Human Research Protections

Basic Information for Researchers and Administrators

AAHRPP TRAINING SERIES

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1. What is AAHRPP accreditation and why is it important to Texas A&M University (TAMU)?

AAHRPP accreditation is the recognized gold standard for adherence to a rigorous set of human subjects protection standards that go beyond federal and state requirements. Accreditation communicates to the public the university's commitment to the protection of human participants in research and instills trust amongst our research collaborators and sponsors.

The accreditation process involves an evaluation of the TAMU Human Research Protection Program (HRPP) and its standard operating procedures, as well as, the site visit which is focused on interviews with selected members of the HRPP, including IRB members, research administrators, Investigators and research staff.

Accreditation largely depends on how well TAMU's policies and procedures address the AAHRPP standards. AAHRPP will check our practices by going through our records, first. Then they will check our knowledge of the policies and procedures through the interviews.

The Texas A&M University Human Research Protection Program (HRPP) originally received full accreditation by the Association for the Accreditation of Human Research Protection Programs in June 2015, for three years. Reaccreditation must be completed by June 2018.

The reaccreditation site visit will take place February 5-6th, 2018. During the site visit AAHRPP reviewers will interview research personnel from Texas A&M University in College Station, the College of Dentistry in Dallas, the School of Law in Fort Worth and branch campuses in Galveston and Qatar.

2. What is a researcher's role in the AAHRPP accreditation process?

Researchers will be interviewed to evaluate how well they understand their responsibilities for protecting humans that volunteer to participate in research. As a researcher, you should:

- Understand the TAMU HRPP structure and know your role within that structure.
- Demonstrate familiarity with the TAMU HRPP Policies and where to access them
- Know the required training and qualifications that apply to all research personnel
- Understand what constitutes Conflict of Interest; know how it is disclosed, managed and reviewed
- Understand and describe the ethical aspects, purpose and value of your work
- Know or understand the regulatory standards that apply to your research
- Know how to recruit participants ethically and in an equitable manner while adhering to inclusion/exclusion criteria necessary to your research.
- Know how to consent participants

- Know how to handle participant complaints
- Know how to report noncompliance, unanticipated problems and other reportable events
- Know your responsibilities and obligations

3. What is the TAMU Human Research Protection Program (HRPP)?

The TAMU Human Research Protection Program (HRPP) is the institution's program that is charged with oversight responsibilities for all human subjects research conducted under its authority. Responsibility for carrying out the HRPP's mission is a team effort. The major components of the team include the following:

- Institutional Official (IO) within the VPR office
- IRB/HRPP staff
- IRB members
- Research Administration
- Department Chairs
- Affiliate member representatives
- Investigators and research staff
- Office of General Counsel
- Sponsored Research Services

a) What is the role of Researchers within the HRPP?

Investigators have primary responsibility for protecting the rights and welfare of humans participating in research. The researcher works with the HRP/IRB Office and other research entities (Research Administration, Sponsored Research Services) to ensure that the rights and welfare of humans are protected. See investigator obligations listed under item 16 of this document.

b) Who is the Institutional Official for Texas A&M University?

The Vice President for Research serves as the Institutional Official. The current IO is the interim VPR, Dr. Karen Butler-Purry. She serves as the Institutional Official for the purposes of AAHRPP Accreditation and as the Signatory Official on TAMU's Federalwide Assurance (FWA).

c) What is the Federalwide Assurance (FWA)?

The FWA is the agreement that TAMU signs with HHS OHRP that allows us to receive federal funding for research. It states that all of the Institution's human subjects research activities, regardless of whether or not the research is subject to Federal Policy, will be guided by the institution's ethical principles. TAMU's ethical principles listed on the FWA include the Belmont Report: Respect, Beneficence and Justice, and the Declaration of Helsinki: Ethical Principles for Medical/Clinical Research Involving Human Subjects).

By signing the FWA the Signatory Official recognizes the institutions responsibility to:

- Provide research investigators, IRB members and staff, and other relevant personnel with appropriate initial and continuing education and training about human subject protections to help ensure that the requirements of the Assurance are satisfied.
- Provide protections for human subjects
- Ensure human research conducted under the auspices of the institution will be reviewed and approved by an IRB
- Ensure the IRB(s) upon which this institution relies will comply with the **Terms of the Federalwide Assurance** when reviewing research covered by this Assurance and possess appropriate knowledge of the local context requirements in which this Institution's research will be conducted.

