inform the regulatory authorities. In addition:
    i. If the investigator terminates or suspends a trial without prior agreement of the sponsor, the investigator should inform the institution where applicable, and the investigator/institution should promptly inform the sponsor and the IRB, and should provide the sponsor and the IRB a detailed written explanation of the termination or suspension.
    ii. If the sponsor terminates or suspends a trial, the investigator should promptly inform the institution where applicable and the investigator/institution should promptly inform the IRB and provide the IRB a detailed written explanation of the termination or suspension.
    iii. If the IRB terminates or suspends its approval opinion of a trial, the investigator should inform the institution where applicable and the investigator/institution should promptly notify the sponsor and provide the sponsor with a detailed written explanation of the termination or suspension.

11. Final Reports by Investigator: Upon completion of the trial, the investigator, where applicable, should inform the institution; the investigator/institution should provide the IRB with a summary of the trial's outcome, and the regulatory authorities with any reports required.

    https://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R2___Step_4.pdf

Appendix A-4 ..... Additional Requirements for Department of Defense (DOD) research

(DoDI 3216.02, "Protection of Human Subjects and Adherence to Ethical Standards in DoD-Conducted and -Supported Research," April 15, 2020 (whs.mil)

1. When appropriate, research protocols must be reviewed and approved by the IRB prior to the Department of Defense approval. Consult with the Department of Defense funding component to see whether this is a requirement.
2. Civilian researchers attempting to access military volunteers should seek collaboration with a military researcher familiar with service-specific requirements.
3. Employees of the Department of Defense (including temporary, part-time, and intermittent appointments) may not be able to legally accept payments to participate in research and should check with their supervisor before accepting such payments. Employees of the Department of Defense cannot be paid for conducting research while on active duty.
4. Service members must follow their command policies regarding the requirement to obtain command permission to participate in research involving human subjects while on-duty or off-duty.
5. Components of the Department of Defense might have stricter requirements for research-related injury than the DHHS regulations.
6. There may be specific educational requirements or certification required.
7. When assessing whether to support or collaborate with this institution for research involving human subjects, the Department of Defense may evaluate this institution's education and training policies to ensure the personnel are qualified to perform the research.
8. When research involves U.S. military personnel, policies and procedures require limitations on dual compensation:
    a. Prohibit an individual from receiving pay of compensation for research during duty hours.
    b. An individual may be compensated for research if the participant is involved in the research when not on duty.
    c. Federal employees while on duty and non-Federal persons may be compensated for blood draws for research up to $50 for each blood draw.
    d. Non-Federal persons may be compensated for research participating other than blood draws in a reasonable amount as approved by the IRB according to local prevailing rates and the nature of the research.
9. When research involves large scale genomic data (LSGD) collected on DOD-affiliated personnel, additional protections are required:
    a. Additional administrative, technical, and physical safeguards to prevent disclosure of DoD-affiliated personnel's genomic data commensurate with risk (including secondary use or sharing of de-identified data or specimens)
    b. Research will apply an HHS Certificate of Confidentiality
10. DoD Component security review
11. When conducting multi-site research, a formal agreement between institutions is required to specify the roles and responsibilities of each party.

12. Surveys performed on DoD personnel must be submitted, reviewed, and approved by the DoD after the research protocol is reviewed and approved by the IRB. When a survey crosses DoD components, additional review is required.
13. The following must be promptly (no longer than within 30 days) reported to the DoD human research protection officer:
    - The results of the IRB continuing review.
    - Change of reviewing IRB.
    - When TAMU is notified by any federal department, agency, or national organization that any part of the HRPP is under investigation for cause involving a DoD-supported research protocol.
14. Other specific requirements of the Department of Defense research be found in the "Additional Requirements for Department of Defense (DOD) Research" section in the IRB's HRP-318 - WORKSHEET - Additional Federal Agency Criteria.

Appendix A-5 ..... Additional Requirements for Department of Energy (DOE) Research

(See DOE Order 443.1C Protection of Human Research Subjects (doe.gov))

