



# Investigator Manual

**DIVISION OF RESEARCH**

Revised April 20, 2018

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	2 of 63

***Table of Contents***

**Scope ..... 4**

**What is the purpose of this manual? ..... 4**

**Definitions ..... 4**

**What is Human Research? ..... 5**

**Who may be a principal investigator for human Research? ..... 5**

**What training do researchers need to conduct Human Research? ..... 6**

**What financial interests do researchers need to disclose conduct Human Research? ..... 7**

**What other approvals are required before initiating Human Research? ..... 7**

**What additional requirements apply to International Research? ..... 8**

**When is a Certificate of Translation Required for Consents or other Study Documents written in another Language? ..... 8**

**How do I submit new Human Research to the IRB? ..... 9**

**When can investigators submit research to an External IRB? ..... 10**

**How do I write an Investigator Protocol? ..... 10**

**How do I create consent or assent documents? ..... 11**

**Should I obtain a Certificate of Confidentiality for my research? ..... 11**

**How do I obtain Institutional Certification for submission of genomic data to an NIH-designated data repository? ..... 12**

**Does my funded project qualify for a ‘Delayed Onset Determination’? ..... 12**

**Is the Primary Awardee of Federal Funds always ‘engaged’ when the project includes Human Research? ..... 14**

**When is written parental permission required for research with minors in an educational setting? 14**

**What else do I need to know when conducting research with minors in an educational setting? .... 14**

**How do I conduct research using genetic information? ..... 15**

**Do I need IRB review for TAMU classroom-based research projects conducted by students? ..... 15**

**Do I need IRB review for TAMU classroom-based research projects conducted by faculty? ..... 16**

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	3 of 63

**What is Community Based Participatory Research? ..... 16**

**Do I need a FDA Investigational New Drug (IND) Application for research with drugs, biologics, dietary supplements or other products? ..... 16**

**When can research that requires and IND begin?..... 17**

**Do I need a FDA IDE for use of an Investigational or Approved Device on Humans? ..... 17**

**When should I register my research with ClinicalTrials.gov?..... 18**

**What is an appropriate recruitment method? ..... 19**

**How do I obtain informed consent from participants? ..... 19**

**Do research participants have to sign a consent document? ..... 20**

**How do I document consent or assent?..... 20**

**How do I obtain a waiver or alteration of informed consent?..... 20**

**When is it Permissible to Use the Short Form Written Consent Process?..... 21**

**How can I use or disclose Protected Health Information for Research and Comply with the Privacy Rule? ..... 21**

**How do I De-identify Protected Health Information under the Privacy Rule? ..... 22**

**How do I obtain an Authorization for Research Uses and Disclosures ..... 23**

**Is a Waiver of HIPAA Authorization Appropriate for my Research?..... 24**

**What is a Limited Data Set and Data Use Agreement? ..... 25**

**What are the different regulatory classifications that research activities may fall under?..... 27**

**What are the decisions the IRB can make when reviewing proposed research?..... 27**

**How does the IRB decide whether to approve Human Research? ..... 28**

**What will happen after IRB review? ..... 28**

**What are my obligations as an investigator in order to conduct human research ..... 29**

**What New Information Items need to be Promptly Reported to the IRB? ..... 30**

**What is an Unanticipated Problem? ..... 32**

**How do I submit a modification? ..... 34**

**How do I submit continuing review? ..... 34**

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	4 of 63

<b>How do I close out a study?</b> .....	35
<b>How long do I keep records?</b> .....	36
<b>How do I get additional information and answers to questions?</b> .....	36
Additional Requirements for DHHS-Regulated Research.....	37
Additional Requirements for FDA-Regulated Research .....	38
Additional Requirements for Clinical Trials (ICH-GCP) .....	46
Additional Requirements for Department of Defense (DOD) research .....	54
Additional Requirements for Department of Energy (DOE) Research .....	56
Additional Requirements for Department of Justice (DOJ) Research .....	58
I. Additional Requirements for DOJ Research conducted in the Federal Bureau of Prisons.....	58
II. Additional Requirements for DOJ Research Funded by the National Institute of Justice.....	61
Additional Requirements for Department of Education (ED) Research.....	62
Additional Requirements for Environmental Protection Agency (EPA) Research.....	63

## 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.

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	5 of 63

## 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 (HRP-310),” located in the IRB Policies & Procedures section of the IRB Web site. This document provides 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 not to conduct Human Research without prior IRB review and approval.

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, iRIS. Determinations are not issued through emails or phone calls.

## 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. Below is a list of who may and may not serve as PI.

<b>Eligible to be a Principal Investigator</b>	<b>With Permission of Dean or Department Head on Case by Case Basis</b>	<b>Not Eligible to be a Principal Investigator</b>
<ul style="list-style-type: none"> <li>• Tenure-track faculty (full, associate, and assistant professors);</li> <li>• Non-tenure-track faculty (full, associate, and assistant professors);</li> <li>• Instructors</li> <li>• Librarians</li> <li>• Faculty Equivalent Research Scientists</li> </ul>	<ul style="list-style-type: none"> <li>• Lecturers</li> <li>• Adjuncts</li> <li>• Visiting faculty</li> <li>• Visiting scholars</li> <li>• Retired faculty</li> <li>• Senior Research Fellow</li> <li>• Senior Staff</li> </ul>	<ul style="list-style-type: none"> <li>• Undergraduate students</li> <li>• Graduate Students</li> <li>• Residents</li> <li>• Post-Doctoral Fellows</li> <li>• Research Assistants</li> <li>• Research Associates</li> <li>• Research Coordinators</li> </ul>

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.