**Texas A&M Agencies, such as the Texas A&M Transportation Institute, Texas A&M Agrilife Research, Texas A&M Agrilife Extension, and Texas A&M Engineering Experiment Service have their own Institutional Official and Federalwide Assurance but through institutional agreements they all rely on the TAMU IRBs to review Human Research and follow TAMU HRPP Policies & Procedures.*

4. What does the IRB do?

The main mission of the Institutional Review Board is to protect the rights, safety and welfare of research subjects. The IRB is formally designated by the institution and given authority through federal regulations to:

- approve, modify or disapprove research,
- conduct continuing review of already approved research,
- suspend or terminate approval of research,
- to observe or have a third part party observe the consent process and the research.

IRBs review and approve research in accordance with Department of Health and Human Services (HHS) regulations in the Common Rule 45 CFR 46. For studies involving products regulated by the Food and Drug Administration (FDA), the IRBs review research according to the requirements in 21 CFR 50, 21 CFR 56, 21 CFR 312, 21 CFR 812. The IRBs also comply with HIPAA regulations in 45CFR 160 and 164 and follow the TAMU HRPP Standard-Operating-Procedures (SOPs).

5. What is the Common Rule?

In 1991, many federal departments and agencies adopted a common set of regulations governing human subjects research. This is known as the Common Rule or 45 CFR Part 46. It was designed to create a uniform human subjects protections system for all federally supported human research. The core regulation is found in Subpart A which describes the authority and function of the IRB.

Subpart A of 45 CFR 46 includes:

- Definitions,
- IRB membership,
- IRB authority, functions and operations
- Review of Research
- Criteria for Approval
- IRB Records
- Requirements for Informed Consent and Documentation of Consent
- Use of federal funds requires a Federal Wide Assurance (FWA)

Extra protections for vulnerable populations are found in:

Subpart B - Additional Protections for Pregnant Women, Human Fetuses and Neonates
Subpart C - Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners
Subpart D - Additional Protections for Children Involved as Subjects in Research

6. Where can I find the TAMU HRPP Standard Operating Procedures (SOP)?

HRPP Standard Operating Procedures are available to investigators at http://rcb.tamu.edu/humansubjects.

Resources include the Investigator Manual (HRP-103) and a **Toolkit** that contains Standard Operating Procedures (SOPs), Checklists, Worksheets and Templates.

In addition to the Investigator Manual and Toolkit, the first point of contact for general questions is normally the HRPP Staff or the IRB.

Additional follow up may be necessary with federal regulatory agencies such as the Office for Human Research Protections (OHRP), the U.S. Food and Drug Administration (FDA) and foreign governmental agencies when conducting research outside the U.S. At times, it may also be necessary to contact the office of General Counsel and the VPR's office.

7. What training and education is required to conduct a research project with human subjects?

Required Training will depend on the type of research project. At a minimum training will include the online training modules through the CITI program. Other required courses may include, Good Clinical Practices, Financial Conflict of Interest and HIPAA in Research training. See SOP HRP-002 Education.

All individuals engaged in or supervising those engaged in human research at TAMU must have the appropriate education, license, or certification appropriate for their field and the proposed research procedures.

8. How do you know what activities are overseen by the HRPP and when should you seek guidance?

Worksheet HRP-310 Human Research Determination provides an algorithm to assist with understanding whether or not an activity is Human Research. The HRPP office makes the ultimate determination in all cases as to whether an activity constitutes Human Research and whether it requires IRB review. Additional guidance is provided in SOP: HRP-093 Activities that Require IRB Review

A request for a determination can be submitted via our online interface iris.tamu.edu. Questions should be directed to HRPP staff but official determinations are made through the online system and are not made through phone or email communications.

9. What is a financial conflict of interest (FCOI) and how do you disclose, manage, minimize or eliminate a FCOI?

Researchers are responsible for knowing when they have a conflicting interest and for disclosing and managing such interests. 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 Financial Conflict of Interest in Sponsored Research and University Rule Financial Conflicts of Interest in Sponsored Research (15.01.03.M1). Investigators can find additional details related to human research in SOP**:** HRP-055 Management of Financial Conflicts of Interests.

Financial Conflict of interests are disclosed via the Financial Disclosure form in Maestro. Financial and Non-financial conflict of interests are also noted in each IRB application and subsequent continuing review(s) as part of the Investigator Attestation. When a potential conflict of interest is noted, the HRPP staff works with the Investigator and the TAMU Conflict of Interest Official (or its equivalent at other TAMU agencies) to execute a management plan. The IRB must review the management plan for appropriateness, before the study can be approved.

10. How do you know that your research is sound in design and minimizes risks to participants?

Investigators and research staff have a responsibility for minimizing risks to participants and for ensuring their rights and welfare (beneficence). Ways to minimize risks include:

- Design and implement protocols that comply with regulatory (**the Common Rule 45CFR46, FDA 21CFR50 and 21CFR51, FERPA, HIPAA**) and institutional policies (**Resources**), as well as the principles of the Belmont Report.

