Investigator Manual

Revised August 23, 2019
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Chapter 1
General Information

1.1 Purpose of this manual
This document “INVESTIGATOR MANUAL (HRP-103)” will help you work with the IRB and the Human Subject Research Office. It will also guide you through policies and procedures related to the conduct of Human Research that are specific to this institution.

University of Miami Investigators must read and understand the information in this manual before conducting human subject research.

1.2 What is Human Research?
The definition of “human subject research” depends upon whether and how the research is regulated. For research that is federally funded, the definition comes from the Common Rule:

Common Rule Definition of Human Subject
Human subject is a living individual about whom an investigator (whether professional or student):

- Obtains information/biospecimens through intervention/interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or
- Obtains, uses, studies, analyzes, or generates identifiable private information/biospecimens.
- Intervention includes physical procedures by which information/biospecimens are gathered (e.g., venipuncture) and manipulations of the subject or the subject’s environment performed for research.
- Interaction includes communication or interpersonal contact between investigator and subject.
- Private information includes information
  - about behavior occurring when an individual can expect that no observation or recording is being done, and
  - provided for specific purposes by an individual who expects the information will not be made public (e.g., a medical record).
- “Identifiable” means the subject’s identity is or may readily be ascertained by the investigator.
- An identifiable biospecimen is a biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen.
When conducting a clinical investigation under FDA jurisdiction, the definition comes from the FDA regulations.

**FDA Definition of Human Subject**

The recipient of the test article or the control.

You can find an algorithm for determining whether an activity is Human Research in “WORKSHEET: Human Research (HRP-310)” on the HSRO website. You can also complete an online survey to help determine whether an activity meets either the DHHS or FDA definition of Human Research. In questionable cases, the IRB makes the ultimate determination whether an activity is Human Research requiring IRB oversight.

You must not conduct Human Research without prior IRB review and approval (or an institutional review and approval of exempt Human Research). If you have questions about whether an activity is Human Research, or if you wish to have a written determination that your project is not human subject research, contact the Human Subject Research Office.

The University of Miami HSRO requires investigators to obtain IRB Approval before conducting human subject research.

### 1.3 What is the Human Research Protection Program

The document “HUMAN RESEARCH PROTECTION PROGRAM PLAN (HRP-101)” describes this institution’s overall plan to protect subjects in Human Research.

- The mission of the Human Research Protection Program;
- The ethical principles that the institution follows governing the conduct of Human Research;
- The applicable laws that govern Human Research;
- When the institution becomes “engaged in Human Research” and when someone is acting as an agent of the institution conducting Human Research;
- The types of Human Research that may not be conducted at the University of Miami; and
- The roles and responsibilities of individuals within the institution.
Protection of human subjects is the responsibility of everyone involved in the research. The PI is ultimately responsible for ensuring subjects’ rights and safety are protected. This is true, even though the IRB oversees the research.

1.4 Who is eligible to be a Principal Investigator

Every research study requires a Principal Investigator (PI). This person takes full responsibility for the conduct of the study. Only one individual can serve as Principal Investigator for a human subject research project. During the conduct of the research, the Principal Investigator has ultimate responsibility for the administrative, fiscal and scientific conduct of the research project.

The HSRO will address all official IRB correspondence to the Principal Investigator.

Jackson Health System (JHS) employees who obtain approval from the JHS Clinical Research Review Committee (CRRC) may also serve as Principal Investigators on studies.

Below is a comprehensive list of who may and may not serve as PI. Unless approved by the Executive Director, HSRO, only UM faculty may serve as Principal Investigators on studies.

**TABLE 1.1 PI ELIGIBILITY**

<table>
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<th>PI Eligible</th>
<th>Case-by-Case Decisions</th>
<th>Not PI Eligible</th>
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<td>• Tenure-track faculty (full, associate, and assistant professors); and • Non-tenure-track research and/or clinical faculty (full, associate, and assistant professors); • Senior research investigators (Faculty with emeritus status or who are tenured and retired but wish to continue as PI) • Jackson employees</td>
<td>• Adjunct faculty • Visiting faculty • Visiting scholars. <strong>Contact the Executive Director of the HSRO via email to request permission for such faculty to conduct research. Please include a letter of support from your Department Chair/Division Chief. Upon approval, upload the confirmation email into the &quot;Supporting Documents&quot; section in your electronic submission.</strong></td>
<td>• Postdoctoral fellows and research assistants (graduate students); • Research associates; and • Graduate and Undergraduate students</td>
</tr>
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Chapter 2

Training and Disclosure Requirements

2.1 Training requirements for investigators and research staff

This section describes the training requirements imposed by the HSRO. You may have additional training imposed by other federal, state, or institutional policies.

2.1.2 Basic Courses in Human Subject Research Training

All personnel involved in human subject research must complete human subject research training before engaging in human subject research activities. This requirement is referred to as becoming “CITI-Certified. The following classes of individuals must complete the required training:

- Investigators
- Sub-investigators
- Research team members listed in the eProst application
- Individuals named as the contact person in the informed consent document and recruitment materials

Investigators are responsible for ensuring all study team members have completed training before submitting an application to the IRB.

The PI and research team members should complete the required training before submitting an application for a new study to the IRB for review. New members of the research team must complete the training before engaging in research activities, including access to and analysis of private identifiable data.

CITI offers the following courses:

- Group 1: HSR Series for Biomedical Researchers - Required for all personnel involved primarily in biomedical research; and for all personnel performing both biomedical and social/behavioral research.
- Group 2: HSR Series for Social-Behavioral-Educational Researchers Basic Course - Required for all personnel involved primarily in social and behavioral research.
Trainees should select the courses most applicable to the types of human subject research conducted at their site. The IRB reserves the right to make this course a requirement for research personnel involved in both biomedical and social/behavioral research.

Recertification is required at three-year intervals for all courses discussed above. The CITI Program offers refresher courses to meet the training requirements. Principal Investigators must ensure that all study team members hold current CITI certification. Failure to maintain such certification is noncompliance with University requirements for the conduct of human subject research.

### 2.1.3 Training for Clinical Trials

In addition to the above courses, investigators and research team members involved in the conduct of a clinical trial must complete training in Good Clinical Practice (GCP). Below is the definition of “clinical trial.”

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

GCP training is a regulatory requirement for NIH-funded clinical trials, including clinical trials with that focus on social-behavioral issues. GCP training consists of basic and refresher courses provided by CITI tailored to different types of research, including:

- GCP for Clinical Trials with Investigational Drugs and Medical Devices (FDA focus)
- GCP for Clinical Trials with Investigational Drugs and Biologics (ICH Focus)
- GCP for Clinical Investigations of Devices
- GCP – Social and Behavioral Research Best Practices for Clinical Research

Trainees should select the courses most applicable to the types of human subject research conducted at their site. As with the basic courses, retraining is required at three-year intervals for all courses discussed above. The CITI Program also offers refresher courses to meet the retraining requirement.

Investigators and research staff must also complete training on Conflicts of Interests as described in the following section.

For questions or concerns related to this issue, please contact the Human Subjects Research Office at 305-2433195 or email our Help desk at hsro@med.miami.edu.
2.2 Financial Disclosure and Training requirements

Investigators and key personnel must comply with the University of Miami COI policy. The Office of Disclosures and Relationship Management (DRM) and the UM COI Committee (COIC) are charged with determining whether relationships with an external entity create a situation that could introduce bias into a research project conducted at the UM or by UM investigators; and, when this bias could occur, to manage it. Additional information is located on the Disclosures and Relationship Management (DRM) website pages.

The DRM shares information about the financial relationship and the determinations made by the COIC with the IRB. The IRB will then review the research and the information provided by the DRM to determine whether risks to subjects continue to be minimized and are reasonable in relation to anticipated benefits to the subjects or others.

Investigators and research team members must complete financial conflicts of interest training when joining the UM and:

- Every four years;
- When financial conflicts policies are revised in a manner that changes investigator requirements
- When found non-compliant with financial conflicts policies and procedures

The training focuses on the federal policies that apply to research and externally funded scholarly activities performed at UM. Additional information including a schedule of seminars to be held on the Gables, Medical and RSMAS campuses can be found in the ULearn System (keyword search “conflict of interest.”)
3.1 Submitting New Human Subject Research

Before submitting the research for initial review, investigators must:

- Ensure all research team members have completed required human subject research training and conflict of interest training
- Obtain the financial interest status (“yes” or “no”) of each research staff
- Obtain the agreement of each research staff to his/her role in the research.

You must submit research proposals to the IRB through the HSRO’s electronic system, eProst. If you do not yet have an eProst account, complete the “New Account Request Form,” located on the landing page of the eProst website. You will need to have a valid C-number in order to request an account.

eProst uses an electronic application. You should use the “New Study SmartForm” for new studies. The New Study SmartForm requires you to list the study personnel. You must ensure that all new personnel have completed required training and have submitted the appropriate disclosures in the UDisclose system.

Once you complete the electronic form, you will need to upload additional documents (protocol, consent document, etc.) requested by the electronic system. When you complete these tasks, the PI must review the submission and click the “Submit” button after ensuring the submission is correct.

You should maintain electronic copies of all information submitted to the IRB so you can use the original versions to document modifications.

Various departments at the University of Miami must be informed about pending human subject research and must complete reviews specific to their department. For example, all cancer studies require review by the Cancer Center’s Protocol Review and Monitoring Committee. Likewise, the Institutional BioSafety Committee (IBC) must review studies involving recombinant DNA. When you complete the application in eProst, the system will inform you if you need to submit documents to one or more ancillary committee. Additional information about the committees can be found here.

3.2 Submitting Modifications

Complete the Modification SmartForm in eProst and attach all requested documents. When revising previously approved documents, use the WORD Track Changes feature to highlight the revisions. When submitting a revised sponsor protocol, you must complete the following:
- Document a summary of the changes and the reasons for the changes on the electronic Smart Form to help the IRB members clearly identify the changes and the reasons for the revision;
- Include a tracked changes version of the protocol and a clean copy of the protocol;
- If the consent document is revised, include a tracked changes version of the consent document.

**Note:** Always save previous tracked changes so you have a clean document before adding new tracked changes for a newly revised document so the reviewers can clearly differentiate language that is new from language that has already been approved.

When the submission is ready, the PI must review the submission and click the “Submit” button after ensuring the submission is correct.

If the modification includes an update to study personnel, you must ensure that all new personnel have completed **required training** and have made the appropriate disclosures in the **UDisclose** system.

If the modification is solely to update the list of study personal, the IRB will acknowledge the update. If the modification is to the research or to any research documents, the IRB will approve the modification when all approval requirements are met.

### 3.3 Submitting Continuing Review Reports

The IRB must conduct “continuing review” of research that involves greater than minimal risk and research subject to FDA regulations. When continuing review is required, your approval letter will include an expiration date. If you do not submit your continuing review application on time, the IRB may restrict your ability to submit new Human Research.

If the approval of Human Research expires all Human Research procedures related to the protocol must cease, including recruitment, advertisement, screening, enrollment, consent, interventions, interactions, and collection or analysis of private identifiable information. Continuing human research procedures after approval has lapsed is a violation of institutional policy and may also violate the terms of your grant and federal regulations.

If current subjects will be harmed by stopping one or more procedures required for the research, immediately contact the IRB chair and provide a written list of the currently enrolled subjects, the procedures that need to be completed and an explanation as to the harm that could occur by not completing the procedures.