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	6 of 63

## 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.

### Investigator and Site Research Staff Group 1 Required Training:

Investigator and Research Staff involved in <b>Clinical Studies</b> (drugs, devices, biologics, invasive procedures) Required Training		
	Course	Timeline
Initial Training	CITI Biomedical Research Basic	Prior to IRB submission of research
	*CITI Good Clinical Practice	Prior to IRB submission of research
	**TRAINTRAQ HIPAA Privacy and Security for Human Research - 2112435	Prior to IRB submission of research
	***TRAINTRAQ Financial Conflicts of Interest in Research - 211716	Prior to IRB submission of research
Refresher Courses	CITI Biomedical Research Refresher	Every 5 years
	**TRAINTRAQ HIPAA Privacy and Security for Human Research - 2112435	Annually or as required
	***TRAINTRAQ Financial Conflicts of Interest in Research - 211716	Every 4 years or upon change

### Investigator and Site Research Staff Group 2 Required Training:

Investigator and Research Staff involved in <b>Social &amp; Behavioral Studies</b> Group 2 (Surveys, Qualitative, Educational, Record Reviews) Required Training		
	Course	Timeline
	CITI Social and Behavioral Research Basic	Prior to IRB submission of research

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	7 of 63

Initial Training	**TRAINTRAQ HIPAA Privacy and Security for Human Research - 2112435	Prior to IRB submission of research
	***TRAINTRAQ Financial Conflicts of Interest in Research - 211716	Prior to IRB submission of research
Refresher Courses	CITI Social and Behavioral Research Refresher	Every 5 years
	**TRAINTRAQ HIPAA Privacy and Security for Human Research - 2112435	Annually or as required
	***TRAINTRAQ Financial Conflicts of Interest in Research - 211716	Every 4 years or upon change

\*When using FDA regulated test articles or 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.

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 in iRIS, 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.

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	8 of 63

**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](mailto:ibc@tamu.edu).

**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](mailto:animalcompliance@tamu.edu).

**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.

## **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. Research projects conducted outside of the United States must be reviewed and approved by the foreign country's equivalent of an IRB, as applicable, before the TAMU IRB will give approval. When there is no equivalent board or group, investigators are asked to rely on local experts or community leaders to provide approval. 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).

Note: Please be aware of any Export Control laws that apply to your project involving a foreign country. Contact the Export Controls Office at (979) 862-6419 or [exportcontrols@tamu.edu](mailto: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



<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	9 of 63

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 submit new Human Research to the IRB?**

- Access the URL <https://iris.tamu.edu>
- Log into iRIS 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 Human Research 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 liaison assigned to your department. This information is posted on the IRB website at <http://rcb.tamu.edu/humansubjects/resources/hssp-staff-contacts>.

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	10 of 63

## **When can investigators submit research to an External IRB?**

TAMU investigators may rely upon the IRB of another organization when they receive a NIH grant or sub-award, or other federal funding that mandates the use of a specific external IRB or the use of a single IRB.

TAMU investigators may rely on an External IRB when the TAMU site is added as a sub-awardee and IRB approval has already been processed by the non-affiliated appropriately qualified IRB and the research is no more than minimal risk.

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 the request.

**The TAMU investigator is required to submit a truncated study application in iRIS to facilitate the evaluation of the external IRB project and to create a record of the activity.** The 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.

## **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. If this is multi-site sponsored research use the protocol provided by the sponsor and provide information about local context and human subjects protections in iRIS.

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.
- For any items described in the sponsor's protocol or other support document submitted with the application, investigators may simply reference the page numbers of these documents within the application rather than repeat information.
- 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

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	11 of 63

- 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.

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

## **Should I obtain a Certificate of Confidentiality for my research?**

A Certificate of Confidentiality (CoC) is a tool for protecting certain information from forced or compelled disclosure, e.g., to oppose a subpoena. The certificate helps researchers protect the privacy of participants enrolled in biomedical, behavioral, clinical and other forms of sensitive health related research. Certificates protect against compulsory legal demands, such as court orders and subpoenas, for identifying information or identifying characteristics of a research participant.

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.

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	12 of 63

- The NIH has recently updated their CoC policy for NIH funded studies. All CoCs issued in the past or in the future, regardless of funding sources, must comply with the requirements of the CoC policy, especially the new disclosure requirements and restrictions.
  - **The new disclosure requirements prohibit disclosure** of the name of research subjects or any identifiable research information, document, or biospecimen to anyone not connected with the research except under very specific circumstances as detailed in the CoC policy.
- Effective October 1, 2017 CoCs will be issued automatically for any NIH-funded project using identifiable, sensitive information that was on-going on/after December 13, 2016
- The CoC will be issued as a term and condition of award
- There will be no physical certificate issued

Read the CoC policy to learn more: <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-17-109.html> and <https://humansubjects.nih.gov/coc/index>

The National Institute of Justice requires a Privacy Certificate if you are working with prisoners. The NIJ Privacy Certificate guidelines can be found at: <http://www.nij.gov/funding/humansubjects/pages/privacy-certificate-guidance.aspx>.

The privacy Certificate is not the same as a Certificate of confidentiality and it is important to complete the application to comply with the confidentiality regulations found in 28 CFR Part 22.

If you are able to obtain a Certificate of Confidentiality or a Privacy Certificate, the IRB will consider that information as part of its review.

## 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.

## 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 iRIS stating that the plans for human subjects are not fully developed and will occur

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	13 of 63

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.