- Ensure that appropriate resources are available to conduct the research (appropriately trained, qualified and licensed personnel, facilities, equipment, etc.).

- Verify procedures are consistent with sound research design by ensuring that the research is reasonably expected to answer the proposed question and that the resulting knowledge is expected to be sufficiently important to justify the research, without unnecessarily exposing subjects to risks.

- Develop plans for protecting participant privacy and the confidentiality of data. In human research, these terms are defined as follows:
  - *Privacy refers to setting or environment* – it relates to individuals having control over the extent, the timing, and circumstances regarding the exposure of themselves or their information within the research setting.
  - *Confidentiality refers to information/data* – it relates to the protection of participant data that has been provided to the researcher with the expectation that it will be protected and not disclosed.

  The IRB determines on a study-by-study basis whether there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data. Such determination depends on the sensitivity of the information collected and the protections put in place to protect it.

- Ensure that recruitment procedures foster equitable selection of participants

- Ensure that the consent process is adequate

- Put in place enhanced protection for participants vulnerable to coercion or undue influence (e.g. children, prisoners, pregnant women, cognitively disabled persons, students, etc.)

- Establish adequate provisions for monitoring participants to identify unknown risks and adverse events. Prepare a plan to review the data collected at appropriate intervals to identify any findings that may present an increase in risk to participants or findings that may challenge data integrity. All studies considered greater than minimal risk must include a data and safety monitoring plan.

To ensure that your research protocol includes all those elements of a sound research design, it is recommended that you complete all required fields in the IRB application and/or to use our protocol templates posted on the HRPP website: Biomedical Protocol Template, Socio-Behavioral Protocol Template, Protocol Existing Data or Specimens.

Additionally, you may consult HRP-314 WORKSHEET: Criteria for Approval found in the toolkit resources.

11. How do you recruit participants equitably?

The chosen study population should be justified by the purpose/nature of the research, the research setting and the potential benefits to that population; not simply by convenience. The benefits of the research should be equally distributed to all eligible individuals and no single group should bear the burden of the risks.

In addition, the recruitment process should be free of coercion or present no undue influence. Special attention should be given to populations that are more susceptible to coercion or undue influence, such as children, prisoners, cognitively disabled individuals, students, economically or educationally disadvantaged participants. Extra measures of protection should be included in the study protocol when vulnerable populations are included in the research.

The IRB reviews recruitment plans, advertisements, proposed payments or extra credits to make sure participants are not unduly influenced to participate, and that they do not take risks that they would not normally take in everyday life or if there were no payments.

Additional resources include SOP: HRP-094 Subject Selection, Recruitment, and Payments, Worksheets: HRP-315 Advertisements HRP-316 Payments, Checklists: HRP-412 Pregnant Women, HRP-415 Prisoners, HRP-416 Children, HRP-417 Cognitively Impaired Adults, Investigator Manual (HRP-103): What is an appropriate recruitment method? (page 18).

12. How do you obtain consent from participants?

Obtaining informed consent is a basic ethical obligation (respect for persons) for researchers. The process of consent should ensure that potential subjects are provided with information about the study in a way that is understandable to them (communicated and written in "lay language" and in the subject's language) allowing them to make an informed and voluntary decision about participation. The consent process should be an ongoing educational interaction between the investigator and the research subject throughout the study.

The amount of information and the manner of presentation (verbal or written) can vary depending on the complexity and risk involved in the study. The consent form serves to document that the subject agreed to participate in the study and also serves for the subject's future reference. Subjects should sign the consent form after the investigator has verbally explained the purpose and procedures involved in the study, answered questions, and provided information that permits the subject to make an informed decision. The consent form must be signed before any study procedures or data collection begin.

Only legally competent adults can give legally effective informed consent. Minors and those individuals who are not competent to provide consent should be given the opportunity to *assent* to participate in the research project.

Assent is an affirmative, knowledgeable agreement to participate in the project. Adequate provisions should be made for soliciting the independent, non-coerced assent from minors or cognitively-impaired persons who are capable of a knowledgeable agreement. Their Legally Authorized Representative (LAR) must be part of the consent process and sign the consent document. For more information about using a LAR in research please see SOP: HRP-013 Legally Authorized Representatives, Children, and Guardians

Additional resources include SOPs: HRP-090 Informed Consent Process for Research and HRP-091 Written Documentation of Consent, Investigator Manual (HRP-103): How do I obtain consent? (page 18-20)

a) What are the required elements of consent?

