



Investigator Manual

Dated: February 27, 2017



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Scope

Throughout this document “organization” refers to University of Miami.

What is the purpose of this manual?

This document, **HRP-103 INVESTIGATOR MANUAL**, is designed to guide you through principles and requirements related to the conduct of Human Research that are specific to this organization.

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

What is Human Research?

HRP-101 HUMAN RESEARCH PROTECTION PROGRAM PLAN defines the activities that this organization considers to be “Human Research.” An algorithm for determining whether an activity is Human Research can be found in **HRP-310 WORKSHEET: Human Research**. Additionally, the Human Subject Research Office has developed a **Not Human Subject Research Self Certification Tool**

(https://umiami.qualtrics.com/SE/?SID=SV_4Iz2NPEhX1kdNIx), which may be accessed from the Online Resources section of the IRB Web site. You may use this tool for guidance as to whether an activity meets either the DHHS or FDA definition of Human Research, keeping in mind that the IRB makes the ultimate determination in questionable cases as to whether an activity constitutes Human Research subject to IRB oversight.

You are responsible not to conduct Human Research without prior IRB review and approval (or an organizational review and approval of exempt Human Research). If you have questions about whether an activity is Human Research, contact the Human Subject Research Office for guidance. If you wish to have a written determination, submit a new study application and upload the Non-Human/Non-Research Determination Application as your protocol to the Human Subject Research Office.

See **HRP-312 WORKSHEET: Exempt Determination** for activities that are exempt from IRB regulatory requirements. Note that you must still submit exempt Human Research for IRB review and approval.

Human Research may be reviewed and approved by an External IRB in certain scenarios. See “When can I submit to an external IRB?” below for those scenarios. If your research does not fit into one of the described scenarios, then your Human Research must be approved by UM.



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What is the Human Research Protection Program?

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

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

Who may be a principal investigator?

Every research study requires a Principal Investigator (PI). This person takes full responsibility for the conduct of the study. Below is a comprehensive list of who may and may not serve as PI.

| <u>PI Eligible</u> | <u>Case-by-case</u> | <u>Not PI Eligible</u> |
|--|--|---|
| <ul style="list-style-type: none"> • 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 | <ul style="list-style-type: none"> • Adjunct (including contributed services) faculty; • Visiting faculty; and • Visiting scholars. • Contact the Vice Provost for Research via email to request permission for such faculty. Please include a letter of support from your Department Chair/Division Chief. If approval is granted, upload the confirmation email into the “Supporting Documents” section in your electronic submission. | <ul style="list-style-type: none"> • Postdoctoral fellows and research assistants (graduate students); • Research associates; and • Undergraduate students |



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What training do my staff and I need to conduct Human Research?

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

Investigators and staff conducting Human Research must complete at least one of the four “Core” courses of the Collaborative Institutional Training Initiative (CITI) human subject online training program and New Investigator training offered by the Office of Clinical Research Operations and Regulatory Support (CRORS), when applicable. Human research protections certification from other equivalent programs may be approved by the Associate Vice Provost for Human Subject Research.

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

Training is valid for a two-year period, after which time the training must be repeated.

All members of the research team involved in the design, conduct, or reporting of the research (or otherwise listed as study team in eProst) must complete training. Members of the research team who have not completed human research protections training may not take part in aspects of the research that involve human subjects.

What financial interests do my staff and I need to disclose in order to conduct Human Research?

Individuals involved in the design, conduct, or reporting of research, research consultation, teaching, professional practice, institutional committee memberships, and service on panels such as Institutional Review Boards or Data and Safety Monitoring Boards are considered to have an institutional responsibility.

All individuals involved in the design, conduct, or reporting of research are required to disclose the financial interests listed in the “Financial Interest Declaration” sections of **HRP-211 FORM: Initial Review** (implemented electronically as the New Study SmartForm) and **HRP-212 FORM: Continuing Review** (implemented electronically as the Mod/CR SmartForm).

- On submission of an initial review.
- At least annually as part of continuing review.
- Within 30 days of discovering or acquiring (e.g., through purchase, marriage, or inheritance) a new financial interest.

Once disclosed in the IRB application, individuals will be directed to the Disclosure Profile System (DPS) to complete their financial interest disclosure. Individuals with reimbursed or sponsored travel by an entity other than a federal, state, or local government agency, higher education institution or affiliated research institute, academic teaching hospital, or medical center



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are required to disclose the purpose of the trip, the identity of the sponsor or organizer, the destination, and the duration of the travel.

Individuals subject to this policy are required to complete financial conflicts of interest training initially, at least every four years, and immediately when:

- Joining the organization
- Financial conflicts policies are revised in a manner that changes investigator requirements
- Non-compliant with financial conflicts policies and procedures

Additional details can be found in **HRP-055 SOP: Financial Conflicts of Interests**.