Two different applications are available for continuing review submissions:
- Continuing Review SmartForm
- Combined Continuing Review and Modification SmartForm
If you need to modify the research at the time of continuing review, you should submit a combined Continuing Review and Modification SmartForm.

To submit a continuing review application, complete the appropriate SmartForm in the electronic IRB system and attach all requested documents. When the submission is ready, the PI must review the submission and click the “Submit” button after ensuring the submission is correct.

3.4 Closing a Study

Investigators must close a study when:

- All interactions and interventions with subjects are completed; and
- The study is no longer accessing private, identifiable information about the subjects.

To close a study, complete the Continuing Review SmartForm in the electronic IRB system, attach all requested supplements, and have the SmartForm submitted by the PI by clicking the “Submit” activity.

3.5 Writing an Investigator Protocol

A research protocol is a document that describes the background, rationale, objectives, design, methodology, statistical considerations, and organization of a research project. After determining that all requirements are met, the IRB will approve the protocol. Unless a revision to the protocol is required to protect subjects from imminent harm, investigators and research staff must comply with the protocol when conducting human subject research. Consequently, it is essential that all individuals listed as study personnel receive training on the protocol requirements. In addition, the HSRO recommends the use of tools, such as visit checklists and pre-written orders to avoid deviations from the protocol.

When conducting industry-sponsored research, the sponsor will provide a protocol. Investigators must write and submit a “Local Addendum” to describe how they will conduct the research at their site. The local addendum will describe local issues such as the process for recruitment and maintaining confidentiality of the data.
Investigators can use one of several protocol templates to create their protocol. These templates are located on the HSRO website. It is important to use a template to ensure that all required information is included.

**TABLE 3.1 PROTOCOL TEMPLATES**

<table>
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<tr>
<th>Protocol</th>
<th>Can be used for a wide range of studies that are not clinical investigations subject to FDA</th>
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<tr>
<td>Template Protocol – Minimal Risk</td>
<td>Should be used for most protocols involving only minimal risk that do not meet any of the categories below</td>
</tr>
<tr>
<td>Template Protocol – NIH-FDA Phase 2 and 3 IND-IDE Clinical Trials</td>
<td>Should be used for clinical investigations involving FDA-regulated products and other bio-medical studies</td>
</tr>
<tr>
<td>Template Protocol – Local Addendum</td>
<td>Should be submitted along with the main sponsor protocol. Provides information that is specific to the research site.</td>
</tr>
<tr>
<td>Template Protocol – Chart Review</td>
<td>For use with research involving only data collection from existing records</td>
</tr>
<tr>
<td>Template Protocol – Survey &amp; Interview</td>
<td>For use with research involving only surveys and/or interviews</td>
</tr>
<tr>
<td>Template Protocol – Biospecimen Research</td>
<td>For use with research involving only existing biospecimens</td>
</tr>
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Use one of the templates above as a starting point. Here are some key points to remember when developing an Investigator Protocol:

- The italicized bullet points in the template serve as guidance to investigators. Follow the guidance and then remove all italicized comments before submitting the protocol to the IRB.
- When writing an Investigator Protocol, always keep an electronic copy. You will need to modify the copy when making changes to the Investigator Protocol.
- If you believe your activity may not be Human Research, click this link to complete an online survey to help determine if the activity meets the definition of Human Subject Research.
- In rare instances, a section in a Template Protocol might not be applicable to your study. If you are certain the section is not applicable, place “N/A” in that section.
• If your research will include any of the following vulnerable populations, you must describe the population in the inclusion criteria of the protocol.
  o Adults unable to provide legally effective consent
  o Individuals who are not yet adults (infants, children, teenagers)
  o Pregnant women
  o Prisoners
• If you are conducting community-based participatory research, you may contact the IRB Office for information about:
  o How to conduct community-based participatory research design
  o Use of community advisory boards
  o Use of participant advocates
  o Partnerships with community-based institutions or organizations.
Chapter 4
Reliances and Cooperative Research for IRB Oversight

Research sites and personnel who are not part of the University of Miami (UM) are not covered by the UM’s IRB review unless the review is coordinated through the UM HSRO. Likewise, if you are collaborating on a study that will involve an external central IRB, the UM HSRO must be involved in the coordination of the central IRB review.

4.1 Requesting an external IRB

The University of Miami permits the use of an external IRB for review and oversight of human subject research only when:

- Required by regulations; or
- Required by the sponsor as a condition of conducting the study.

If you are interested in obtaining review from an external IRB for research, you will need to complete the FORM: Reliance Application (HRP 216). You may submit this form through eProst or via email.

HSRO staff will review the form and determine whether the research qualifies for a reliance. Once the HSRO makes this determination, we will contact you with a response and provide further directions.

When an independent, commercial IRB completes the review, the HSRO charges a one-time $1000 administrative fee for processing submissions for external review.

If the research qualifies for a reliance, the following actions must happen:

- HSRO staff will determine whether the UM HSRO has a reliance agreement in place and will follow-up with the reviewing institution if an agreement is needed.
- The HSRO staff will provide a signed HRP-216 or a Cede Review Letter to the reviewing IRB.
- Prior to conducting the review, the reviewing IRB may require information about the University of Miami’s local context. Click Here to find more information about required language for consent documents, local context and state law requirements.
The UM site must:
  o Submit the study through eProst;
  o Obtain all required ancillary reviews and approvals;
  o Ensure documents are submitted to the reviewing IRB;
  o Ensure the consent document includes language required by the UM HSRO;
  o Submit the following approved documents into eProst after the reviewing IRB has completed the review:
    ▪ Protocol
    ▪ Consent Document(s)
    ▪ Recruitment Materials
    ▪ Subject-facing documents
  o Refrain from starting the research until you receive acknowledgement from the UM HSRO;
  o Refrain from starting the research until each step above is completed

During the course of the research, you must submit the following as a modification in eProst:
  o Any document that needs to be uploaded into Velos;
  o Reports of non-compliance that could meet the UM’s definitions of serious or continuing non-compliance;
  o IRB suspensions or terminations of study approval;
  o IRB determinations of:
    ▪ Serious non-compliance;
    ▪ Continuing non-compliance;
    ▪ Unanticipated problems involving risks to subjects or others;
  o Study closures

4.2 Obligations of investigators when relying on an external IRB

When relying on an external IRB for oversight of research conducted at the UM, investigators must:
1) Obtain appropriate approvals from the University of Miami HSRO and all required ancillary committees prior to seeking review by another IRB.
2) Comply with the determinations and requirements of the reviewing IRB.
3) Provide the reviewing IRB with requested information about local requirements or local research context issues relevant to the IRB’s determination prior to IRB review.
4) Report the following to the reviewing IRB:
   a. Changes in local policies that impact IRB review;
b. Conflicts of interests along with the COIC Management Plan reviewing IRB and you must comply with the management plan;
c. Any proposed changes to the research prior to implementing such changes without prior IRB review and approval, except where necessary to eliminate apparent immediate hazards to the participants;
d. Any unanticipated problems involving risks to participants or others according to the requirements specified in the reliance agreement;
e. Non-compliance, participant complaints, protocol deviations or other events according to the requirements specified in reviewing IRB’s SOPs or the reliance agreement.
f. Data safety monitoring reports in accordance with the reviewing IRB’s reporting policy.
5) Cooperate with all other reporting requirements of the reviewing IRB.
6) When enrolling participants, obtain consent from subjects or the subject’s legally authorized representative (LAR) in compliance with applicable regulations, the reviewing IRB’s requirements, the protocol, and the University of Miami requirements [SOP: INFORMED CONSENT PROCESS FOR RESEARCH (HRP-90)].
7) Maintain records of documentation of consent for each participant, as required by applicable regulations, the protocol, the reviewing IRB and the University of Miami requirements;
8) Provide the name and contact information for an individual the IRB can contact for questions and instructions.

### 4.3 Requesting the UM IRB to serve as the IRB

When considering whether to use the UM IRB as the reviewing IRB, investigators should be aware that they will incur additional responsibilities. For example, the UM investigator, or an established coordinating center, will be responsible for coordinating the submissions from each site and submitting information into the UM HSRO’s electronic system, ePROST. In addition, the UM investigator will be responsible for ensuring that participating sites receive IRB communications, such as approval letters and approval documents, unless another mechanism is used.

If you are interested in using the UM IRB to review a multi-site study or reviewing the research activities of a collaborating independent external investigator, you will need to complete the FORM: HRP-217 External Site application for UM IRB Review. HSRO staff will review the completed form and determine whether the research qualifies for a reliance. Once the HSRO makes
this determination, we will contact you with a decision and provide instructions on how to proceed.

If the research qualifies for a reliance, the following actions will happen:

- HSRO staff will determine whether the UM HSRO has a reliance agreement in place with each of the relying sites and will follow-up with the sites if an agreement is needed.
- The UM site must submit the study through the UM HSRO’s electronic system, eProst.
- The UM site or a coordinating center must complete a submission through eProst.
- Each site must complete and the local team must submit FORM: HRP-218 Relying Site Information Questionnaire.
- A Responsible Party from each site must sign a Cede Review Letter for the specific study and the letter must be uploaded into the site’s submission in the eProst system.

4.4 Obligations of a Lead PI for a Multi-Site study reviewed by UM IRB

When you are the Lead PI for a Multi-Study reviewed by the UM IRB, you will have the following additional responsibilities:

1) Coordinating with HRSO personnel to determine whether the University of Miami’s IRB can act as the single IRB for all or some institutions participating in the study or if a different, external IRB will assume oversight.

2) Identifying all sites that will be engaged in the human research and requiring review and oversight by the University of Miami IRB.

3) Provide to the reviewing IRB a description of the roles and responsibilities of key stakeholders and the plan for communicating and coordinating key information to and from study teams at relying sites and the UM IRB or HRSO.

4) Unless other arrangements are in place:
   a. Provide relying site investigators with the policies of the UM HSRO.
   b. Establish a process for obtaining and collating information from all sites and submitting this information to the reviewing IRB; (This information includes site-specific variations in study conduct, such as the local consent process and language, subject identification and recruitment processes and local variations in study conduct)
   c. Prepare and submit IRB applications on behalf of all sites. Submissions include initial review, modifications, personnel updates, reportable new information and continuing review reports;
   d. Report the absence of continuing review information from relying sites if they do not provide the required information prior to submission of the continuing review materials to the reviewing IRB. Notifying the relying site of their lapse in approval and applicable corrective actions.
   e. Submit reportable new information from relying sites to the reviewing IRB in accordance with the terms outlined in the authorization agreement or communication plan.
f. Provide relying site investigators with the IRB-approved versions of all study documents;

g. Provide investigators with all determinations and communications from the reviewing IRB.

h. Provide approval documents and communications so the to the relying institution, reviewing IRB or regulatory agencies upon request.

i. Ensuring that consent forms used by relying sites follow the consent template approved by the reviewing IRB and include required language as specified by the relying sites.

j. Respond to questions or information requests from study teams or the IRB or HRPP staff at relying sites; and

k. Ensure that all sites receive a request to rely on the reviewing IRB and that all institutional requirements are satisfied before a study is activated at a relying site.
Chapter 5
IRB Review of Human Subject Research

The IRB follows policies and procedures to conduct research. These policies are included in Standard Operating Procedures (SOPs) located on the HSRO Website. This chapter describes what investigators should expect from IRB review.