Delayed Onset Human Research Status is valid for up to one year.

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 iRIS.

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.

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	14 of 63

## **Is the Primary Awardee of Federal Funds always ‘engaged’ when the project includes Human Research?**

OHRP’s published guidance indicates that a direct federal awardee (contract, grant or cooperative agreement) institution is considered engaged in humans subjects research even when all activities involving human subjects are carried out by employees or agents of another institution.

The investigator is required to submit an application to TAMU IRB when they are the primary awardee of any federal grant that involves human subjects research at any site. The investigator is also responsible for uploading a copy all sub-awardee IRB approval letters into iRIS.

Even if the TAMU investigator receives de-identified data, de-identified tissue samples or de-identified cell lines but is the primary awardee of a federal grant that includes human subjects research, an IRB application is required in iRIS.

## **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;

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	15 of 63

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.

### **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.

### **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.

However, 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. The IRB staff works with the Office of Graduate and Professional Studies (OGAPS) to ensure these student projects are compliant with TAMU policies.

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

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	16 of 63

## 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.

## 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 a 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:

- 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.



Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	17 of 63

- 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 a 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:

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	18 of 63

- 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?**

You must register your research with ClinicalTrials.gov if you are acting as the study sponsor and your research meets the requirements for an 'Applicable Clinical Trial'. If you are required to register your research with ClinicalTrials.gov, you must also include a statement indicating so in your consent document. This statement is provided for you in the "Biomedical Template Consent Document (HRP-592)".

Applicable Clinical Trials include the following:

- Trials of drugs and biologics: Controlled clinical investigations, other than phase 1 clinical investigations, of drugs or biological products subject to Food and Drug Administration (FDA) regulation
- Trials of devices (1) Controlled trials with health outcomes of devices subject to FDA regulation, other than small feasibility studies, and 2) [pediatric postmarket surveillance](#) required by FDA

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

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	19 of 63

- The trial is conducted under an FDA investigational new drug application or investigational device exemption
- The trial involves a drug, biologic, or device that is manufactured in the United States or its territories and is exported for research

Go to the following website for additional information: <https://clinicaltrials.gov/ct2/manage-recs/fdaaa>

**NIH funded Studies - Registration and reporting on Clinicaltrials.gov** is applicable to all NIH funded clinical trials instead of a subset of applicable clinical trials. The lead investigator will be responsible for registration no later than 21 days after enrolling the first subject, updating the information on the website at least once every 12 months and providing a summary of the results no later than one year after completion of the study.

<https://grants.nih.gov/policy/clinical-trials/reporting/steps.htm>

## **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 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 in iRIS. 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 iRIS. These IRB-stamped approved documents from iRIS 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.

## **How do I obtain informed consent from participants?**

You must describe your process for obtaining informed consent from participants in your application or 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 the SOP: Informed Consent Process for Research (HRP-090); and sections 5, 6 and 7 of WORKSHEET: Criteria for Approval (HRP-314)" for elements to include in your consent process.

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	20 of 63

## **Do research participants have to sign a consent document?**

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. Include information about consent documentation in your application or protocol.

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

- The research must be no more than 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)

Remember that you must provide a copy of the signed and dated consent document to the participant or representative. You must also keep a copy of each signed consent document with your study records.

## **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;

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	21 of 63

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.

## When is it Permissible to Use the Short Form Written Consent Process?

When an investigator does not have an IRB-approved consent document translated into the language understandable to a subject and there is an unusual situation where the window of opportunity for a subject to participate in any benefits of the research is brief, the IRB finds that the use of the short form consent document may be permissible. This usually occurs in a clinical setting. Investigators must obtain IRB approval prior to using the short written consent process.

A short form is a written consent document stating that the elements of informed consent, as required by the Department of HHS and the FDA, have been presented orally to either the participant or the participant's legally authorized representative. You may use a short form as described in HRP-317: WORKSHEET: Short Form of Consent Documentation. You must have the English short form translated into the appropriate language prior to submitting your request to the IRB.

Because time is of the essence when there is a valid request to use the short form consent process, the IRB prioritizes the review to avoid denying the non-English speaking participant an opportunity to participate when they may receive benefit. However, once the participant is enrolled, the investigator is expected to adhere to the IRB's standard requirements for non-English speaking participants.

**If you expect to enroll more than one participant with limited English proficiency or if your study is being conducted internationally, you are expected to translate all study documents provided to participants into the appropriate language.** If you are using a commercial translation service and wish to reduce costs, it is recommended that you obtain IRB approval for your English-language document(s) first. Then, have your document(s) translated. Translated document(s) require IRB approval. This is accomplished by submitting a Modification in iRIS that includes a valid Certificate of Translation.

## How can I use or disclose Protected Health Information 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

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	22 of 63

PHI can be used or disclosed for activities preparatory to research and for research on decedents' information.

## **How do I De-identify Protected Health Information under the Privacy Rule?**

Covered entities may use or disclose health information that is de-identified without restriction under the Privacy Rule. Covered entities seeking to release this health information must determine that the information has been de-identified using either statistical verification of de-identification or by removing certain pieces of information from each record as specified in the Rule.