1. Research that involves one or more of the following must be submitted to the appropriate IRB for human subjects research review and determination :
    a. Study of humans in a systematically modified environment. These studies include but are not limited to intentional modification of the human environment:
        i. Study of human environments that use tracer chemicals, particles or other materials to characterize airflow.
        ii. Study in occupied homes or offices that:
            1. Manipulate the environment to achieve research aims.
            2. Test new materials.
            3. Involve collecting information on occupants' views of appliances, materials, or devices installed in their homes or their energy-saving behaviors through surveys and focus groups.
    b. Use of social media data.
    c. Human Terrain Mapping (HTM).
    d. All exempt HSR determinations must be made by the appropriate IRB and/or IRB office.
2. Personally identifiable information collected and/or used during HSR projects must be protected in accordance with the requirements of DOE Order 206.1, Department of Energy Privacy Program, current version. The Central DOE IRBs require submission of DOE's HRP- 490-CHECKLIST-Reviewing Protocols that use Personally Identifiable Information (PII) if your research includes PII.
3. You must report the following to the DOE human subjects research Program Manager (and, when an NNSA element is involved, the NNSA HSP Program Manager) prior to initiation of any new human subjects research project, even if it meets the regulatory definition of exempt human subjects research as outlined in 10 CFR Part 745.104, involving:
    a. An institution without an established Institutional Review Board (IRB);
    b. A foreign country;
    c. The potential for significant controversy (e.g., negative press or reaction from stakeholder or oversight groups);
    d. Research subjects in a protected class (prisoners, children, individuals with impaired decision making capability, or DOE/NNSA federal or DOE/NNSA contractor employees as human subjects, who may be more vulnerable to coercion and undue influence to participate) that is outside of the reviewing IRB's typical range/scope; or
    e. The generation or use of classified information.
4. The IRB must be notified immediately and the DOE HSP Program Manager (and, when an NNSA element is involved, the NNSA HSP Program Manager) must be notified within 48 hours and consulted regarding planned corrective actions if any of the following occur:
    a. Adverse events. Notify the IRB for all adverse events and the DOE/NNSA HSP Program Manager if the IRB determines them to be significant, as defined in DOE Order 443.1C.

b. Unanticipated problems and complaints about the research.
c. Any suspension or termination of IRB approval of research.
d. Any significant non-compliance with HSP Program procedures or other requirements.
e. Any finding of a suspected or confirmed data breach involving PII in printed or electronic form. Report immediately to the IRB, the DOE/NNSA HSP Program Manager(s), and the DOE-Cyber Incident Response Capability, in accordance with the requirements of the CRD associated with DOE O 206.1.
f. Serious adverse events and corrective actions taken must be reported immediately to the IRB and the DOE/NNSA HSP Program Manager(s). The time frame for "immediately" is defined as upon discovery.

5. Requirements for human participant protections for classified research apply to all classified research conducted or supported by the DOE and its national laboratories, including contracts, and including Human Terrain Mapping research.
6. Researchers conducting human subjects research in any other country or on citizens or other individuals residing in that country must be cognizant of country-specific human subjects research requirements and consult the IRB regarding applicability of such requirements.
7. No human subjects research conducted with DOE funding, at DOE institutions (regardless of funding source), or by DOE or DOE contractor personnel (regardless of funding source or location conducted), whether done domestically or in an international environment, including classified and proprietary research, may be initiated without both a Federalwide Assurance (FWA) or comparable assurance (e.g., Department of Defense assurance) of compliance and approval by the cognizant Institutional Review Board (IRB) in accordance with 10 CFR §745.103. Human subjects research involving multiple DOE sites (e.g., members of the research team from more than one DOE site and/or data or human subjects from more than one DOE site) must be reviewed and approved by one of the Central DOE IRBs prior to initiation, or if authorized by the DOE and/or NNSA HSP Program Manager, other appropriate IRB of record. In all cases, an IRB Authorization Agreement (IAA) or Memorandum of Understanding (MOU) must be in place between the organization(s) conducting the HSR and the organization responsible for IRB review.
8. Human subjects research that involves DOE Federal and/or contractor employees must first be reviewed and approved by the appropriate DOE IRB (the DOE site IRB or one of the Central DOE IRBs), or if deemed more fitting by the Federally assured DOE site or Headquarters, other appropriate IRB of record, in accordance with an IAA or MOU negotiated between the DOE site or Headquarters and the organization responsible for IRB review.
9. Classified and unclassified human subjects research that is funded through the Strategic Intelligence Partnership Program (SIPP) must be reviewed and approved by the Central DOE IRB-Classified.
10. If applicable, federally funded HSR must comply with the requirements of the Paperwork Reduction Act.
11. Other specific requirements of the DOE research can be found in the "Additional Requirements for Department of Energy (DOE) Research" section in the IRB's HRP-318 - WORKSHEET - Additional Federal Agency Criteria.