5.1 Levels of IRB Review

When the HSRO receives a submission, the first task is to determine whether the proposed project is, indeed, human subject research. If we determine that it meets the definition of human subject research, the next task is to determine the level of review. The following are descriptions of the various levels of review available:

- **Not “Human Research:”** Activities that do not meet the definition of “research” and/or do not include “human subjects,” as defined by regulations, are not subject to IRB oversight or review. Click this link to access a survey to help you determine if the project is human subject research. If you need a letter from the IRB indicating a proposed project is not human subject research, print the report provided to you after completing the survey and submit the report via email to the HSRO. If you have additional questions about a project, contact the IRB Office.

- **Exempt:** Certain categories of Human Research may be exempt from regulation but require IRB review. It is the responsibility of the institution, not the investigator, to determine whether Human Research is exempt from IRB review. A single designated reviewer will review the submission rather than the convened board.

- **Review Using the Expedited Procedure:** Certain categories of non-exempt Human Research may qualify for review using the expedited procedure, meaning that a single designated reviewer will review the submission rather than the convened board.

- **Review by the Convened IRB:** The convened IRB must review non-exempt Human Research that does not qualify for review using the expedited procedure. In most instances, research requiring review by a convened IRB involves greater than minimal risk.

4.2 Criteria for Approval

The Belmont Report is a document that describes the basic ethical principles that should underlie the conduct of biomedical and behavioral research involving human subjects. The Federal regulations incorporate the ethical principles found in the Belmont. Included in the regulations are the criteria below that must be met before an IRB can approve a regulated research study that includes human subjects:

(a) ...IRB shall determine that all of the following criteria are met:
1. Risks to subjects are minimized by using:
   i) procedures consistent with sound scientific design and which do not unnecessarily expose subjects to risk
   ii) whenever appropriate by using procedures already being performed on subjects for diagnostic or treatment purposes
2. Risks to subjects are reasonable in relation to the anticipated benefits ...
3. Selections of subjects is equitable
4. Unless the IRB waives the requirement informed consent will be sought from each prospective subject or the subject's legally authorized representative
5. Informed consent will be appropriately documented
6. When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects
7. When appropriate, there are adequate protections to protect privacy of subjects and to maintain the confidentiality of data.
   (b) When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of the these subjects.

See [Section 46.111 of the Common Rule](https://www.hhs.gov/ohrp/policy/index.html) and [21 CFR 56.111](https://www.ecfr.gov/cgi-bin/text-idx?c=ecfr&rgn=div9&node=se21.1.56&rgn=div9&node=se21.1.56#se21.1.56p111)

The criteria for IRB approval can be found in the “[WORKSHEET: Criteria for Approval (HRP-314)](https://www.hhs.gov/ohrp/policy/index.html)” for non-exempt Human Research.

The IRB must ensure that additional criteria are met before approving regulated research that will include children, prisoners, pregnant women and neonates.

HRP 314 references other checklists that might be relevant. These worksheets and checklists are available on the [HSRO Website](https://www.hhs.gov/ohrp/policy/index.html).

The IRB uses the checklists and worksheets for initial review, continuing review, review of modifications and review of new information.

You should refer to checklists and worksheets when you write your protocol and consent document so you can ensure your documents satisfies the criteria for IRB approval and other requirements the IRB must follow.

### 4.3 IRB Determinations

According to federal regulations, the IRB may approve research, require modifications to the research before it can be approved, table or disapprove research. The regulations require the IRB to make additional determinations in certain circumstances. The following is list of determinations the IRB may make:
• **Approval:** When all criteria and other requirements are met, the IRB makes this determination. You will receive an approval letter explaining the requirements you must follow during the conduct of the research.

• **Modifications Required to Secure Approval:** The committee makes this determination when IRB members require specific modifications to the research before granting final approval. You will receive a letter explaining the modifications that are required and should follow the directions in the letter to submit the modifications.

• **Tabled:** When the IRB cannot approve the research at a meeting because of issues with the IRB, such as loss of quorum. When taking this action, the IRB automatically schedules the research for review at the next meeting. Investigators do not need to take any action when a tabling action occurs.

• **Deferred:** When the IRB determines that the committee is unable to approve research and suggests significant modifications that might make the research approvable, the Committee will defer the review. You will receive a letter explaining the reasons for the decision and recommending revisions to the research to make it approvable. You should revise the research as recommended or respond to the IRB in person or in writing if you disagree with the IRB’s determination.

• **Disapproval:** When the IRB determines that it is unable to approve research and cannot describe modifications that might make the research approvable, the Committee will disapprove the research. 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.

• **Serious Non-Compliance:** Made when the Compliance Review Committee or the IRB determines an investigator or research team member failed to comply with regulations, university policies, or the requirements/determinations of the IRB, when, in the judgment of the institution, such failure substantially increases risks to subject welfare/safety, subject rights, or data integrity. Serious noncompliance may also involve compromising the effectiveness of UM’s human subject research protection program.

• **Continuing Non-Compliance:** Made when the Compliance Review Committee or the IRB determines there is a recurring pattern of behavior or noncompliance during the conduct of the research; that, if not remediated, may compromise subject welfare/safety, subject rights, or data integrity.

• **Unanticipated Problems Involving Risks to Subjects or Others:** Made when information reviewed is (1) unanticipated, (2) related to the research, and (3) indicates that subjects or others are at increased risk of harm.

• **Waiver of Consent:** In most instances, consent from subjects is required before involving the subjects in research procedures. However, regulations allow the IRB to waive the
requirement for consent in limited circumstances. See “CHECKLIST: Waiver of Alteration of the Consent Process (HRP-410)” to see the requirements for approval of this waiver.

- **Waiver of Documentation of Consent**: When research involves greater than minimal risk, regulations usually require a signed and dated consent document from the subject. However, regulations allow the IRB to waive the requirement for the signature when the study involves only minimal risk and additional criteria are satisfied. See “CHECKLIST: Waiver of Written Documentation of the Consent Process (HRP-411)” to see the requirements for approval of this waiver.

- **Waiver of the requirement for a HIPAA Authorization**: In most instances, investigators cannot look at a patient’s medical record for research purposes without a signed authorization from the subject. However, the IRB can waive the requirement for an authorization when specific regulatory requirements are met. See CHECKLIST Waiver of HIPAA Authorization (HRP-441) to see the requirements for approval of this waiver.

- **Non-Significant Risk Device Determination**: FDA regulations allow investigators to study “Non-Significant Risk” (NSR) devices without an investigational device exemption (IDE), and requires the IRB to make a determination as to whether the investigational device involves significant risk or NSR. See “CHECKLIST: Non Significant Risk Device (HRP-441)” to see the requirements for this determination.

- **Inclusion of Cognitively Impaired Subjects**: The International Conference on E-6(R2), is an international guidance document that describes the requirements for the conduct of clinical research of investigational drugs. This guidance includes requirements for including adults who are cognitively impaired in clinical trials. The UM IRB applies the requirements for all human subject research. See “CHECKLIST: Inclusion of Cognitively Impaired Adults (HRP-417)” to see the requirements for this determination.

- **Inclusion of Prisoners in Research**: Investigators cannot include prisoners as subjects in some federally-funded human subject research unless specific requirements are met. The UM IRB applies some of these requirements to research that is not federally funded. See “CHECKLIST: Research Involving Prisoners (HRP-415)” to see the requirements for this determination.

- **Inclusion of Pregnant Women in Research**: Investigators cannot include pregnant women or fetuses as subjects in some federally-funded human subject research unless specific requirements are met. See “CHECKLIST: Research Involving Pregnant Women (HRP-412)” to see the requirements for this determination.
• **Inclusion of Fetuses in Research** - Investigators cannot include non-viable neonates and neonates of uncertain viability as subjects in some federally-funded human subject research unless specific requirements are met. See “CHECKLIST: Research Involving Non-Viable Neonates (HRP-413)” and “CHECKLIST: Research Involving Neonates of Uncertain Viability (HRP-414)” to see the requirements for these determinations.

• **Inclusion of Children in Research** - Investigators cannot include children in FDA-regulated research and some federally-funded human subject research unless specific requirements are met. The HSRO extends the requirements to most human subject research. See “CHECKLIST: Research Involving Children (HRP-416)” to see the requirements for this determination.

### 5.4 What will happen after IRB review?

The IRB will provide a written decision indicating the IRB’s determinations. You will receive a notice by email when this letter is available in the electronic system. These letters usually include additional requirements that you must adhere to, so it is important that you carefully read the letter.

- **APPROVAL:** When the IRB approves the Human Research: The Human Research may commence once you have received all other required institutional approvals (ancillary approvals). IRB approval of research involving greater than minimal risk will expire within a year of approval. You must submit a Continuing Review Application at least 45-days before the expiration date to obtain approval to continue the study, so it is important to note the expiration date. Finalized documents (e.g. consent templates) approved during the review, will be located in the eProst documents.

- **MODIFICATIONS REQUIRED TO SECURE APPROVAL:** This determination means the IRB approved the research, but the approval will not be effective until you make specific modifications to the research. You must make the requested modifications and submit them to the IRB. If you make all requested modifications, the approval will be effective and the IRB will issue a final approval letter. Research cannot commence until you receive the final approval letter. If you do not agree to make the modifications, write a memo to the IRB explaining the reasons why you cannot make the modifications and submit the memo to the IRB through eProst.

- **DEFERRAL:** This determination means the IRB cannot approve the research at this time. The IRB will provide a statement of the reasons for deferral, suggestions to make the study approvable, and give you an opportunity to respond in writing or in person. You will need to submit a modification in response to the deferral. In most cases, if you address the IRB’s reasons for the deferral, the IRB can approve the project.

- **DISAPPROVAL:** This determination means the IRB cannot approve the research and could not provide specific suggestions for modification to make the study approvable. The IRB will provide a statement of the reasons for disapproval and give you an opportunity to respond in writing or in person.
In all cases, you have the right to address your concerns to the IRB directly at an IRB meeting.
Chapter 6
Recruiting and Screening Research Subjects

6.1 Basic Principles of Recruitment

Identification, initial contact, screening and recruitment of potential human subjects form the foundation of the informed consent process. The research team and the IRB should consider the following ethical questions when evaluating recruitment strategies:

- **Equitable selection of participants**: Does the recruitment strategy help ensure that selection of research participants is equitable and appropriate for the study?

- **Respect for privacy**: Does the recruitment strategy respect an individual's reasonable expectations for privacy? If the research team asks questions for screening, will the questions be asked in a private setting where others will not overhear the answers? If you recruit patients from a recruitment database in the clinic, have those patients given their permission beforehand for this use of their medical information?

- **Lack of undue influence and coercion**: Will you introduce the study in a balanced presentation that allow subjects ample time to consider participation without undue pressure? Consider the following:
  - **Sufficient time**: Will the potential subject have sufficient time to comprehend the study and to discuss the study with their family before they are asked to agree to participate?
  - **Who is making the request**: Subjects may believe they will face adverse consequences if they say “no” to a person in authority. Will potential subjects be put in a situation where they have to say “no” to their physician or their professor? How will you minimize undue influence and coercion in these situations?
  - **Inducements**: Are inducements such as compensation emphasized or are they of such value that potential subjects may not consider the risks associated with participation?

- **Unbiased presentation**: Is all recruitment information accurate, balanced and free of misleading emphases that make the study excessively attractive? Is the information as complete as appropriate for each stage of recruitment?