The simplest way of de-identifying data under The Privacy Rule is by removing all 18 elements that could be used to identify the individual or the individual's relatives, employers, or household members; these elements are enumerated in the Privacy Rule. The covered entity also must have no actual knowledge that the remaining information could be used alone or in combination with other information to identify the individual who is the subject of the information. Under this method, the identifiers that must be removed are the following:

1. Names.
2. All geographic subdivisions smaller than a state, including street address, city, county, precinct, ZIP Code, and their equivalent geographical codes, except for the initial three digits of a ZIP Code if, according to the current publicly available data from the Bureau of the Census:
  - a. The geographic unit formed by combining all ZIP Codes with the same three initial digits contains more than 20,000 people.
  - b. The initial three digits of a ZIP Code for all such geographic units containing 20,000 or fewer people are changed to 000.
3. All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death; and all ages over 89 and all elements of dates
4. Telephone numbers.
5. Facsimile numbers.
6. Electronic mail addresses.
7. Social security numbers.
8. Medical record numbers.
9. Health plan beneficiary numbers.
10. Account numbers.
11. Certificate/license numbers.
12. Vehicle identifiers and serial numbers, including license plate numbers.
13. Device identifiers and serial numbers.
14. Web universal resource locators (URLs).
15. Internet protocol (IP) address numbers.

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	23 of 63

(including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older.

16. Biometric identifiers, including fingerprints and voiceprints.
17. Full-face photographic images and any comparable images.
18. Any other unique identifying number, characteristic, or code, unless otherwise permitted by the Privacy Rule for re-identification.

## **How do I obtain an Authorization for Research Uses and Disclosures**

Another method of using or disclosing PHI under The Privacy Rules is to have research participants agree to the uses and disclosures of their PHI by signing an Authorization form for uses and disclosures not otherwise permitted by the Rule. The Privacy Rule establishes the right of a research subject to authorize a covered entity to use and disclose his/her PHI for research purposes. This requirement is in addition to the informed consent requirements.

A valid Privacy Rule Authorization is an individual's signed permission that allows a covered entity to use or disclose the individual's PHI for the purposes, and to the recipient or recipients, as stated in the Authorization. When an Authorization is obtained for research purposes, the Privacy Rule requires that it pertain only to a specific research study, not to nonspecific research or to future, unspecified projects.

The Privacy Rule considers the creation and maintenance of a research repository or database as a specific research activity, but the subsequent use or disclosure by a covered entity of information from the database for a specific research study will require separate Authorization unless the PHI use or disclosure is permitted without Authorization in the form of a waiver approved by an IRB or Privacy Board. If an Authorization for research is obtained, the actual uses and disclosures made must be consistent with what is stated in the Authorization. The signed Authorization must be retained by the investigator for 6 years from the date of creation or the date it was last in effect, whichever is later.

An Authorization must contain the following specific core elements and required statements stipulated in the Rule:

### **Authorization Core Elements:**

- A description of the PHI to be used or disclosed, identifying the information in a specific and meaningful manner.
- The names or other specific identification of the person or persons (or class of persons) authorized to make the requested use or disclosure.

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	24 of 63

- The names or other specific identification of the person or persons (or class of persons) to whom the covered entity may make the requested use or disclosure.
- A description of each purpose of the requested use or disclosure.
- Authorization expiration date or expiration event that relates to the individual or to the purpose of the use or disclosure ("end of the research study" or "none" are permissible for research, including for the creation and maintenance of a research database or repository).
- Signature of the individual and date. If the individual's legally authorized representative signs the Authorization, a description of the representative's authority to act for the individual must also be provided.

#### **Authorization Required Statements:**

- A statement of the individual's right to revoke his/her Authorization and how to do so, and, if applicable, the exceptions to the right to revoke his/her Authorization or reference to the corresponding section of the covered entity's notice of privacy practices.
- Whether treatment, payment, enrollment, or eligibility of benefits can be conditioned on Authorization, including research-related treatment and consequences of refusing to sign the Authorization, if applicable.
- A statement of the potential risk that PHI will be re-disclosed by the recipient. This may be a general statement that the Privacy Rule may no longer protect health information disclosed to the recipient.

### **Is a Waiver of HIPAA Authorization Appropriate for my Research?**

Many health research projects and protocols cannot be undertaken using health information that has been de-identified. Also, it may not be feasible for a researcher to obtain a signed Authorization for all PHI the researcher needs to obtain for the research study.

To address these and other situations that may arise in the course of a research project, the Privacy Rule contains criteria for waiver or alterations of Authorizations by an IRB or Privacy Board. The Privacy Rule adds to federal research requirements when a researcher requests a waiver or an alteration of Authorization. When a covered entity has used or disclosed PHI for research with an IRB or Privacy Board approval of waiver or alteration of Authorization, documentation of that approval must be retained by the covered entity for 6 years from the date of its creation or the date it was last in effect, whichever is later.

An IRB or Privacy Board may approve a waiver or an alteration of the Authorization requirement in whole or in part for research uses and disclosures of PHI. A complete waiver occurs when the IRB or Privacy Board determines that no Authorization will be required for a covered entity to use and disclose PHI for a particular research project. A partial waiver of Authorization occurs when an IRB or Privacy



Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	25 of 63

Board determines that a covered entity does not need Authorization for all PHI uses and disclosures for research purposes, such as disclosing PHI for research recruitment purposes. An IRB or Privacy Board may also approve a request that removes some PHI, but not all, or alters the requirements for an Authorization (an alteration).

**Note: IRB approval of a HIPAA Authorization or a waiver of a HIPAA Authorization does not mean that you have unrestricted approval to access or use PHI held by a Covered Entity. The Covered Entity holding the PHI may have additional requirements that must be met before you can access or use that information.**

## What is a Limited Data Set and Data Use Agreement?

**Limited Data Set** - Refers to PHI that excludes 16 categories of direct identifiers and may be used or disclosed, for purposes of research, public health, or health care operations, without obtaining either an individual's Authorization or a waiver or an alteration of Authorization for its use and disclosure, with a data use agreement

**Data Use Agreement** - An agreement into which the covered entity enters with the intended recipient of a limited data set that establishes the ways in which the information in the limited data set may be used and how it will be protected.