How do I submit new Human Research to the IRB?

Log in to eProst/IRB 7 and complete the new study smart form attaching all requested supplements (e.g. protocol, consent form, questionnaires, etc.). Execute the “Submit” activity so the application is submitted for review (departmental, ancillary, IRB). Maintain electronic copies of all information submitted to the IRB in case revisions are required. Before submitting the research for initial review, you must:

- 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.
- Ensure all research staff are CITI certified in the Human Subject Research (HSR) Series, Conflict of Interest and, if applicable, Good Clinical Practice (GCP)

How do I submit a grant-only submission to the IRB?

Umbrella grants, training grants, and just-in-time grants, unless accompanied by a protocol describing all elements of the research (including the informed consent process and document, if required) are technically not Human Research according to the definitions above.

What IRB fees apply to my research?

The University of Miami, Vice Provost for Research Office, HSRO/IRB Department will assess fees for all types of reviews (Full Board, Expedited and Exempt) where a determination has been made by the HSRO/IRB. Additional details related to fees and how they will be billed may be found in Appendix A-9, “IRB Fees and Related Financial Billing Information.”

When can I submit to an external IRB (“outgoing”)?

You can submit a study to be conducted at UM for review by an external IRB only if your research fits into one of the scenarios described in **HRP-095 SOP: External IRB Review**.



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When can I submit a multi-site study to the UM Central IRB (“incoming”)?

You can submit multi-site studies to UM Central IRB for single IRB review only if your research fits into one of the scenarios described in **UM CIRB Manual for Investigators and Networks**.

How do I write an Investigator Protocol?

Use an appropriate **HRP-503(x) TEMPLATE PROTOCOL** as a starting point for drafting a new Investigator Protocol, and reference the instructions in italic text for the information the IRB requires when reviewing research. Here are some key points to remember when developing an Investigator Protocol:

- The italicized bullet points in **HRP-503(x) TEMPLATE PROTOCOL** serve as guidance to investigators when developing an Investigator Protocol for submission to the IRB. All italicized comments are meant to be deleted prior to submission.
- For any items described in the sponsor’s protocol or other documents submitted with the application, investigators may simply reference the applicable sections of these documents within the Investigator Protocol rather than repeat information.
- When writing an Investigator Protocol, always keep an electronic copy. You will need to modify this copy when making changes to the Investigator Protocol.
- If you believe your activity may not be Human Research, you may use the **Not Human Subject Research Self-certification Tool** (available from the Online Resources page of the HSRO web site) prior to developing your Investigator Protocol and print your results for verification. Although not required by University policy, if you require further confirmation of such a determination from the IRB, complete a **HRP-211 FORM: Initial Review** (*implemented electronically as the New Study SmartForm*)” and attach the completed Not Human Subject Research Self-certification with your Investigator Protocol.
- Note that, depending on the nature of your research, certain sections of the template may not be applicable to your Investigator Protocol. Indicate this as appropriate.
- You may not involve any individuals who are members of the following populations as subjects in your research unless you indicate this in your inclusion criteria as the inclusion of subjects in these populations has regulatory implications.
 - Adults unable to provide legally effective consent
 - Individuals who are not yet adults (infants, children, teenagers)
 - Pregnant women
 - Prisoners



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- If you are conducting community-based participatory research, you may contact the Human Subject Research Office for information about:
 - Research studies using a community-based participatory research design
 - Use of community advisory boards
 - Use of participant advocates
 - Partnerships with community-based organizations

Should I obtain a Certificate of Confidentiality for my research?

A Certificate of Confidentiality is a tool for protecting certain information from forced or compelled disclosure, e.g., to oppose a subpoena. Please consult the NIH Certificate of Confidentiality Kiosk at <http://grants.nih.gov/grants/policy/coc/index.htm> for more information about what research qualifies for a Certificate of Confidentiality and how one can be obtained. If you are able to obtain a Certificate of Confidentiality, the IRB will consider that information as part of its review.

How do I research using genetic information?

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

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

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

How do I create a consent document?

Use an appropriate version of **HRP-502(x) TEMPLATE CONSENT DOCUMENT** found in the IRB Library within eProst/IRB7 or on the [Consent Templates](#) page within the [Online Resources](#) section of the [HSRO website](#) to create a consent document. For more information, please reference **HRP-091 SOP: Written Documentation of Consent**.