6.2 Identifying Potential Subjects
• **Medical Record Review** – Review of medical records is one method of identifying potential subjects. However, patients’ medical records are private information and you must not view a patient’s medical record unless you have the authority. The following are the different avenues you can use to identify subjects.

  o **Clinician’s own Patients:** Clinicians may review medical information of their own patients to identify and contact potential study subjects.

  o **Preparatory to Research Exception:** Investigators may use the exception to the requirement for an HIPAA Authorization for purposes preparatory to research by completing and submitting to the IRB (via email) Certification for Reviews Preparatory to Research (Form E). This certification allows you to review medical records, but you must not copy, write down or otherwise collect identifiable information from the records, or contact patients about participation. This Certification can be used to determine whether a study is feasible.

  o **Waiver of Authorization for Recruitment:** Investigators may request a Waiver of Authorization for Recruitment by documenting the request in their protocol. This waiver allows you to review information in the medical record, record the minimum necessary information necessary needed to contact a potential subject and to make that contact.

  o **Consent to Contact:** Investigators can submit a request to obtain a list of potential participants through the Consent to Contact initiative. Through this initiative you can receive a list of patients meeting specific inclusion/exclusion criteria.

  o **Referrals:** May be from non-investigator healthcare providers, snowball sampling, participants referring other participating. Investigators may provide their colleagues with a “Dear Patient” letter describing the study or researcher may provide information sheets about the study to colleagues or associates. Please note that referral fees are prohibited.

  o **IRB-approved Screening/Recruitment Database:** You could submit a protocol to the IRB to obtain approval to maintain a database of potential research participants who have agreed to be contacted for studies and have signed a consent document and HIPAA authorization for this purpose, when applicable. Investigators contact these potential subjects about particular studies in accord with their protocol and the (typically signed) consent of the prospective subject. In many cases, prospective participants may have given permission to be contacted for future studies by means of check-off box in a consent form for a previous study.
6.3 Recruitment Plan and Materials

The IRB must approve the recruitment method and all recruitment materials before the materials are used. You should describe your recruitment process in your protocol and submit recruitment materials with your application. The IRB application should describe how you will use the materials (e.g. newspaper, Internet, radio). You must submit any additions or changes to these documents to the IRB and obtain approval before implementing the changes.

Recruitment materials may include:
- Letters, emails or information sheets that you will send or give to potential subjects.
- Advertisements
- Scripts or guides that will be used for in-person or telephone recruitment interviews
- Printouts of web postings or pages used for direct recruitment.

Recruitment materials (advertisements) should usually include the following information:
- An accurate description of the research purpose
- Name and address of the investigator or facility (including university affiliation and/or department)
- Condition under study
- Eligibility criteria
- Time commitments required
- Location of the research
- Person to contact for further information

Recruitment materials should NOT usually include coercive language:
- Claims that a device or drug is safe and effective
- The words “new treatment,” “new medication,” or “new drug” if the test article is investigational
- Promises of “free medical treatment”
- Amount of payment, dollar signs, or the words “free” in large or bold face type
- Statements or implications indicating a favorable outcome or other benefits beyond what is outlined in the consent document and protocol
- Claims, either explicitly or implicitly, that the test article is known to be equivalent or superior to any other drug, biologic, or device
- Exculpatory language that appears to waive any rights of the prospective participants or indicate that the investigator, sponsor or University cannot be held liable or at fault for any research-related event.

6.4 Screening Subjects

Screening includes collecting data directly from prospective subjects through written screening tools or questionnaires, or accessing private information such as medical test results for purposes of determining eligibility. Screening activities are reviewed as part of the overall
recruitment and consent process, The IRB evaluates the process with respect to the protection of privacy and confidentiality of those who are screened.

The protocol should include the following information with respect to screening procedures:

- The screening materials that may be used
- Data, if any, that will be collected during screening
- Whether the investigator intends to retain data from subjects who are ineligible upon screening; and if so, why and how the data collected during the screening procedures will be stored.

Points to consider:

- To protect the individual’s privacy, ask the eligibility questions before asking for the subject identifiers such as name and contact information. If the potential subject is not eligible, do not collect the identifying information.
- Screening questions should be limited to the information needed to determine whether the potential subject should come to the research site for the consent process and screening/study procedures.
- HIPAA regulations apply to the screening process if it involves review of medical records. Investigators must obtain prospective HIPAA authorization or apply for a waiver of HIPAA authorization and informed consent.
- Some sites use an Eligibility Log. If the log includes identifiable information about potential subjects who have not signed a consent form or authorization, the monitor cannot see that information. For best practice, the Eligibility Log should include only coded information and a link to the individual’s identity can be kept in a separate file if it is needed.
Informed Consent is a voluntary agreement from a research subject to participate in research. It is not merely a form. Instead, it is a process through which the subject gains an understanding of the research, its risks and potential benefits. Unless the IRB waives the requirement for informed consent, obtaining such consent is essential. Moreover, consent is an ongoing process as the subject progresses through the research.

Subjects’ participation must be free from undue pressure or coercion. This principle is especially true for vulnerable populations such as children, prisoners and adults with limited capacity to consent. These subjects might not be able to consent on their own behalf, but they should be allowed an opportunity to agree or disagree to participation when they have some capacity to understand the risks and procedures associated with participation.

Federal regulations and ICH E-6(R2) set out the information that must be included in an informed consent document. Investigators and IRB members refer to the requirements as the “elements of consent.” The regulations includes a list of elements that are required during every consent process as well as a list of elements that are required under certain circumstances. The University of Miami requires additional elements to be included in consent documents. “WORKSHEET: INFORMED CONSENT (HRP 314b)” includes all of the elements and is a helpful tool for use when drafting a consent document. In addition, when drafting a new consent document, investigators should use an HSRO Consent Template, which include language to satisfy all of the required elements.

Signature blocks on the consent document are very important. Prior to submitting the consent template for approval, investigators are encouraged to assess whether the blocks intended for subject signatures are consistent with the research being done. For example, if the study will not include subjects who lack capacity to consent for themselves, the signature block should not include a line for a legally authorized representative to sign on the subject’s behalf.

### 7.1 Categories of Consent/Assent Processes and Documents

**Consent** – An adult subject, capable of giving permission to participate in a research study, can provide consent. The subject must be 18 years of age and competent to make the decision to participate.

**Parental Permission** – When children/minors are included in research, the parent/guardian must sign a parental permission consent document. Some situations require permission from at least one parent, while other situations require permission from both parents. Florida law requires parental permission before a minor can be included in human subject research.
Assent – When an individual is unable to consent for his or her self, the investigator must obtain that individual’s agreement to participate in a study whenever possible. This agreement is referred to as assent.

Verbal Consent – During a verbal consent process, the prospective subject is provided with all of the required elements of consent verbally or by providing to them an Information Sheet. If the subject agrees to participate, the individual obtaining consent should document the consent process in the research record. This process can be used only when the IRB has approved a Waiver of Documentation of Consent.

Short Form – A “short form” is generally used when there is a language barrier and an English IRB-approved consent is orally translated in the subject’s native language. See Section 8.4.8 Obtaining Consent with the Short Form below.

Information/Fact Sheet – An information sheet may be used as a form of consent in certain circumstances where a signature could compromise the participant or in studies where signed consent is not required by regulations (See Waiver of Documentation of Consent below).

Waiver of Documentation of Informed Consent – A waiver of documentation of informed consent can be obtained when (1) the written consent is the only link to the study and record of subjects name could compromise the participant; or (2) the study involves only minimal risk and the research does not include any procedures for which written consent is required. When the IRB approves a waiver of documentation of consent, the required elements of consent must be provided to the subject. If the subject agrees to participate, s/he can consent verbally. The individual obtaining consent should document the process in the research record.

Waiver of Informed Consent or Alternation of the Requirements for Informed Consent – An IRB may approve a waiver of informed consent or a waiver of one of the required elements of informed consent, when specific regulatory requirements are met. When the IRB approves a waiver of informed consent, the investigator may involve human subjects in the research without obtaining consent from the subject. When the IRB approves a waiver of one or more of the elements of consent, the information provided to the subject does not have to include the element(s) waived by the IRB.

7.2 Consent Templates

The FDA and the federal funding agencies have specific requirements for the information that must be provided to subjects during the consent process.

Consent templates that comply with the requirements are available on the HSRO Website. For some funded studies, sponsors may provide a sample or draft consent documents; however, the UM IRB that reviews the study is the final authority on the content of the consent documents for use in obtaining consent from prospective study participants.

For studies that are subject to the requirements of the FDA regulations, Investigational New Drug Applications (IND) submitted to FDA are not required to contain a copy of the consent document. If the sponsor submits a copy, or if FDA requests a copy, the Agency will review the document and may comment on the document's adequacy.
For significant risk medical devices, the FDA considers the consent document to be a part of the investigational plan in the Application for an Investigational Device Exemption (IDE). FDA always reviews these consent documents. The Agency's review is generally limited to ensuring the presence of the required elements of informed consent and the absence of exculpatory language. Sponsors must subject any substantive changes to the document to FDA for review and approval.

The FDA is usually unaware of studies involving non-significant risk (NSR) device studies and does not review or approve consent documents for these studies.

7.3 Elements of Consent

Consent must be obtained in a manner that provides the subject with sufficient opportunity to discuss and consider whether or not to participate, while minimizing coercion and undue influence. Subjects must be able to understand the language used in a consent document. Consent must be provided in sufficient detail and the language/format must be organized and presented in a way that does not merely provide a list of isolated facts. Instead, the language must facilitate the prospective subject’s understanding of why one might or might not want to participate.

7.3.1 Required elements for all studies:
Subjects who agree to participate in non-exempt research must receive the following information as part of the consent process.

- A statement that:
  - the study involves research and explains the purposes of the research
  - explains the expected duration of the subject’s participation
  - explains the procedures to be followed
  - identifies any procedures that are experimental

- A description of reasonably foreseeable risks or discomforts to the subject.
- A description of any benefits to the subject or others, which may reasonably be expected from the research.
- A description of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.
- A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained.
- A statement that:
  - participation is voluntary
  - refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled
  - the subject may discontinue participation at any time without loss of benefits to which the subject is otherwise entitled.
7.3.2 Additional elements that must be included, when applicable

- A statement that:
  - the particular treatment or procedure may involve risks to the subject, which are currently unforeseeable
  - if the subject is or becomes pregnant, the particular treatment or procedure may involve risks to the embryo or fetus, which are currently unforeseeable
- Anticipated circumstances under which the subject’s participation may be terminated by the investigator without regard to the subject’s consent.
- Any additional costs to the subject that may result from participation in the research.
- The consequences of a subject’s decision to withdraw from the research and procedures for orderly termination of participation by the subject.
- A statement that significant new findings developed during the course of the research, which may relate to the subjects willingness to continue participation will be provided to the subject.
- The approximate number of subjects involved in the study.

7.3.3 Required elements for studies involving greater than minimal risk

- Whether any compensation is available if injury occurs and, if so, what it consists of, or where further information may be obtained
- Whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained.

NOTE: The UM consent templates include template language for the section above. Revisions to the template language require approval from the UM General Counsel.

7.3.4 Required elements for FDA-regulated studies (Including ICH E-6(R2))

- The possibility that the Food and Drug Administration may inspect the records.
- A description of the probability of random assignment to each treatment, when applicable.¹
- A statement that the data collected on the subject to the point of withdrawal will remain part of the study database and may not be removed.
- A description of the subjects’ responsibilities²
- A statement that the investigator will ask a subject who is withdrawing whether the subject wishes to provide consent for further data collection from routine medical care.
- A statement indicating the IRB approved the research.
- A statement that monitors, auditors, the IRB and regulatory authorities will be granted direct access to the subject’s original medical records for verification of clinical trial

¹ ICH E-6(R2)
² Ibid.
procedures and data, without violating the confidentiality of the subject, to the extent permitted by applicable laws and regulations and that, by signing the consent and authorization documents, the subject or LAR is authorizing the such access.