The Privacy Rule permits a covered entity, without obtaining an Authorization or documentation of a waiver or an alteration of Authorization, to use and disclose PHI included in a limited data set. A covered entity may use and disclose a limited data set for research activities conducted by itself, another covered entity, or a researcher who is not a covered entity if the disclosing covered entity and the limited data set recipient enter into a data use agreement. Limited data sets may be used or disclosed only for purposes of research, public health, or health care operations. Because limited data sets may contain identifiable information, they are still PHI.

A limited data set is described as health information that excludes certain, listed direct identifiers (see below) but that may include: **city; state; ZIP Code; elements of date; and other numbers, characteristics, or codes not listed as direct identifiers.** The direct identifiers listed in the Privacy Rule's limited data set provisions apply both to information about the individual and to information about the individual's relatives, employers, or household members. The following identifiers must be removed from health information if the data are to qualify as a limited data set:

1. Names.
2. Postal address information, other than town or city, state, and ZIP Code.
3. Telephone numbers.
10. Certificate/license numbers.
11. Vehicle identifiers and serial numbers, including license plate numbers.
12. Device identifiers and serial numbers.

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	26 of 63

- |                                     |  |
|-------------------------------------|--|
| 4. Fax numbers.                     | 13. Web universal resource locators (URLs).                        |
| 5. Electronic mail addresses.       | 14. Internet protocol (IP) address numbers.                        |
| 6. Social security numbers.         | 15. Biometric identifiers, including fingerprints and voiceprints. |
| 7. Medical record numbers.          | 16. Full-face photographic images and any comparable images.       |
| 8. Health plan beneficiary numbers. |  |
| 9. Account numbers.                 |  |

A data use agreement is the means by which covered entities obtain satisfactory assurances that the recipient of the limited data set will use or disclose the PHI in the data set only for specified purposes. Even if the person requesting a limited data set from a covered entity is an employee or otherwise a member of the covered entity's workforce, a written data use agreement meeting the Privacy Rule's requirements must be in place between the covered entity and the limited data set recipient.

The Privacy Rule requires a data use agreement to contain the following provisions:

- Specific permitted uses and disclosures of the limited data set by the recipient consistent with the purpose for which it was disclosed (a data use agreement cannot authorize the recipient to use or further disclose the information in a way that, if done by the covered entity, would violate the Privacy Rule).
- Identify who is permitted to use or receive the limited data set.
- Stipulations that the recipient will
  - Not use or disclose the information other than permitted by the agreement or otherwise required by law.
  - Use appropriate safeguards to prevent the use or disclosure of the information, except as provided for in the agreement, and require the recipient to report to the covered entity any uses or disclosures in violation of the agreement of which the recipient becomes aware.
  - Hold any agent of the recipient (including subcontractors) to the standards, restrictions, and conditions stated in the data use agreement with respect to the information.
  - Not identify the information or contact the individuals.

If a covered entity is the recipient of a limited data set and violates the data use agreement, it is deemed to have violated the Privacy Rule. If the covered entity providing the limited data set knows of a pattern of activity or practice by the recipient that constitutes a material breach or violation of the data use

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	27 of 63

agreement, the covered entity must take reasonable steps to correct the inappropriate activity or practice. If the steps are not successful, the covered entity must discontinue disclosure of PHI to the recipient and notify HHS.

## **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 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, iRIS. Determinations cannot be issued through emails or phone calls.

- **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.
- **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.

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	28 of 63

- Modifications Required to Secure Approval: Made when IRB members require specific minor 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 the 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 the 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 approvals have been met. IRB approval is usually good for a period of time that is limited to 12 months or less, and is noted in the 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.

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	29 of 63

- 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 in a modification 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 your concerns to the IRB directly at an IRB meeting. Please contact the IRB staff to make arrangements to address the convened board.

## **What are my obligations as an investigator in order to conduct human research**

1) Ensure that Research Staff continue to remain 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 for the duration of the study.

a) Delegate responsibilities to Research Staff in accordance with staff experience, training, and qualifications.

b) Assure that all research procedures are performed with appropriate supervision and only by individuals who are licensed or otherwise qualified to perform them in the state of Texas and according to institutional policies.

c) Monitor the research study and perform quality assurance activities to ensure that participants are protected and that data are reliable.

2) Update the IRB office with any changes to the list of study personnel, by submitting a 'Personnel Change Request' form or an IRB Amendment in iRIS

3) Personally conduct or supervise the Human Research.

a) Conduct the Human Research in accordance with the relevant current protocol as approved by the IRB.

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 modify the Human Research without prior IRB review and approval unless necessary to eliminate apparent immediate hazards to participants.

d) Protect the rights, safety, and welfare of participants involved in the research.

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	30 of 63

- e) Make arrangements for oversight of the research and protection of participants in the event that you become temporarily unavailable to personally conduct or oversee the research.
- 4) Obtain the legally and ethically effective informed consent of research participants according to the plan approved by the IRB. a) Ensure that only qualified Research Staff obtain informed consent.
- 5) Maintain accurate and complete research records.
- 6) Submit to the IRB:
- a) Proposed modifications as described in this manual. (See “How do I submit a modification?”)
  - b) A continuing review application as requested in the approval letter. (See “How do I submit continuing review?”)
  - c) A continuing review application when the Human Research is closed. (See “How Do I Close Out a Study?”)
  - d) Reportable New Information. Reports of new information should be submitted within five business days. (See “What new information needs to be reported to the IRB?”)
- 7) 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.
- 8) Do not accept or provide payments to professionals in exchange for referrals of potential participants (“finder’s fees.”)
- 9) Do not accept payments designed to accelerate recruitment that were tied to the rate or timing of enrollment (“bonus payments.”)
- 10) See additional requirements of various federal agencies in Appendix A. These represent additional requirements and do not override the baseline requirements of this section.