Appendix A-6 ..... Additional Requirements for Department of Justice (DOJ) Research

Additional Requirements for DOJ Research conducted in the Federal Bureau of Prisons

1. Implementation of Bureau programmatic or operational initiatives made through pilot projects is not considered to be research.
2. The project must not involve medical experimentation, cosmetic research, or pharmaceutical testing.
3. The research design must be compatible with both the operation of prison facilities and protection of human subjects.
4. Investigators must observe the rules of the institution or office in which the research is conducted.
5. Any investigator who is a non-employee of the Bureau of Prisoners must sign a statement in which the investigator agrees to adhere to the requirements of 28 CFR §512.
6. The research must be reviewed and approved by the Bureau Research Review Board.
7. Incentives cannot be offered to help persuade inmate subjects to participate. However, soft drinks and snacks to be consumed at the test setting may be offered. Reasonable accommodations such as nominal monetary recompense for time and effort may be offered to non-confined research subjects who are both: No longer in Bureau of Prisons custody. Participating in authorized research being conducted by Bureau employees or contractors.
8. A non-employee of the Bureau may receive records in a form not individually identifiable when advance adequate written assurance that the record will be used solely as a statistical research or reporting record is provided to the agency.
9. Except as noted in the consent statement to the subject, you must not provide research information that identifies a subject to any person without that subject's prior written consent to release the information. For example, research information identifiable to a particular individual cannot be admitted as evidence or used for any purpose in any action, suit, or other judicial, administrative, or legislative proceeding without the written consent of the individual to whom the data pertain.
10. 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.
11. If you are conducting a study of special interest to the Office of Research and Evaluation but the study is not a joint project involving Office of Research and Evaluation, you may be asked to provide Office of Research and Evaluation with the computerized research data, not identifiable to individual subjects, accompanied by detailed documentation. These arrangements must be negotiated prior to the beginning of the data collection phase of the project.
12. Required elements of disclosure additionally include:
    a. Identification of the investigators.
    b. Anticipated uses of the results of the research.
    c. A statement that participation is completely voluntary and that the subject 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, an investigator may not guarantee confidentiality when the subject indicates intent to commit future criminal conduct or harm himself or herself or someone else, or, if the subject is an inmate, indicates intent to leave the facility without authorization.
e. A statement that participation in the research project will have no effect on the inmate subject's release date or parole eligibility.

13. You must have academic preparation or experience in the area of study of the proposed research.
14. The IRB application must include a summary statement, which includes:
    a. Names and current affiliations of the investigators.
    b. Title of the study.
    c. Purpose of the study.
    d. Location of the study.
    e. Methods to be employed.
    f. Anticipated results.
    g. Duration of the study.
    h. Number of subjects (staff or inmates) required and amount of time required from each.
    i. Indication of risk or discomfort involved as a result of participation.
15. The IRB application must include a comprehensive statement, which includes:
    a. Review of related literature.
    b. Detailed description of the research method.
    c. Significance of anticipated results and their contribution to the advancement of knowledge.
    d. Specific resources required from the Bureau of Prisons.
    e. Description of all possible risks, discomforts, and benefits to individual subjects or a class of subjects, and a discussion of the likelihood that the risks and discomforts will actually occur.
    f. Description of steps taken to minimize any risks.
    g. Description of physical or administrative procedures to be followed to: Ensure the security of any individually identifiable data that are being collected for the study.
    h. Destroy research records or remove individual identifiers from those records when the research has been completed.
    i. Description of any anticipated effects of the research study on organizational programs and operations.
    j. Relevant research materials such as vitae, endorsements, sample consent statements, questionnaires, and interview schedules.
16. The IRB application must include a statement regarding assurances and certification required by federal regulations, if applicable.
17. You must assume responsibility for actions of any person engaged to participate in the research project as an associate, assistant, or subcontractor.

18. At least once a year, you must provide the Chief, Office of Research and Evaluation, with a report on the progress of the research.
19. At least 12 working days before any report of findings is to be released, you must distribute one copy of the report to each of the following: the chairperson of the Bureau Research Review Board, the regional director, and the warden of each institution that provided data or assistance.
20. You must include an abstract in the report of findings.
21. In any publication of results, you must acknowledge the Bureau's participation in the research project.
22. You must expressly disclaim approval or endorsement of the published material as an expression of the policies or views of the Bureau.
23. Prior to submitting for publication the results of a research project conducted under this subpart, You must provide two copies of the material, for informational purposes only, to the Chief, Office of Research and Evaluation, Central Office, Bureau of Prisons.
24. Other specific requirements of the Department of Justice (DOJ) Research Conducted within the Federal Bureau of Prisons (BOP) can be found in the “Additional Requirements for Department of Justice (DOJ) Research Conducted within the Federal Bureau of Prisons (BOP)” section in the IRB’s “WORKSHEET: Additional Federal Criteria (HRP-318).”