- For controlled drug/biologic/device trials (except Phase I drug trials) and pediatric device surveillance trials: “A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.”

7.3.5 Required elements for federally funded studies

- The informed consent must begin with a concise/focused presentation of the key information that is likely to assist a subject in understanding the reasons why one might or might not want to participate.
- A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions.
- When the research involves biospecimens, the following statements must be included:
  - A statement that the subject’s biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit.
  - A statement as to whether the research will or might include whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen).
- If private identifiable information or identifiable biospecimens are being collected, one of the following statements must be included:
  - A statement that identifiable private information and/or identifiable biospecimens might be used for future research studies or distributed to another investigator for future research after removing the identifiers, without additional informed consent from the subject; or
  - A statement that the subject’s information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies.

7.3.6 Required elements for research subject to the European Data Privacy Rule (GDPR)

- A statement indicating that personal data will be collected, used or created to conduct the research.
- If sensitive data are being collected, explicit consent is requested.
- The duration for which personal data will be retained.
- Information on how personal data will be protected.
- The following notices of subjects’ rights:
Right to access, correct or withdraw personal data
Right to restrict the types of activities the research team can do with the data
Right to object to using data for specific types of activities
Right to withdraw consent to use data for purposes outlined in the consent document

- When applicable, a statement indicating personal data will be transferred to the US and the US does not protect personal data in the same way it is protected in the European Union or European Economic Area.
- When applicable, a statement that treatment decisions that could significantly affect a person will be based solely on personal data and the decision is automated (e.g. computer randomization).
- The Privacy Officer’s Contact Information for questions, complaints or if the subject wants to make a request relating to the rights.

7.4 Making a consent document readable

The UM Institutional Review Boards (IRB) asks that research teams make every effort to ensure that informed consent documents be written at an approximate 8th grade level when tested against the Flesch-Kincaid (FK) grade level readability test. The IRB recommends the use of this tool as it is available as a feature within Microsoft Word’s Spelling and Grammar check. The IRB recognizes that some consent forms are of such a technical nature that it may not be possible to keep to an approximate 8th grade reading level. Investigators may discuss problems with keeping consent text at a low reading level with the staff at the HSRO.

Testing readability:
1. Click the File tab, and then click Options.
2. Click Proofing.
3. Under When correcting spelling and grammar in Word, make sure the Check grammar with spelling box is selected.
4. Select Show readability statistics.
5. Click OK.

After you enable this feature, open a file that you want to check, and check the spelling. When Word finishes checking the spelling and grammar, it displays information about the reading level of the document.

The FK is only one of many available readability formulas. Other formulas are located HERE.
7.5 Translation Requirements for Consent Documents

<table>
<thead>
<tr>
<th>Subjects Abilities and Limitations</th>
<th>Consent Process</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subject cannot Read English but can read another language</td>
<td>Consent document and other subject facing documents must be in the language the subject can read</td>
</tr>
<tr>
<td>Subject cannot read English but fully comprehends spoken English</td>
<td>Read the consent form to the subject in English in the presence of a witness. Obtain the witness’s signature on the consent document. Note the subject's ability to understand English in the research record.</td>
</tr>
<tr>
<td>The subject does not understands or read English. The subject speaks and understand a different language but cannot read documents written in that language.</td>
<td>Read the IRB-approved translated consent form to the subject in the presence of a witness. Obtain the witness’s signature on the consent document. Note the subject's ability to (1) understand the different language and (2) the translated consent document was provided to the subject.</td>
</tr>
</tbody>
</table>

Exceptions to the above requirements:

- A subject requires rapid entry into a study for his/her well-being but the study does not have a consent form translated in the subjects’ language.
- The investigator is uncertain whether non-English speaking subjects might enroll in the study, or believe that the majority of subjects will speak/comprehend English. This instance is rare at the University of Miami.

In these instances, use the “short form process” described in Section 8.7 below. However, if the study involves more than minimal risk, you should carefully consider whether you are able to obtain informed consent in this manner and you should restrict the use of the short form process to situations where there is a prospect of direct benefit to the subject that is not otherwise available.

Obtaining translations

- Do not send documents for translation until the IRB has approved the document.
- IND/IDE Studies: Certified Translators must translate the document. Submit an “Affidavit of Accuracy” from the translator when submitting the translated document for approval.
• Non-IND/IDE Studies: An individual fluent in the translated language must translate the English document into the second language and a second individual who is fluent in both languages must provide a “back translation.” Submit both “forward” and “back” translations to the IRB for approval with (1) an attestation that the translation was performed independent of the other translation, is accurate, (2) an attestation that the “back” translation was performed without referring to the English version of the document. Both attestations should include the date the translation was completed.

7.6 Documenting Consent Using a Full Consent Document

When obtaining consent from a prospective subject, you must:
• Discuss each element of consent with the prospective subject or LAR.
• Allow an opportunity for the subject or LAR to ask questions and provide answers to each question.
• Assess whether the subject/LAR comprehends important aspects of the research by asking questions such as:
  o Why are we asking you to be in this research?
  o Why are we conducting this study?
  o What happens if you don’t want to be in this research?
  o What happens if you decide to leave this research without completing all of the visits?
  o If you participate in this study, what risks will you face?
  o What should you do if you believe you are injured as a result of your participation in this study?
• If the subject/LAR agrees to participation, the subject/LAR must sign and personally date the consent document.
• After the subject/LAR completes the signature process, the individual obtaining consent must sign and personally date the consent document.
• The subject must receive a copy of the signed and dated consent document.
• The individual obtaining consent should then document the consent process in the research record. The HSRO recommends that investigators include the following information in their documentation:
  o Whether the most current version of the consent form was used to obtain consent;
  o Whether the individual obtaining consent reviewed the consent form with the subject/LAR;
  o If an LAR provided consent on behalf of the subject, whether the IRB approved the enrollment of subjects who cannot personally consent;
Whether the subject’s/LAR’s comprehension was assessed to ensure that the subject/LAR understands the research and the risks and benefits involved in the study;

Whether the subject had any questions; and if so, a statement that all of the subject’s questions were answered;

Whether the subject was given time to review the consent form and to discuss participation in this study with family members/others;

Whether the subject agreed to participate in the study and signed/dated the most current valid IRB approved consent form *prior to participating in any procedures performed solely for the research*;

Whether the subject/LAR was given a copy of the signed and dated consent document;

Whether the research involves the use, disclosure or creating of identifiable health information;

Whether the subject/LAR signed and dated the UM HIPAA Authorization Form (From B):

Whether the subject/LAR received a copy of Form B.

The HSRO recommends investigators to develop and use a consent checklist or template language to document informed consent to ensure that the above information is documented.

### 7.7 Documenting Consent with the Short Form

A “short form” is generally used when there is a language barrier and an English IRB-approved consent is orally translated in the subject’s native language. If there is occasional need to enroll subjects who are not fluent in English or Spanish, investigators must use a written short form in conjunction with the written IRB-approved English version of the Informed Consent Form. Investigators can find translated versions of Short Form on the [IRB website](#).

The following is an outline of the process for enrolling subjects with the short form:

- A translator must orally translate the entire IRB-approved English version of the consent form to the subject in a language the subject understands.

- Whenever, possible, the Short Form must be translated into a language the subject understands. If the Short Form is not translated into a language the subject understands, the translator must orally translate the entire English version of the Short Form in a language the subject understands.

- A witness who is fluent in English and the language the subject understands must observe the entire consent process. The translator may serve as the witness.
The individual delegated to obtain consent and the witness must sign the IRB-approved English version of the consent form.

The subject and the witness to the consent process must sign the Short Form.

The individual obtaining consent must give copies of both the signed and dated consent form and Short Form to the subject or the subject’s LAR.

The research team must place the original signed consent form and Short Form should be placed in the subject’s research record.

The individual obtaining consent should document in the research record that consent was obtained as described in Section 7.5 above.

### 7.8 Obtaining Parental Permission

In Florida, minors (those under 18 years of age) generally may not consent to medical care or treatment, or research involving medical care or treatment, without a parent or legal guardian’s consent. However, the Florida statutes regarding the removal of “Disability of Nonage of Minors” (Title XLIII, Chapter 743) describe conditions when the requirement(s) for parental consent are waived by law.

IRBs are required to make adequate provisions for soliciting the permission of each child's parent(s), LAR or guardian, based on the level of risk and expected direct potential benefit to the child, as noted below. The IRB may not require less than outlined below, but may determine that more stringent requirements are appropriate.

<table>
<thead>
<tr>
<th>Regulatory Category of Permitted Research with Children</th>
<th>Requirements for Parental Permission</th>
</tr>
</thead>
<tbody>
<tr>
<td>Greater than Minimal Risk, Direct Benefit to Subject [45 CFR 46.405, 21 CFR 50.52]</td>
<td>One parent/legal guardian may be sufficient but IRB must determine whether one or two is required</td>
</tr>
<tr>
<td>Greater than Minimal Risk, No Direct Benefit to Subject, but Likely to Yield Generalizable Knowledge about Subject’s Condition [45 CFR 46.406, 21 CFR 50.53]</td>
<td>Both parents/legal guardians, unless one parent is deceased, unknown, incompetent, not reasonably available, or does not have legal responsibility for the custody of the child.</td>
</tr>
<tr>
<td>Greater than Minimal Risk, No Direct Benefit to Subject, but Results May Alleviate Serious Problems of Children’s Health or Welfare [45 CFR 46.407, 21 CFR 50.54]</td>
<td>Both parents/legal guardians, unless one parent is deceased, unknown, incompetent, not reasonably available, or does not have legal responsibility for the custody of the child.</td>
</tr>
</tbody>
</table>
IMPORTANT NOTE: When there is only one living parent or guardian or one parent has sole custody after a divorce, the investigator and/or IRB may determine that single-parent or single guardian permission is sufficient.

If there are two parents available to give permission but they disagree about allowing their child to participate in the study, the child may not be enrolled unless that disagreement can be resolved. This rule applies to all permissible categories—even if only one parent’s signature is required, when both parents are involved in the decision, they must agree for the child to be enrolled. If a parent who was not involved or available for the original consent later becomes involved or available, the two parents must then agree.

7.9 Obtaining and Documenting Assent

Obtaining Assent from Children

The Federal regulations require that “adequate provisions [be] made for soliciting the assent of the children, when in the judgment of the IRB the children are capable of providing assent... [taking] into account the ages, maturity, and psychological state of the children involved” [45 CFR 46.408; 21 CFR 50.55(a)].

In most instances a child’s refusal to participate in a research study should be honored. Parents may overrule a child’s dissent only when the IRB waives the requirement for assent and the IRB may waive the requirement for assent in the following circumstances:

- The capability of some or all of the children is so limited that they cannot reasonably be consulted; or
- The intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research.

When research involves the provision of experimental therapies for life-threatening diseases such as cancer; however, researchers should be sensitive to the fact that parents may wish to go to extremes, even when the likelihood of success is marginal and the probability of extreme discomfort is high. Should the child not wish to undertake such experimental therapy, and if, for example, the child is a mature adolescent and death is imminent, the child's wishes should be respected.