The Common Rule (45 CFR 46.116 (a)) requires that informed consent includes:

- A statement that the study involves **research**;
- Information on the **purpose** of the research;
- The expected **duration** of subject participation;
- A description of the **procedures** (identification of experimental procedures);
- A description of reasonably foreseeable **risks** or harms;
- A description of any **benefits** to subjects or others;
- Disclosure of appropriate **alternative treatments/procedures**, if the research involves clinical treatment;
- A description of how the **confidentiality** of records will be maintained;
- A description of procedures related to **compensation for injury,** if the research is more than minimal risk;
- **Contact information** for the PI and HRPP/IRB; and
- A statement that participation is **voluntary** and that the subject may **withdraw** at any time with no penalty or loss of benefits.

Additional elements of consent are required for FDA-regulated research (see Worksheet: HRP-314 Criteria for Approval Section 7)

To ensure that all required elements are included, it is recommended to use the TAMU HRPP Templates found in the HRPP Toolkit: Assent Form, Assent Script, Simple survey consent script, Informed Consent Document for Social and Behavioral Research, Informed Consent Document for Biomedical Research

b) Does the consent process always involve documenting (signing) a consent form?

In some situations, the IRB may waive the requirement for obtaining a signed informed consent document (45 CFR 46.117(c)). Worksheet: HRP-411 Waiver of Written Documentation of Consent

Waiver of documentation of consent is allowed if:

- The only record linking the subject and the research would be the consent document and potential harm may result from a breach of confidentiality (the subjects would be placed at risk by documents linking them with an illegal or stigmatizing characteristic or behavior). For example, survey or interview studies that contain highly sensitive (e.g., criminal behavior, sexual behavior) questions, or
- The research presents no more than minimal risk of harm to the subjects and involves no procedures for which written consent is normally required outside of the research context. For example, online surveys about topics that could not reasonably damage a participant's reputation or employability or be otherwise stigmatizing.

In cases where the documentation requirement is waived, the IRB will usually require the investigator to provide subjects with a written statement regarding the research (the documentation may also be referred to as a "consent script" or "information sheet").

c) Can the consent process be waived altogether or altered?

Some research projects would not be possible if informed consent were required. The IRB may approve a consent procedure that does not include, or which alters, some or all of the elements of informed consent, or may waive the requirements to obtain informed consent (45 CFR 46.116(d)). Worksheet: HRP-410 Waiver of Alteration of Consent Process.

The regulations state that informed consent may be waived in full or in part if the research is not FDA regulated and if IRB determines that:

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

Examples of studies in which all elements of consent have been waived include retrospective analysis of data or specimens that were previously collected for non-research purposes.

13. How to enhance protection for participants vulnerable to coercion or undue influence (e.g. children, prisoners, pregnant women, cognitively disabled persons, etc.)?

Federal Regulations outline specific requirements for conducting human research with children, prisoners, pregnant women, and mentally disabled persons.

Children, prisoners and mentally disabled persons are more susceptible to coercion or undue influence, and how they are recruited and consented may affect their freedom to participate and remain in a research study.

Additional groups of participants may also be susceptible to coercion and undue influence such as students, economically or educationally disadvantaged participants.

Pregnant women need special protections in that research participation may affect their unborn child.

When research involves vulnerable participants, or those vulnerable to coercion or undue influence, the researcher should consider:

- The extent to which proposed participants are already burdened by poverty, illness, poor education, or chronic disabilities.
- Inconvenience to participants (i.e., the time required, travel involved, restrictions on diet, or other activities), and any discomfort, or potential embarrassment in addition to the risks associated with the research procedures.
- Whether it would be possible to conduct the study with other, less vulnerable participants, and whether that would entail additional expense or inconvenience.
- Whether the convenience of the researcher, or possible improvement in the quality of the research, justifies the involvement of participants who may be susceptible to pressure or who are already burdened.
- Whether it is possible to reduce pressure on certain groups of participants to participate in research (such as by consulting with a representative of the group beforehand)
- Whether the selection process overprotects vulnerable participants, such that they would be denied opportunities to participate in research.
- Whether recruitment materials and consent documents are appropriate for the population, and do not include exculpatory language

In certain cases, it may be necessary to consult with experts in specialized areas on protecting vulnerable populations.

Additional resources include WORKSHEETS: HRP-412 Pregnant Women, HRP-415 Prisoners, HRP-416 Children, HRP-417 Cognitively Impaired Adults; SOP: HRP-013 Legally Authorized Representatives, Children, and Guardians

14. How to process participants concerns, complaints, or requests for information?

The research team should address participants concerns, complaints and questions quickly. When the research team cannot resolve a subject's complaint or concern, it should be reported to the IRB.