## What New Information Items need to be Promptly Reported to the IRB?

New safety, risk and compliance related information, including Unanticipated Problems, require prompt reporting to the IRB. Within 5 business day of being notified of the reportable new information item, a Reportable New Information Report is to be submitted through iRIS.

**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.

Include any new information items that fall into one or more of the following categories below:

- 1) Harm experienced by a subject or other individual, which in the opinion of the investigator are **unexpected** and **related** or possibly to the research procedures including unanticipated problems.
  - a) 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.

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	31 of 63

- b) A harm is “**related**” or possibly related to the research procedures if in the opinion of the investigator, the research procedures more likely than not caused the harm.
- 2) Information that indicates a new or increased risk, or a new safety issue including unanticipated problems. For example:
    - a) 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).
    - b) 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
    - c) Withdrawal, restriction, or modification of a marketed approval of a drug, device, or biologic used in a research protocol
    - d) Protocol deviation that harmed subjects or others or that indicates subjects or others might be at increased risk of harm
    - e) Complaint of a subject that indicates subjects or others might be at increased risk of harm or at risk of a new harm
    - f) Any changes significantly affecting the conduct of the research
  - 3) 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.
  - 4) Audit, inspection, or inquiry by a federal agency or any other outside entity and any resulting reports (e.g. FDA Form 483.)
  - 5) Written reports of study monitors.
  - 6) Failure to follow the protocol due to the action or inaction of the investigator or research staff whether planned or unplanned (deviations).
  - 7) Breach of confidentiality (inappropriate disclosure of or access to confidential information).
  - 8) Change to the protocol taken without prior IRB review to eliminate an apparent immediate hazard to a subject.
  - 9) Incarceration of a subject in a study not approved by the IRB to involve prisoners.
  - 10) Complaint of a subject that cannot be resolved by the research team.
  - 11) Premature suspension or termination of the protocol by the sponsor, investigator, or institution.
  - 12) 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.)

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	32 of 63

## **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.

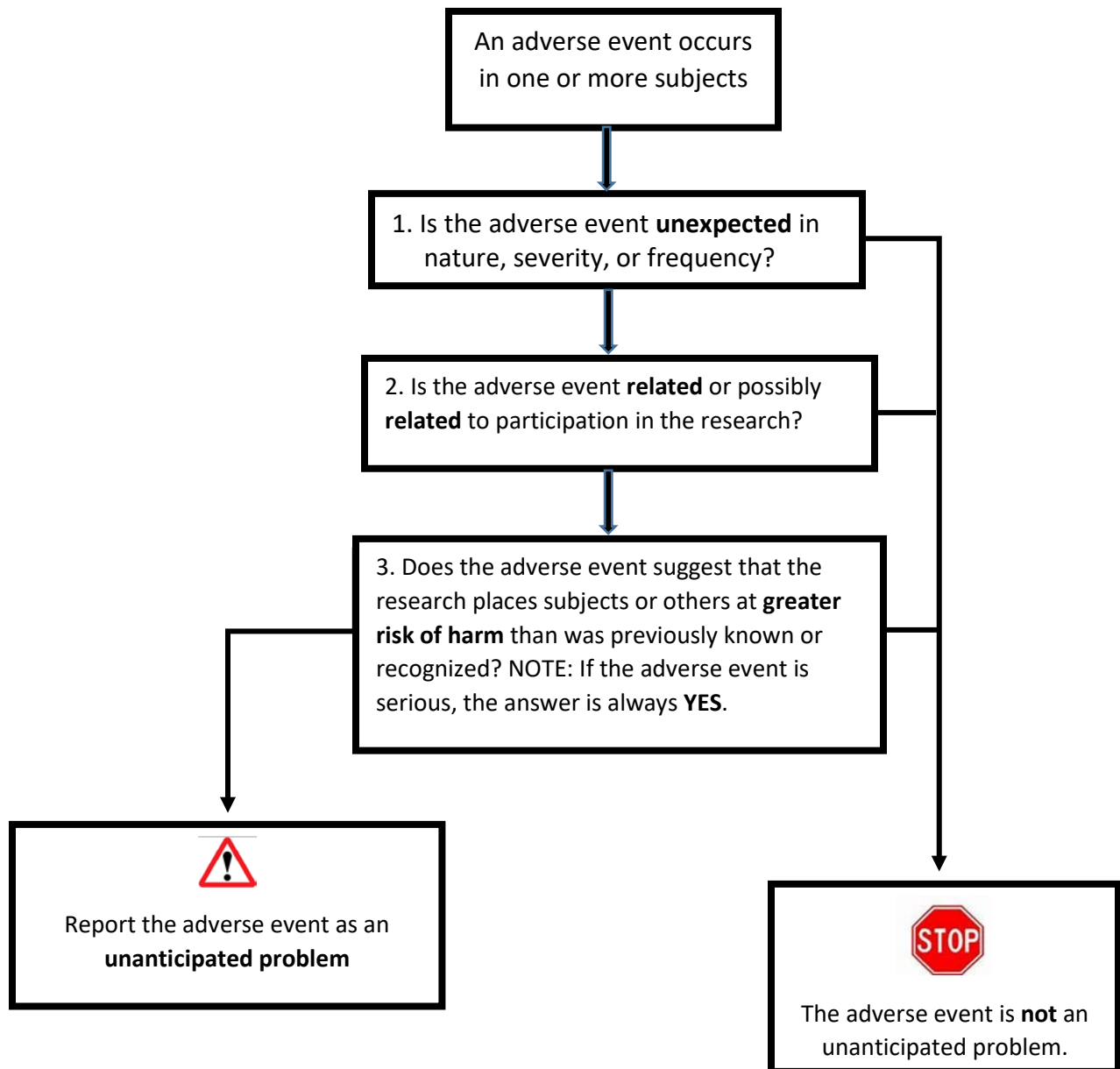
See flow chart below.



Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	33 of 63

### Unanticipated Problem Flow Chart

**Ask all three questions**



<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	34 of 63

## How do I submit a modification?

- Access the URL <https://iris.tamu.edu>
- Log into iRIS using your NetID or UIN/SSO login and password.
- From the 'Study Assistant' menu click 'My Studies'.
- Select the study you would like to modify.
- You will first need to modify the IRB application and/or consent documents and any other study documents, as applicable, to reflect the proposed changes.
- Then select 'IRB Amendment' from the list of 'Protocol Items'.
- Select 'Add a new Form'
- Complete each section of the online IRB Amendment Form.
- Attach any updated documents (IRB Application, Consent Documents, Protocol, any other study document)
- Click 'Save and Continue to the Next Section' after the form is complete.
- Select 'Save and Continue', then 'Sign off and Submit'

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?

- Access the URL <https://iris.tamu.edu>
- Log into iRIS using your NetID or UIN/SSO login and password.
- From the 'Study Assistant' menu click 'Upcoming Renewals'
- Select the study you would like to renew.
- Then select 'IRB Continuing Review Form' from the list of forms.
- Select 'continue'
- Complete each section of the online IRB Continuing Review Form
- Attached already approved documents (consent documents and all other study documents) that you wish to use in the upcoming approval. Those documents will be re-assessed and stamped approved again.
- Select 'Save and Continue', then 'Sign off and Submit'
- Select all Investigators to include in the sign off.
- Then click 'Save and Continue' as needed.
- Complete your sign off as prompted.
- The continuing review will not be submitted to the IRB until all Investigators have logged into iRIS and completed their assigned sign offs.

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?'

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	35 of 63

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 until the completed 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. If current subjects will be harmed by stopping Human Research procedures that are available outside the Human Research context, provide these on a clinical basis as needed to protect current subjects. If current subjects will be harmed by stopping Human Research procedures that are not available outside the Human Research context, immediately contact the IRB chair and provide a written list of the currently enrolled subjects and why they will be harmed by stopping Human Research procedures.

## How do I close out a study?

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

- Access the URL <https://iris.tamu.edu>
- Log into iRIS using your NetID or UIN/SSO login and password.
- From the 'Study Assistant' menu click 'My Studies'.
- Select the study you would like to close.
- Select 'IRB-Completion/Not Initiated Report Form' from the list of 'Protocol Items'
- Select 'Add a new Form'
- Complete each sections of the form and 'Save and Continue'
- Then click 'Sign off and Submit'
- Assign personnel sign off, 'Save and Continue' and complete and save your sign off as prompted.

The IRB may request additional information to ensure that the study is in good standing and ready to be closed. Once the submission is approved, the study is considered Closed by the IRB and will be archived. If an investigator wishes to resume the research after the study has been closed or if the study is closed in error, **a new study will have to be submitted.**

Once a study has been closed, investigators may keep the data collected. All identifiable information should be removed before closure. Clinical trials may need to keep data that can be linked back to the subject for a period of time specified by the sponsor. This data must be stored in a manner that is consistent with the protections provided in IRB-approved protocol. Investigators should continue to honor any confidentiality protections of the data. Investigators should also honor any other commitments that were agreed upon as part of the approved research. For example, providing

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	36 of 63

information about the study results to research participants or honoring reimbursement commitments for participation.

### **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.

### **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 <http://vpr.tamu.edu/compliance/rcc/irb/sops>.

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

750 Agronomy Rd. Suite 2701

College Station, TX 77843-1186

Mail Stop: 1186 TAMU

Phone: 979.458.4067

Email: [irb@tamu.edu](mailto:irb@tamu.edu)

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	37 of 63

## Additional Requirements for DHHS-Regulated Research

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. 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.

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	38 of 63

## Additional Requirements for FDA-Regulated Research

1. When a subject withdraws from a study:<sup>1</sup>
  - 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 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:<sup>2</sup>
    - 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.

---

<sup>1</sup> <http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126489.pdf>

<sup>2</sup> <http://www.accessdata.fda.gov/SCRIPTS/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.7>

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	39 of 63

- 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<sup>3</sup>
- 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.
- c. Follow FDA requirements for control of the investigational drug<sup>4</sup>
- 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<sup>5</sup>
- i. Disposition of drug:

---

<sup>3</sup> <http://www.accessdata.fda.gov/SCRIPTS/cdrh/cfdocs/cfcr/CFRSearch.cfm?fr=312.60>

<sup>4</sup> <http://www.accessdata.fda.gov/SCRIPTS/cdrh/cfdocs/cfcr/CFRSearch.cfm?fr=312.61>

<sup>5</sup> <http://www.accessdata.fda.gov/SCRIPTS/cdrh/cfdocs/cfcr/CFRSearch.cfm?fr=312.62>

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	40 of 63

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<sup>6</sup>
- 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.