There is no regulatory requirement for a child to sign an assent document. Instead, the investigator must comply with the IRB’s requirements for documenting that assent was obtained. In some situations, the IRB may require the investigator to provide written information for the child to read. In other instances, the IRB will rely on the individual obtaining consent to explain the study to the child, assess the child’s comprehension of the study and obtain agreement from the child when the child can relate sufficient information about the study to demonstrate adequate
comprehension. The IRB may require the child to indicate his/her assent by signing a document such as an Assent Form or by signing a signature block on the Informed Consent form. As an alternative, the IRB may require the individual obtaining assent to document in the research record or on the informed consent document that assent was obtained.

**Important Note:** When a subject enrolls in a study as a child and reaches age 18 while continuing to participate in the study, the investigator must obtain informed consent from the new adult before having the subject participate in any procedures performed solely for research purposes.

**Assent from Adult Subjects**
Assent from adult subjects who lack capacity to personally consent is not discussed in the federal regulations; however, ICH E6(R2) Section 4.8.12 requires investigators to obtain assent from these subjects after informing them about the trial to the extent compatible with their understanding. When the adult subject is capable, the investigator should have the subject sign and personally date an assent block located in the informed consent document.
Chapter 9
Required IRB Reports

The IRB requires investigators to submit reports of events as part of the IRB’s responsibilities for oversight of the study. In addition, the IRB must report to applicable regulatory authorities the following determinations:

- Serious or Continuing Non-compliance
- Suspensions Approval
- Terminations of Approval
- Unanticipated Problems Affecting Subjects or Others

9.1 Reports of New or Increased Risk (Submit within 5 business days)

Investigators are required to submit reports of new or increased risk of a study to the IRB within five (5) business days. The following are various methods sites receive information about new or increased risk. If you are reporting one of these events, select “Risk” on the RNI Form.

Examples of New or Increased Risk

| Updated Investigator Brochure that includes revisions to risk profile or expected adverse reactions | Sponsor report or letter that identifies a new expected adverse event |
| Updated package insert or device label that includes revisions to risk profile or expected adverse reactions | Investigator finding that indicates revisions to the risk profile or expected adverse reactions |
| Safety monitoring report that identifies a new expected adverse event | Publication that identifies a new expected adverse event or indicates a new treatment for the condition under investigation has been cleared for marketing |
| Withdrawal, restriction, or modification of a marketed approval of a drug, device, or biologic used in a research protocol | Protocol violation that harmed subjects or others or that indicates subjects or others might be at increased risk of harm |
| Complaint of a subject that indicates subjects or others might be at increased risk of harm or at risk of a new harm | Harm experienced by a subject/other individual, which the sponsor believes is unexpected and probably related to the research procedures.³ |

³ “Unexpected” harm - when new information indicates that a previously known harm occurs more frequently or more severely than previously expected; “Probably related:” if the sponsor believes the research procedures more likely than not caused the harm.
Protocol change implemented without prior IRB review to eliminate an immediate hazard to a subject | Unanticipated adverse device effect

9.2 Reports of External Serious Adverse Events/IND Safety Letters

Do not submit reports of external adverse events that have not been analyzed by the sponsor, and the sponsor does not state:

1. The event is unexpected;
2. The event is related to the study; and
3. The existence of the event means there is a new risk to subjects or others that was previously not known.

Refer to FDA guidance for more information on this requirement.

9.3 Reports of Non-Compliance (Submit within 10 business days of knowledge)

Examples of Non-Compliance (Submit within 10 business days of knowledge)

<table>
<thead>
<tr>
<th>Non-compliance or an allegation of non-compliance with the protocol, regulations, or with the requirements or determinations of the IRB when the non-compliance was the result of action or inaction on behalf of the investigator or the study team (including departments that provide support for the research such as the Investigational Drug Services)</th>
<th>Written reports of study monitors that describe protocol deviations or other non-compliance that is the result of action or inaction of the investigator or study team (including departments that provide support for the research such as the Investigational Drug Services)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Internal or external audit, or inspection, by a federal agency and any resulting reports of non-compliance</td>
<td>Breach of confidentiality</td>
</tr>
</tbody>
</table>

4 Any serious adverse effect on health/safety; any life-threatening problem, death caused by, or associated with, a device, if the effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the protocol, or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects).
### 9.4 Other Required Reports (Submit within 10 business days of knowledge)

<table>
<thead>
<tr>
<th>Subject complaint that the study team cannot resolve</th>
<th>Premature suspension or termination of the protocol by the sponsor, investigator or institution</th>
</tr>
</thead>
</table>
Chapter 10
Investigator Responsibilities

10.1 General Responsibilities

Principal Investigators are required to personally conduct or supervise the Human Subject Research. Principal Investigators must understand that the PI is responsible for non-compliance of any study team member. In addition, the PI is responsible for complying with the requirements outlined in this chapter.

1. Protect the rights, safety and welfare of subjects involved in the research.
2. Do not start Human Research activities until:
   a) You have received and read the final IRB approval letter;
   b) You have received all other required institutional approvals, including approvals of departments or divisions that require approval prior to commencing research that involves their resources.
3. Ensure that there are adequate resources to carry out the research safely. Resources include sufficient investigator time, appropriately qualified research team members, equipment, and space.
4. Prior to delegating research staff to conduct protocol-related procedures, ensure each staff member is qualified to conduct research procedures. “Qualified” means a research staff member has:
   a) Has the necessary licensure or other qualifications to fulfill the role;
   b) Completed the disclosure certification process using the UDisclose System at least once a year, and has updated their disclosure certifications, when necessary.
   c) Completed all required institutional training; and
   d) Received training on the specific procedures they will conduct and has demonstrated an ability to comply with the requirements.
5. Update the IRB office with any changes to the list of study personnel after ensuring the requirements in #3 above are met.
6. Comply with the most current version of the IRB-approved protocol, applicable federal regulations, local laws, institutional requirements and IRB requirements. Do not purposefully deviate from the protocol unless one of the following requirements are met:
   a) The deviation is necessary to protect a subject from imminent harm; or
   b) The sponsor and IRB (and FDA if under an IDE) approve of the deviation.
7. Do not modify any IRB-approved document or make any revisions to the Human Research without prior IRB review and approval unless the revision is necessary to eliminate apparent immediate hazards to subjects.
8. When required by the IRB, ensure that consent is obtained in accordance with the relevant current IRB-approved protocol and informed consent document.
9. Submit to the IRB:
   a) Proposed modifications as described in this manual. (See “Modifications”)


b) A continuing review application as requested in the approval letter. (See “Continuing review reports”)
c) Reports required by the IRB (See Chapter 9)
d) A continuing review application when the Human Research is closed. (See “Closing a Study?”)

10.2 Additional Responsibilities for FDA-regulated products

Clinical investigations involving investigational drugs and devices are subject to FDA jurisdiction and must be conducted in compliance with FDA regulations:

- **21 CFR §50** Protection of Human Subjects (includes the requirements for informed consent and involvement of children in a clinical trial)
- **21 CFR § 54** Financial Disclosures by Clinical Investigators
- **21 CFR § 56** Institutional Review Boards
- **21 CFR § 312** Investigational New Drug Applications (includes requirements for conducting a clinical investigation of an investigational drug or biologic)
- **21 CFR § 812** Investigational Device Exemptions (includes the requirement for conducting a clinical investigation of an investigational device.

Investigators must be familiar with and understand the information included in these regulations, when they are applicable to the research being conducted. Specifically, the investigator must understand:

- IRB Review and Oversight
  - Must be obtained before starting a clinical investigation or before implementing changes to an investigation, unless the change is needed to eliminate an imminent hazard to subjects. Note: According to the FDA, planned protocol deviations require prior-IRB approval.
- Supervision of the Clinical Trial
  - Investigators are required to personally supervise clinical investigations, including:
• Training, delegation and oversight of study team members
• Protecting the rights, welfare and safety of subjects in the investigation

Investigational Product Control and Accountability
  o Investigators must follow FDA requirements for control of the investigational drug\(^5\)
    ▪ Administer the drug only to subjects under the investigator's personal supervision or under the supervision of a sub-investigator responsible to the investigator.
    ▪ Do not provide an investigational drug or device to any person not authorized to receive it.
• Maintain records of receipt and disposition of the investigational product, including dates, quantity, and use by subjects.
• Return or dispose of unused supplies of the investigational product as directed by the sponsor.

Comply with the Protocol
  o Do not implement any revisions to the protocol without obtaining IRB and sponsor approval unless the revision is necessary to eliminate an imminent hazard to subjects.

Case Histories
  o Maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation. Case histories include:
    ▪ Case report forms and supporting data including
    ▪ Signed and dated consent forms
    ▪ Medical records
    ▪ Physician progress notes
    ▪ Checklists used to maintain compliance
    ▪ Nurses' notes.
  o The case history for each individual must document that informed consent was obtained prior to participation in the study.

Investigator Reports
  o All clinical investigations
    ▪ Financial Disclosure
      o Provide the sponsor with sufficient accurate financial information to allow complete and accurate certification or disclosure statements as required under 21 CFR § 54 Financial Disclosure by Clinical Investigators
      o 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.

\(^5\) [http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.61]
Progress reports to the sponsor for collecting and evaluating the results obtained.

Final report to the sponsor shortly after completion of the investigator's participation in the investigation.

Continuing Review, reports of unanticipated problems involving risks to subjects or others and all other reports required by the IRB.

- Investigations of drugs and biologics
  - Adverse event reports to the sponsor
    - Serious adverse events must be reported promptly

- Investigations of Devices
  - Unanticipated adverse device effects: to the sponsor and IRB no event later than 10 working days after the investigator first learns of the effect.
  - Deviation from the protocol to protect the life or physical well-being of a subject in an emergency to the sponsor and IRB for device studies
  - Withdrawal of IRB approval: To the sponsor, within 5 working days, a withdrawal of approval of a device study by the IRB.
  - 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.

- Record Keeping and Record Retention (See Section 10.5)

10.3 ICH Guideline for Good Clinical Practice E6(R2)

Most industry sponsors require investigators to comply with ICH Guideline for Good Clinical Practice E6 (R2). This guideline is guidance in the United States but is considered law in some other countries. Sponsors who want to submit marketing applications in countries that require compliance with this guideline must ensure investigators understand and comply with the guidance during the conduct of their trials.

Much of the information in this guidance is similar to the FDA regulations discussed above. However, in several areas the guidance differs or includes much more detail on the requirements. For example, the guidance includes a section entitled, Essential Documents for the Conduct of a Clinical Trial, which describes the documents that must be available for “evaluation of the conduct of the trial and the quality of the data produced.” In addition the guidance requires inclusion of additional information in the information consent document.

10.4 Issues to Consider when a Subject Withdraws From a Study

1. For research that is subject to FDA regulations, the data collected on the subject to the point of subject withdrawal remains part of the study database and may not be removed.⁶

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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 that the 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 federal regulation, including the FDA regulations, investigators, in consultation with the funding entity, 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 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 subject chooses the latter, research activities involving other components of the clinical trial, such as follow-up data collection activities (imaging, laboratory studies, etc.), 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.

5. If a subject withdraws from the interventional portion of the study, but agrees to continue in the 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 if this subject will participate in data collection that is not described in the original informed consent form). IRB approval of informed consent documents is required.

6. 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.