Additional Requirements for DOJ Research Funded by the National Institute of Justice

1. The project must have a privacy certificate approved by the National Institute of Justice Human Subjects Protection Officer.
2. All investigators and research staff are required to sign employee confidentiality statements, which are maintained by the responsible investigator.
3. The confidentiality statement on the consent document must state that confidentiality can only be broken if the subject reports immediate harm to subjects or others.
4. Under a privacy certificate, investigators and research staff do not have to report child abuse unless the subject signs another consent document to allow child abuse reporting.
5. A copy of all data must be de-identified and sent to the National Archive of Criminal Justice Data, including copies of the informed consent document, data collection instruments, surveys, or other relevant research materials.
6. Other specific requirements of the Department of Justice (DOJ) Research Funded by the National Institute of Justice can be found in the “Additional Requirements for Department of Justice (DOJ) Research” section in the IRB’s “WORKSHEET: Additional Federal Criteria (HRP-318).”

Appendix A-7 ..... Additional Requirements for Department of Education (ED) Research

1. Each school at which the research is conducted must provide an assurance that they comply with the Family Educational Rights and Privacy Act (FERPA) and the Protection of Pupil Rights Amendment (PPRA).

2. Provide a copy of all surveys and instructional material used in the research. Upon request parents of children[17] involved in the research[18] must be able to inspect these materials.

3. The school in which the research is being conducted must have policies regarding the administration of physical examinations or screenings that the school may administer to students.

4. Other specific requirements of the Department of Education (ED) Research can be found in the "Additional Requirements for Department of Education (ED) Research" section in the IRB's "WORKSHEET: Additional Federal Criteria (HRP-318)."

[17] Children are persons enrolled in research not above the elementary or secondary education level, who have not reached the age or majority as determined under state law.

[18] Research or experimentation program or project means any program or project in any research that is designed to explore or develop new or unproven teaching methods or techniques.

Appendix A-8 ..... Additional Requirements for Environmental Protection Agency (EPA) Research

1. Research conducted, supported, or intended to be submitted to EPA is subject to Environmental Protection Agency Regulations.

2. Intentional exposure of pregnant women or children to any substance is prohibited.

3. Observational research involving pregnant women and fetuses are subject to additional DHHS requirements for research involving pregnant women (45 CFR §46 Subpart B) and additional DHHS requirements for research involving children (45 CFR §46 Subpart D.)

4. Research involving children must meet category #1 or #2.

5. Other specific requirements of the Environmental Protection Agency (EPA) Research can be found in the "Additional Requirements for Environmental Protection Agency (EPA) Research and Research Intended to be Submitted to the Environmental Protection Agency" section in the IRB's "WORKSHEET: Additional Federal Criteria (HRP-318)."

Appendix A-9 ..... Single IRB Studies

1. That National Institutes of Health expects that all sites participating in multi-site studies involving non-exempt human subjects research funded by the NIH will use a single Institutional Review Board (sIRB) to conduct the ethical review required by the Department of Health and Human Services regulations for the Protection of Human Subjects at 45 CFR Part 46.
    a. This policy applies to the domestic sites of NIH-funded multi-site studies where each site will conduct the same protocol involving non-exempt human subjects research, whether supported through grants, cooperative agreements, contracts, or the NIH Intramural Research Program. It does not apply to career development, research training or fellowship awards.
    b. This policy applies to domestic awardees and participating domestic sites. Foreign sites participating in NIH-funded, multi-site studies will not be expected to follow this policy.
    c. Exceptions to the NIH policy will be made where review by the proposed sIRB would be prohibited by a federal, tribal, or state law, regulation, or policy. Requests for exceptions that are not based on a legal, regulatory, or policy requirement will be considered if there is a compelling justification for the exception. The NIH will determine whether to grant an exception following an assessment of the need.
2. The Office for Human Research Protections expects that all sites located in the United States participating in cooperative research must rely upon approval by a single IRB for that portion of the research that is conducted in the United States. The reviewing IRB will be identified by the Federal department or agency supporting or conducting the research or proposed by the lead institution subject to the acceptance of the Federal department or agency supporting the research.

    The following research is not subject to this provision:
    a. Cooperative research for which more than single IRB review is required by law (including tribal law passed by the official governing body of an American Indian or Alaska Native tribe); or
    b. Research for which any Federal department or agency supporting or conducting the research determines and documents that the use of a single IRB is not appropriate for the particular context.
    c. For research not subject to paragraph (b) of this section, an institution participating in a cooperative project may enter into a joint review arrangement, rely on the review of another IRB, or make similar arrangements for avoiding duplication of effort. Consultation with the TAMU HRPP is required prior to entering into any arrangement.