Resources are available to subjects on the HRPP website and via our Participant Brochure HRP-104, as well as in our consent templates. Our templates include ways to contact the research team for questions, concerns or complaints and to report when the research may have caused harm.

In addition our consent templates include ways to contact someone other than the research team (the HRPP/IRB office) when the research team cannot be reached, the questions, concerns or complaints are not being answered by the research team, to talk to someone other than the research team about participants rights or to provide input about the research.

15. How to report noncompliance, unanticipated problems and other reportable events?

Once approval to conduct research is granted, the researcher must keep the IRB informed of new information or modifications to the approved protocol or supporting documents. Modifications should be submitted to the IRB via an Amendment form. New Information should be submitted to the IRB via a Reportable New Information form in iRIS.

New information that requires prompt reporting to the IRB (within 5 days of discovery) include:

- Harm experienced by a subject or other individual, which in the opinion of the investigator are **unexpected** and **probably related** to the research procedures.
    - 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.
    - 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.
- Information that indicates a new or increased risk, or a new safety issue. For example:
    - New information that indicates an increase in the frequency or magnitude of a previously known risk, or uncovers a new risk (e.g., an interim analysis, safety monitoring report, publication in the literature, sponsor report, or investigator finding).
    - An investigator drug 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
    - Withdrawal, restriction, or modification of a marketed approval of a drug, device, or biologic used in a research protocol

  - Protocol deviation that harmed subjects or others or that indicates subjects or others might be at increased risk of harm
  - Complaint of a subject that indicates subjects or others might be at increased risk of harm or at risk of a new harm
  - Any changes significantly affecting the conduct of the research
- Non-compliance with the federal regulations governing human research or with the requirements or determinations of the IRB or the institution, or an allegation of such non-compliance.
- Audit, inspection, or inquiry by a federal agency or any other outside entity and any resulting reports (e.g. FDA Form 483.)
- Written reports of study monitors.
- Failure to follow the protocol due to the action or inaction of the investigator or research staff whether planned or unplanned (deviations).
- Breach of confidentiality (inappropriate disclosure of or access to confidential information).
- Change to the protocol taken without prior IRB review to eliminate an apparent immediate hazard to a subject.
- Incarceration of a subject in a study not approved by the IRB to involve prisoners.
- Complaint of a subject that cannot be resolved by the research team.
- Premature suspension or termination of the protocol by the sponsor, investigator, or institution.
- 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)

16. What are your obligations as a Researcher?

Principal investigators must perform the research procedures or delegate to authorized research staff all necessary tasks to carry out the research, including:

- Obtaining IRB approval before research begins;
- Obtaining informed consent of participants prior to initiating study procedures;
- Conducting continuing review within the time intervals required by the IRB;
- Informing the IRB of any disapprovals, suspensions, or terminations to active research studies; and
- Creating and maintaining accurate records.

The PI is also ultimately responsible for proper conduct of the study and is accountable for regulatory violations. Related obligations, include:

- Appropriate training for all study team members on protocol procedures and safety issues;

- Adhering to the approved protocol and not deviating unless it is necessary to eliminate apparent immediate hazard to the subject
- Assurance that all research procedures are performed with appropriate supervision
- Inform the HRPP/IRB office with any changes the list of study personnel, study protocol and study documents, changes in funding, changes in financial interests, discovery of any new information.
- Cooperating with investigations/inspections conducted by the TAMU HRPP.

TAMU requirements and obligations are outlined similarly in our Investigator Manual (HRP-103) (page 28).

17. Why does the IRB require a copy of the grant, contract or funding agreement?

Federal regulations [45 CFR 46.103(f)] require that each grant application or proposal for federally supported human subjects research be reviewed and approved by an IRB. The IRB reviews the grant to ensure that grant is consistent with the research application and protocol.

Additionally, AAHRPP standards require that contracts and funding agreements include provisions to protect subjects, when appropriate. Areas of a contract that often affect research participants and the informed consent document include: subject injury provisions, plans to disseminate the findings, results of sponsor safety monitoring, data confidentiality and types of bonuses.

18. What other approvals does the HRPP need to verify before the research can be approved?

Many different components across the university work together to ensure that research projects maintain compliance with all applicable regulations and safety requirements. Often human research protocols involve testing, procedures, settings or articles that need additional compliance verification that is outside the scope of the IRB or HRPP staff. When this occurs, these additional offices are contacted to verify compliance within their areas. These offices include: BioSafety, Export Control, Radiation Safety and Animal Welfare.

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