---

<sup>6</sup> <http://www.accessdata.fda.gov/SCRIPTS/cdrh/cfdocs/cfcr/CFRSearch.cfm?fr=312.64>



<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	41 of 63

- 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<sup>7</sup>
  - 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<sup>8</sup>
  - 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<sup>9</sup>
  - i. If the investigational drug is subject to the Controlled Substances Act, the investigator must take adequate precautions, including storage of the

---

<sup>7</sup> <http://www.accessdata.fda.gov/SCRIPTS/cdrh/cfdocs/cfcr/CFRSearch.cfm?fr=312.66>

<sup>8</sup> <http://www.accessdata.fda.gov/SCRIPTS/cdrh/cfdocs/cfcr/CFRSearch.cfm?fr=312.68>

<sup>9</sup> <http://www.accessdata.fda.gov/SCRIPTS/cdrh/cfdocs/cfcr/CFRSearch.cfm?fr=312.69>

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	42 of 63

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.<sup>10</sup>

- 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 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<sup>11</sup>

- 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.

---

<sup>10</sup> <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcr/CFRSearch.cfm?fr=812.100>

<sup>11</sup> <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcr/CFRSearch.cfm?fr=812.110>

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	43 of 63

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:<sup>12</sup>
    - 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.
    - 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

---

<sup>12</sup> <http://www.accessdata.fda.gov/SCRIPTS/cdrh/cfdocs/cfcr/CFRSearch.cfm?fr=812.140>

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	44 of 63

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<sup>13</sup>
- 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.
- e. Prepare and submit the following complete, accurate, and timely reports<sup>14</sup>
- i. Unanticipated adverse device effects. An investigator must submit to the sponsor and to the reviewing IRB a report of any unanticipated adverse device

---

<sup>13</sup> <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=812.145>

<sup>14</sup> <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=812.150>

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	45 of 63

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.

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	46 of 63

## 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.
  - 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.

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	47 of 63

- 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.

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	48 of 63

- 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.



<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	49 of 63

- 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.

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	50 of 63

- 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.

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	51 of 63

- 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.

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	52 of 63

- 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.

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	53 of 63

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](https://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R2_Step_4.pdf)

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	54 of 63

## Additional Requirements for Department of Defense (DOD) research

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. 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.
3. 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.
4. Components of the Department of Defense might have stricter requirements for research-related injury than the DHHS regulations.
5. There may be specific educational requirements or certification required.
6. 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.
7. 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.
8. The investigator must notify the Department of Defense Human Research Protection Official (HRPO) promptly (within 30 days) of the following items:
  - When significant changes to the research protocol are approved by the IRB.
  - The results of the Continuing Review
  - If the IRB used to review and approve the research changes to a different IRB

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	55 of 63

9. 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 “WORKSHEET: Additional Federal Criteria (HRP-318)” and the [DOD Directive 321602.pdf](#)

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	56 of 63

## Additional Requirements for Department of Energy (DOE) Research

1. Research that involves one or more of the following is considered by DOE to be human subjects research and requires IRB review:
  - a. Intentional modification of the human environment
  - b. Study of human environments that use tracer chemicals, particles or other materials to characterize airflow.
  - c. Study in occupied homes or offices that:
    - i. Manipulate the environment to achieve research aims.
    - ii. Test new materials.
    - iii. 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.
2. You must complete and submit to the IRB the DOE "Checklist for IRBs to Use in Verifying that HS Research Protocols are In Compliance with DOE Requirements" ([http://human.subjects.energy.gov/other-resources/documents/IRB-template-for-reviewing-PII-protocols-2010\\_ac.pdf](http://human.subjects.energy.gov/other-resources/documents/IRB-template-for-reviewing-PII-protocols-2010_ac.pdf)) if your research includes Personally Identifiable Information. Please indicate with each item in the checklist where this is addressed within the protocol you have submitted to the IRB for review.
3. You must report the following within ten business days to the Department of Energy human subjects research program manager:
  - a. Any significant adverse events, unanticipated risks; and complaints about the research, with a description of any corrective actions taken or to be taken
  - b. Any suspension or termination of IRB approval of research
  - c. Any significant non-compliance with HRPP procedures or other requirements.
4. You must report the following within three business days to the Department of Energy human subject research program manager.
  - a. Any compromise of personally identifiable information must be reported immediately.
5. Research involving human participants also includes studies of the intentional modification of the human environment; generalizable includes the study of tracer chemical, particles or other materials to characterize airflow.



<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	57 of 63

6. Generalizable also includes studies in occupied home or offices that:
  - a. Manipulate the environment to achieve research aim;
  - b. Test new materials;
  - c. Involve collecting information on occupants' views of appliances, materials; or
  - d. Devices installed in their homes or their energy-saving behaviors through surveys and focus groups.

Generalizable should be viewed in terms of the contribution to knowledge with the specific field of study.

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

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	58 of 63

## Additional Requirements for Department of Justice (DOJ) Research

### I. 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

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	59 of 63

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.

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	60 of 63

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.

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	61 of 63

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).”

## II. [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).”

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	62 of 63

## 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<sup>15</sup> involved in the research<sup>16</sup> 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).”

---

<sup>15</sup> 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.

<sup>16</sup> 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.

<b>Investigator Manual</b>		
NUMBER	DATE	PAGE
HRP-103	5/30/2017	63 of 63

## 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)."