10.5. Maintaining Research Records

Principal investigators are reasonable for the creation and maintenance of research records and documents. Such records and documents (including data collected pursuant to research) are the property of the University. Until the temporal requirements for record/document retention are met, investigators and others may not remove or destroy research records or documents (or copies of such records or documents) without written consent. Investigators must maintain human research records for the time specified by federal regulations and the clinical trial agreement. If the requirements between the regulations and agreements differ, investigators must maintain the records for the maximum time required. The following are the regulatory requirements for maintaining specific documents:
## Minimum Retention Requirements for Human Subject Research Records

<table>
<thead>
<tr>
<th>Jurisdiction</th>
<th>Document Examples</th>
<th>Time Frame</th>
</tr>
</thead>
<tbody>
<tr>
<td>Federally funded Human Research Records</td>
<td>All research documents, including protocols, signed and dated consent documents, source documents, etc.</td>
<td>At least 3 years from study closure date</td>
</tr>
<tr>
<td>Research under FDA Jurisdiction</td>
<td>All research documents, including protocols, signed and dated consent documents, source documents, etc.</td>
<td>At least 2 years after the date a marketing application is approved for the drug under study; or, if no application will be filed or is not approved for such indication, 2 years after the study is discontinued and FDA is notified. If industry sponsored, you should comply with the Clinical Trial Agreement and contact the sponsor before destroying records.</td>
</tr>
<tr>
<td>Documents subject to the Federal Privacy Rule (HIPAA)</td>
<td>Signed authorizations for use and disclosure of protected health information.</td>
<td>Six years after completion of the research</td>
</tr>
<tr>
<td>Research covered by a clinical trial agreement or other funding agreement</td>
<td>All research documents, including protocols, signed and dated consent documents, source documents, etc.</td>
<td>As required by the agreement – As a best practice, you should contact the sponsor before destroying records</td>
</tr>
</tbody>
</table>
Chapter 11
Privacy and Confidentiality

Before approving research involving human subjects, the IRB must determine that the subjects’ privacy and confidentiality are protected.

Privacy is the control over the extent, timing, and circumstances of sharing oneself (physically, behaviorally, or intellectually) with others. For example, persons may not want to be seen entering a place that might stigmatize them, such as a substance abuse treatment center or a pregnancy counseling center that is clearly identified by signs on the front of the building. The evaluation of privacy also involves consideration of how the researcher accesses information from or about potential participants (e.g., recruitment process). IRB members consider strategies to protect privacy interests relating to contact with potential participants, and access to private information.

Confidentiality pertains to the treatment of information that an individual has disclosed in a relationship of trust with the expectation that it will not be shared with others without permission. For example, the when recording research data, the HSRO usually requires investigators to remove the identifiers from subject information, apply a code as needed and maintain the link between the subject’s identity and the code in a separate location.

11.1 HIPAA Privacy and Security Rules

The HIPAA Privacy and Security Rules affects research that uses, creates, or discloses Protected Health Information (PHI). Investigators must meet specific requirements before accessing PHI. Similarly, investigators must protect PHI that they access, use or create from inadvertent or malevolent access.

Investigators are responsible for identifying in the IRB application all proposed access to PHI which will occur during the course of the research, including:

- Access to paper and electronic medical records for the purpose of subject identification or screening;
- Any intended addition of information into medical records; and
- Any collection or use of human specimens with individually identifiable health information attached.

Investigators must use one of the following provisions to access, use or create PHI while conducting research at the UM:

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7 Any identifiable health information that is used, maintained, stored, or transmitted by a HIPAA-covered entity
Authorization - Each participating subject (or the subject’s legally authorized representative) signs and dates a completed written authorization (FORM B), permitting the use and disclosure of the participant’s information for the research purposes;

Limited Data Set with Data Use Agreement - The information is furnished to the investigator in a limited data set that does not contain direct identifiers and the recipient signs a Data Use Agreement;

Certification for Reviews Preparatory to Research (FORM E) – Permits access to PHI for subject identification, assessing feasibility and other activities in preparation for research after submitting the Certification to the IRB and receiving an acknowledgement;

Investigator Certification for Research with Decedents’ Information (Form D) – Access to PHI relating to deceased individuals is permitted when an investigator submits a completed and signed FORM D to the IRB and receives an acknowledgement from the IRB:

Waiver of Authorization – Approved by the IRB or Privacy Board when regulatory requirements are satisfied.

Patients have a right to receive an accounting of disclosures of PHI except for disclosures for treatment, payment, healthcare operations, pursuant to an authorization and disclosures in a limited data set. Investigators must follow UHealth polices when accessing PHI through a waiver of authorization or through one of the other exceptions listed above.

De-identified health information is not subject to HIPPA. Information is considered de-identified under HIPAA when it does not include any of the identifiers listed below.

<table>
<thead>
<tr>
<th>Geographic subdivisions smaller than a state (address, city zip code)</th>
<th>Certificate/license numbers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dates relating to the subject except for year for individuals &lt; age 90</td>
<td>Device identifiers and serial numbers</td>
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<tr>
<td>Telephone numbers</td>
<td>Web Universal Resource Locators (URLs)</td>
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<td>Fax numbers</td>
<td>Internet Protocol (IP) address numbers</td>
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<tr>
<td>Email addresses</td>
<td>Biometric identifiers, including finger and voice prints</td>
</tr>
<tr>
<td>Social Security Numbers</td>
<td>Full face photographic images and any comparable images;</td>
</tr>
<tr>
<td>Medical record numbers</td>
<td>Any other unique identifying number, characteristic, or code except a code assigned to allow for information de-identified to be re-identified by the covered entity.</td>
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<tr>
<td>Health plan beneficiary numbers</td>
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<tr>
<td>Account numbers</td>
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<tr>
<td>Vehicle identifiers, serial numbers, including license plate numbers</td>
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“SOP: Privacy & Security Procedures For Human Subject Research (HRP-098)” describes the procedures investigators, IRB Members and HSRO staff must follow when research involves the use or creation of PHI.

11.2 Federal Education Records Act (FERPA)

The purpose of the Family Educational Rights and Privacy Act (FERPA) (20 U.S.C. § 1232g; 34 CFR Part 99) is to protect all student and parent information maintained in an Education Record.

The law applies to all schools that receive funds from the U.S. Department of Education (ED). FERPA regulates the disclosure of Personally Identifiable Information from youth. The purpose of FERPA is to protect all student and parent information maintained in an Education Record.

Education Records are records that contain information directly related to a student and maintained by an educational agency or institution or by a party acting for the agency or institution. Protected records include Education Records held by public elementary and secondary schools, school districts, intermediate education agencies, state education agencies, and any public or private agency or institution that uses funds from ED.

Investigators are responsible for adhering to the requirements of FERPA when accessing Education Records. FERPA stipulates that an educational institution has the authority to determine what information may be accessed from an Education Record. If an institution denies an investigator access to information in an Education Record, the IRB cannot overrule the decision.

FERPA regulations specify that a parent or adult student must provide a signed and dated written consent before the institution can disclose Personally Identifiable Information from Education Records, unless the disclosure falls within one of few exceptions allowed under FERPA. Before accessing education records, investigators must discuss the access with the UM Registrar, even when the records already in the investigator’s possession.

The HSRO will comply with FERPA requirements when reviewing research protocols that involve access to student Education Records. In most instances, the IRB will not be able to waive consent for access to student records for research purposes.

11.3 Certificates of Confidentiality

A Certificate of Confidentiality (CoC) adds a layer of privacy protection for participants enrolled in research involving sensitive information. A CoC primarily protects against compulsory legal demands, such as court orders and subpoenas, for identifying information or identifying characteristics of a research participant. All studies funded by the NIH have a CoC. In addition, some non-NIH-funded studies may obtain a CoC when the research gathers information about subjects that might be damaging, and which will only exist in the research study records (that is, the information is not already in other records that are subject to subpoena). To obtain a CoC for
non-NIH funded research, go to the NIH’s CoC Kiosk and complete the steps to submit your application electronically. After the CoC is received, the NIH will provide you with a form that must be signed by the PI and the University of Miami Institutional Official.

If your study is covered by a CoC, you must understand and comply with your responsibilities associated with the CoC. One responsibility is to include language in the consent form about the CoC. The required language is included in the HRP 502 — TEMPLATE CONSENT DOCUMENT.

Additional guidance on CoCs is found on the NIH Website.

### 11.4 General Data Privacy Rule (GDPR)

The GDPR applies to human research involving personal data about individuals located in (but not necessarily citizens or residents of) the European Union member states and the European Economic Area. The GDPR also regulates personal data processed by entities located in the European Union and European Economic Area. The following states adopted the GDPR:

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<th>Austria</th>
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<td>Republic of Cyprus</td>
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<tr>
<td>Spain</td>
<td>Sweden</td>
<td>United Kingdom</td>
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When research data about human subjects is transferred to one of the states listed above, the recipient must comply with the GDPR.

The GDPR is much broader than the HIPAA Privacy and Security Rules and applies to most information that directly or indirectly could identify an individual. This includes names, addresses, phone numbers, dates of birth, as well as IP addresses, cookie identifiers, device information, advertising identifiers, financial information, geo-location information, social media information, consumer preferences, etc.

In most instances, the GDPR requires consent and/or notice to individuals before investigators can process personal data subject to the GDPR.

If you plan to collect, obtain or create personal data about individuals who are located in one of the countries listed above, you must contact the University of Miami Data Privacy Office. Click HERE for more information about the GDPR.
Chapter 12

Emergency/Treatment Use of an Unapproved Drug, Biologic or Device

12.1 Emergency Use of an Unapproved Drug, Biologic or Device

The regulations allow clinicians to use an unapproved drug, biologic or device without prior IRB approval in limited circumstances; however, the clinician must comply with FDA requirements in these situations.

When seeking to use an unapproved product, it is critical that the patient and his/her licensed physician consider all possible risks because the FDA has not determined whether the products are safe. Such products may, or may not, be effective in the treatment of the condition.

When you decide that the investigational product is the best option for the patient, contact the FDA to obtain approval.

   a) For an investigational drug or biologic call (888) 463-6332 or email druginfot@fda.hhs.gov
   b) For an investigational device call (301) 796-7100 or email dice@fda.hhs.gov.

You can also submit an Emergency Use Request Form to the IRB via email at cmg345@med.miami.edu.

The next step is to contact the sponsor and obtain agreement for the use of the investigational product.

As time permits, complete WORKSHEET: Emergency Use (HRP-322) and contact the HSRO or an IRB chair immediately to discuss the situation. WORKSHEET Emergency Use (HRP-322) outlines the criteria for use of an unapproved drug, biologic or device without IRB approval. An Emergency Use Request Form can be used to notify the IRB. Please email the report to the IRB. IRB Office number is 305-243-3195.

If time permits, you must obtain informed consent from the patient using TEMPLATE CONSENT DOCUMENT – Emergency Use (HRP 506). If the patient is not able to provide informed consent due to incapacity and there is insufficient time to obtain consent from a legally authorized representative, see the instructions below.

You must report the use of the unapproved drug, biologic or device to the IRB through an eProst submission within five business days using the electronic Report of New Information SmartForm. Regulations require that you submit this report even when you discussed the use of the investigational product with the sponsor and IRB Chair. If you fail to submit the report within five days, you will be restricted from submitting new Human Research until the IRB receives this report. Use the form, Emergency Use Report, to report the use. Please email the report to the IRB.
Finally, according to the FDA, the emergency use provision can be used only once. If there is any possibility that you will need to use the same investigational product with the same patient or with a different patient, you must submit a protocol to the IRB and obtain an IND or IDE from the FDA. The FDA regulations have provisions for expanded access use through a treatment protocol.