Appendix A-10.....Additional Requirements for Research Subject to EU General Data Protection Regulations (GDPR)

1. Human Research involving personal data about individuals located in (but not necessarily citizens of) European Union member states, Norway, Iceland, Liechtenstein, and Switzerland is subject to EU General Data Protection Regulations.
2. For all prospective Human Research subject to EU GDPR, contact the TAMU Privacy Officer at privacy@tamu.edu to ensure that the following elements of the research are consistent with institutional policies and interpretations of EU GDPR:
    a. Any applicable study design elements related to data security measures.
    b. Any applicable procedures related to the rights to access, rectification, and erasure of data.
    c. Procedures related to broad/unspecified future use consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens.
3. Where FDA or DHHS regulations apply in addition to EU GDPR regulations, ensure that procedures related to withdrawal from the research, as well as procedures for managing data and biospecimens associated with the research remain consistent with Appendices A-1 and A-2 above.

Appendix A-11.....Emergency/Disaster Preparedness Considerations for Investigators Conducting Human Research

Investigators conducting human research should be aware of the following additional considerations associated with managing Human Research during an emergency/disaster scenario (e.g., extreme weather events, natural disasters, man-made disasters, infectious disease pandemics, etc.) related to investigators' ongoing interactions with research subjects and the institutional review board (IRB) in such cases.

During Emergency/Disaster Scenarios: Deciding Whether a Study-Specific Risk Mitigation Plan for Ongoing Research Is Needed

In general, investigators should develop a study-specific emergency/disaster risk mitigation plan for their research unless one of the following is true:

- Research does not involve in-person interaction with research subjects.
- Research can be conducted as written while adhering to additional institution-level and HRPP-level guidance and requirements regarding the emergency/disaster event.
- The research is externally sponsored, and the sponsor has developed a protocol-specific risk mitigation plan for the research.
- The research has been voluntarily placed on hold for recruitment and all research procedures (except for necessary follow-up procedures to be done consistently with additional institution-level and HRPP-level guidance and requirements regarding the emergency/disaster event).

Tools and Resources for Developing Study-Specific Emergency/Disaster Risk Mitigation Plans for Ongoing Research

Review "HRP-108 - FLOWCHART - Study-Specific Emergency-Disaster Risk Mitigation Planning" and "HRP-351 - WORKSHEET - Protocol-Specific Emergency-Disaster Risk Mitigation Plan" for general guidance on developing study-specific risk mitigation plans.

Voluntary Holds on Human Research Activities

Investigators may voluntarily elect to place all recruitment, enrollment and research procedures on temporary hold during emergency/disaster scenarios if doing so will better ensure the safety of research subjects and would not create any additional risks to the safety and welfare of research subjects. Such voluntary holds on research activity do not require IRB notification or review.

Submitting Study-Specific Emergency/Disaster Risk Mitigation Plans for IRB Review

If immediate modification of the research is necessary to eliminate an apparent immediate hazard to a subject, take action and notify the IRB within five business days following the standard pathway to submit reportable new information.

For all other study modifications made to ensure the ongoing safety of research subjects during emergency/disaster scenarios, submit a study amendment and all relevant new or modified study materials to the IRB prior to implementation.

Other Reportable New Information Considerations During Emergency/ Disaster Scenarios

The IRB's list of reportable events includes two items for which additional clarification and guidance may be helpful during emergency/disaster scenarios:

- ***"Failure to follow the protocol due to the action or inaction of the investigator or research staff."*** Emphasis on action or inaction of the investigator or research staff has been added because this requirement does not include action or inaction of the research subject. For example, study teams may notice an increase in the number of subjects who do not arrive for scheduled research visits under emergency/disaster circumstances. Failure of a research participant to appear for a scheduled research visit is not noncompliance due to action or inaction by the investigator or research staff, and therefore does not require reporting to the IRB.
- ***"Change to the protocol taken without prior IRB review to eliminate an apparent immediate hazard to a subject."*** During emergency/disaster scenarios, there will be cases where there is sufficient time to receive IRB approval of any proposed modifications to previously approved research, and in such cases, investigators should follow standard IRB procedures for submitting modifications. However, there may be other cases where investigators conducting research with procedures that impact the health and wellbeing of participants must make more immediate changes to the protocol or investigational plan to minimize or eliminate immediate hazards or to protect the life and well-being of research participants. Such changes may be implemented without IRB approval, but are required to be reported to the IRB within five business days afterward in accordance with IRB policies and procedures for submitting reportable new information. These procedures are generally related to protocols involving medical treatments or interventions.