See SOP Emergency Use and Expanded Access (HRP-023) and FDA Guidance on Expanded Access for additional information.

### 12.2 Exception to Informed Consent Requirement for Emergency Use

The FDA regulations allow the use of an investigational product without informed consent when the investigator, and a physician who is not involved in the study, certify the following in writing:

1. The human subject is confronted by a life-threatening situation necessitating the use of the test article;
2. Informed consent cannot be obtained from the subject because of an inability to communicate with, or obtain legally effective consent from the subject;
3. Time is not sufficient to obtain consent from the subject's legal representative; and
4. There is available no alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the subject.

If the investigator is not able to obtain the second opinion due to time constraints and the above requirements are met, the investigator must:

1. Make and document the required determinations above;
2. Have a physician who is not part of the research review and evaluates the documentation;
3. Have the physician sign the document indicating his/her concurrence;
4. Submit the document to the IRB by completing and emailing the form, Emergency Use Report;
5. If the investigational product is a device, the investigator must submit a report of the use of the product without informed consent to the sponsor.

This process is described in “SOP: EMERGENCY AND TREATMENT USE OF INVESTIGATIONAL DRUGS, BIOLOGICS AND DEVICES (HRP-23).”

### 12.3 Treatment (Compassionate) Use

Under FDA regulations (21 CFR § 312.300), expanded access (often referred to as “treatment use” or “compassionate use”) is a potential pathway for a patient with an immediately life-threatening condition or serious disease or condition to gain access to an investigational medical
product (drug, biologic, or medical device). This access is for treatment outside of clinical a trial when no comparable or satisfactory alternative therapy options are available. While expanded access is not a clinical investigation, FDA submission and IRB review are required.

The IRB will require an eProst submission for initial review that includes:

- Protocol
- TEMPLATE CONSENT DOCUMENT – Emergency Use (HRP 506) revised to indicate the use is for non-emergency treatment use.
- Information about the investigational product such as an investigator brochure.

If the need for the investigational product is urgent, the IRB will forego the requirement for a formal protocol but will require sufficient information to make the determinations required under 21 CFR § 56.111 (Criteria for Approval). In these instances, the IRB will require:

- Information about the efficacy and risks of the investigational product
- Information about the patient’s condition supporting a finding that the patient has a condition for which no other comparable treatment or therapy is available
- FDA approval of use of the investigational product (IND or IDE)
- The procedures the physician will follow, including the procedures to monitor patient safety during and after use of the investigational product.

Click HERE for information about the FDA’s requirements,

12.4 Right to Try

The “Right to Try Act” (H.R.878 - Right to Try Act of 2017) allows investigational drugs, biological products or devices without FDA approval under the following conditions:

- To be eligible for “Right to Try,” the patient must:
  - Be diagnosed with a life-threatening disease or condition;
  - Have exhausted approved treatment options and is unable to participate in a clinical trial involving the eligible investigational drug (this must be certified by a physician who is in good standing with their licensing organization or board and who will not be compensated directly by the manufacturer for certifying);
  - The subject or their LAR must provide written informed consent for use of the investigational drug;
- The investigational drug or biologic must meet the following criteria:
  - A Phase 1 clinical trial must have been completed;
  - The drug/biologic/device must not have been approved FDA approved for any use;
  - One of the following must be met:
    - An application has been filed with the FDA;
    - The drug/biologic is undergoing a clinical trial subject to an IND that is intended to provide data to support FDA;
Clinical trials are ongoing and have not been discontinued or placed on hold by the FDA.

UM strongly encourages the use of the expanded use pathway initiated by the FDA (described in Section 11.1 above) for patients who seek unapproved medications for life-threatening diseases or conditions. Therefore, physicians should gently inform patients who invoke the Right to Try Act of the following:

- The Act does not require institutions to accede to requests for unapproved drugs
- UM follows Federal research regulations, and
- Efforts to obtain unapproved drugs should be made to the FDA under its emergency use expanded access program.
Chapter 13
Requirements for Federally Funded Research

13.1 Department of Defense (DOD)

1. Service Members as Subjects
   - Service members may need to obtain permission to participate in research involving human subjects, even when the service member is off-duty.

2. Payments to Subjects
   - DOD employees may not be able to legally accept payments to participate in research and should check with their supervisor before accepting such payments.
   - Military personnel must not receive payment for participating in research procedures during duty hours.
   - Military personnel may receive payment for participating in research procedures when not on duty.
   - Federal employees may receive up to $50 for blood each blood draw, even while on duty.

3. Reporting Requirements
   The following must be reported promptly (within 30 days) to the DOD human research protection officer:
   - When significant changes to the research protocol are approved by the IRB.
   - The results of IRB continuing review
   - Change of reviewing IRB
   - When the institution or investigator is notified by any Federal Department, agency or national organization that any part of the HRPP is under investigation for cause involving a DOD supported research protocol.

Other specific requirements of the Department of Defense research be found in the “Additional Requirements for Department of Defense (DOD) Research” section in the HSRO’s “WORKSHEET: Additional Federal Criteria (HRP-318)” and in “SOP: NEW INFORMATION (HRP-024).”

13.2 Department of Energy (DOE)

1. Research that involves one or more of the following is considered by DOE to be human subjects research and requires IRB review:
   - Intentional modification of the human environment
   - Study of human environments that use tracer chemicals, particles or other materials to characterize airflow.
• Study in occupied homes or offices that:
  o Manipulate the environment to achieve research aims.
  o Test new materials.
  o 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. If the research includes use of personally identifiable information, investigators must complete and submit to the IRB and the DOE “DOE Institutional Review Board Template for Reviewing Human Subjects Research Protocols that Utilize Personally Identifiable Information (PII).”

3. The IRB must report the following to the Department of Energy human subjects research program manager within 48 hours:
   • Any significant adverse events, unanticipated risks; and complaints about the research, with a description of any corrective actions taken or to be taken
   • Any suspension or termination of IRB approval of research
   • Any significant non-compliance with Human Research Protection Program procedures or other requirements.

4. Any compromise of personally identifiable information must be reported immediately upon discovery.

5. Requirements for human participant protections for classified research apply to all research conducted or supported by the DOE, including contracts, and including Human Terrain Mapping research.

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 HSRO’s “WORKSHEET: Additional Federal Criteria (HRP-318).”

13.3 Department of Justice (DOJ) and Bureau of Prisons

1. The Department of Justice (DOJ) has not promulgated the 2018 revisions to the Common Rule. All DOJ founded research must follow the old 2018 Common Rule.

2. DOJ funded research projects must:
   • Not involve medical experimentation, cosmetic research, or pharmaceutical testing.
   • Be compatible with both the operation of prison facilities and protection of human subjects.
   • Research conducted in within the Bureau of Prisons must be reviewed and approved by the Bureau Research Review Board.
3. 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.

4. Payments to Subjects
   - The only incentives allowable to confined inmate subjects are soft drinks and snacks to be consumed at the test setting.
   - Nominal monetary compensation for time and effort may be offered to non-confined research subjects who are no longer in custody.

5. Records and Confidentiality
   - DOJ funded research must have a privacy certificate approved by the National Institute of Justice Human Subjects Protection Officer
     o 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.
   - 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.
   - A non-employee of the Bureau of Prisons 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.
   - Written consent from the subject is required before investigators release or share any identifiable information for any reason, judicial, administrative or legislative proceedings.
   - Records that contain non-disclosable information directly traceable to a specific person may not be stored in, or introduced into, an electronic retrieval system.
   - All investigators and research staff are required to sign employee confidentiality statements, which are maintained by the investigator.
   - The following must be sent to the National Archive of Criminal Justice Data in a de-identified manner:
     o All data
     o Informed consent document
     o Data collection instrument
     o Surveys
     o Other relevant research materials.

6. IRB Application
   For research conducted within the Bureau of Prisons, investigators must submit a summary statement to the Bureau of Prisons IRB, which includes:
   - Names and current affiliations of the investigators
• Title of the study
• Purpose of the study
• Location of the study
• Methods to be employed
• Anticipated results
• Durations of the study
• Number of subjects (staff or inmates) and the amount of time required from each
• Description of risk or discomfort involved as a result of participation.
• A Comprehensive statement that includes the following:
  o Review of related literature.
  o Detailed description of the research method.
  o Significance of anticipated results and their contribution to the advancement of knowledge.
  o Specific resources required from the Bureau of Prisons.
  o 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.
  o Description of steps taken to minimize any risks.
  o Description of physical or administrative procedures to be followed to:
    i. Ensure the security of any individually identifiable data that are being collected for the study.
    ii. Destroy research records or remove individual identifiers from those records when the research has been completed.
  o Description of any anticipated effects of the research study on institutional programs and operations.
  o Relevant research materials such as vitae, endorsements, sample consent statements, questionnaires, and interview schedules.

7. Reporting Requirements
• Progress Reports to the Chief, Office of Research and Evaluation, are due annually.
• 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.
  o An abstract must be included in the report of findings.

8. Requirements for publication
• Investigators must acknowledge the Bureau's participation in the research project in all publications
• Investigators must expressly disclaim approval or endorsement of the published material as an expression of the policies or views of the Bureau.
• 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.

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 HSRO’s “WORKSHEET: Additional Federal Criteria (HRP-318).”

13.4 Department of Education (ED)

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. 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.
3. Parents or children involved in ED funded research must be able to inspect copies of all surveys and instructional material used in the research.

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 HSRO’s “WORKSHEET: Additional Federal Criteria (HRP-318).”

13.5 Environmental Protection Agency (EPA)

1. Research conducted, supported, or intended to be submitted to EPA is subject to Environmental Protection Agency Regulations and must be approved by the EPA Human Subjects Research Review Official (HSRRO) before the research may begin.
2. Research involving 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. If proposed research involves children, the risk of the research must be minimal or there must be a potential for direct benefit to the child.

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
Chapter 14
HSRO Resources and Contact Information

Much of the information you need can be found on the HSRO website, including:

**HSRO Forms and Templates** – This is where you will find the following forms:

- HIPAA Forms (Form B, Form D and Form E)
- Cooperative Research Forms – External IRB Reliance Application, External Site Application, IRB Authorization agreement
- Emergency Use Request and Emergency Use Report (including translated forms), cooperative research, and emergency use of an investigational product. Corporate Research forms, & Emergency Use forms.
- Protocol Templates
- Consent Templates

**HSRO Standard Operating Procedures** – This where you can find this manual and copies of the HSRO Standard Operating Procedures.

For general questions about submission and procedures, call (305) 243-3195.

A list of HSRO personnel is located on the [HSRO Website](#).

If you have questions, concerns, complaints, allegations of undue influence, allegations or findings of non-compliance, or input regarding the Human Research Protection Program that cannot be addressed by contacting the IRB Office, Contact the [Vice Provost for Research](#).
Chapter 15
Obtaining Additional Information

15.1 Common Rule

2018 45 CFR 46
Pre-2018 45 CFR 46

15.2 FDA Regulations

21 CFR 56 – Institutional Review Boards
21 CFR 312 – Investigational New Drugs
21 CFR 812 – Investigational Device Exemptions
21 CFR 812 Subpart H – Humanitarian Use Devices

15.3 FDA Information Sheet Guidance for Institutional Review Boards (IRBs), Clinical Investigators, and Sponsors

15.4 ICH E6(R2) Good Clinical Practice