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Note that all long form consent documents and all summaries for short form consent documents must contain all of the required and all additional appropriate elements of informed consent disclosure. Review the “Long Form of Consent Documentation” section in **HRP-314 WORKSHEET: Criteria for Approval** to ensure that these elements are addressed. When using the short form of consent documentation, the appropriate signature block from **HRP-502(x) TEMPLATE CONSENT DOCUMENT** should be used on the short form.

We recommend that you date the revisions of your consent documents to ensure that you use the most recent version approved by the IRB. The IRB will watermark consent documents with IRB approval dates.

How do I obtain informed consent from subjects?

You must describe your process for obtaining informed consent from subjects for participation in Human Subject Research. The process you employ for obtaining informed consent will depend on the research setting and your subject population. The consent process is distinct from the consent document. For more information, please reference **HRP-090 SOP: Informed Consent Process for Research**. When written documentation of consent is a requirement for IRB approval, the subject or Legally Authorized Representative (LAR) must sign a consent document, but only after you have led subjects through your approved consent process.

When should I register my research with ClinicalTrials.gov?

You must register your research with ClinicalTrials.gov if it meets the requirements for submission. Please see the ClinicalTrials.gov website for more information:

<https://clinicaltrials.gov/ct2/manage-recs/background>

If you are required to register your research with ClinicalTrials.gov, you must also include a statement indicating so in your consent document. This statement is provided for you in **HRP-502a TEMPLATE CONSENT DOCUMENT (Biomedical Studies)**.

What if I want to enroll participants with limited English proficiency?

Participants who have limited English proficiency may be enrolled in your research provided that you have the resources to communicate effectively with subjects during recruitment, while obtaining consent, and for the duration of the research. You may request IRB authorization to use a short form as described below in the “How do I document consent or assent?” section to document consent. Consult **HRP-317 WORKSHEET: Short Form of Consent Documentation** for more information. The IRB Office has also provided Short Form consent templates in several language for your convenience, which can be found at the following webpage: <http://hsro.med.miami.edu/resources>.

Generally speaking, if you expect to enroll more than one participant with limited English proficiency or if your study is being conducted internationally, you are expected to translate your



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approved consent document into the appropriate language for your research. To reduce translation costs, if you are using a commercial translation service, it is recommended that you first obtain IRB approval for your English-language consent document. After you receive IRB approval, translate your document, and submit that document in IRB7 with a modification, including a Certificate of Translation. For descriptions of the minimum accepted methods of translation, please reference **Investigator Guidance: Translation Requirements** (<http://hsro.med.miami.edu/documents/Guidance-TranslationRequirements-rev12.22.2015.pdf>).

Please consult the following webpage for a non-exclusive list of translation services:
<http://hsro.med.miami.edu/resources/translations>.

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

Submitted activities may fall under one of the following four regulatory classifications:

- **Not “Human Research”**: Activities must meet the organizational definition of “Human Research” to fall under IRB oversight. Activities that do not meet this definition are not subject to IRB oversight or review. Review **HRP-310 WORKSHEET: Human Research** for reference. Contact the Human Subject Research Office in cases where it is unclear whether an activity is Human Research.
- **Exempt**: Certain categories of Human Research may be exempt from regulation but do require IRB review. It is the responsibility of the organization, not the investigator, to determine whether Human Research is exempt. Review **HRP-312 WORKSHEET: Exemption** for reference on the categories of research that may be exempt.
- **Review Using an Expedited Procedure**: Certain categories of non-exempt Human Research may qualify for review using an expedited procedure, meaning that the project may be approved by a single designated IRB reviewer, rather than the convened board. Review **HRP-313 WORKSHEET: Eligibility for Review Using the Expedited Procedure** for reference on the categories of research that may be reviewed using the expedited procedure.
- **Review by the Convened IRB**: Non-Exempt Human Research that does not qualify for review using the expedited procedure must be reviewed by the convened IRB.

Note: Worksheets are available in the library within the [eProst/IRB7](#).

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

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

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



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- Approve with modification: Made when IRB members make specific modifications to the research in order to grant approval.
- Require Modifications to Secure Approval: Made when IRB members require specific modifications to the research before approval can be finalized.
- Table: Made when the IRB cannot approve the research at a meeting for reasons unrelated to the research, such as loss of quorum. When taking this action, the IRB automatically schedules the research for review at the next meeting.
- Defer: Made when the IRB determines that the board is unable to approve research and the IRB suggests modifications the might make the research approvable. When making this motion, the IRB describes its reasons for this decision, describes modifications that might make the research approvable, and gives the investigator an opportunity to respond to the IRB in person or in writing.
- Disapprove: Made when the IRB determines that it is unable to approve research and the IRB cannot describe modifications the might make the research approvable. When making this motion, the IRB describes its reasons for this decision and gives the investigator an opportunity to respond to the IRB in person or in writing.

How does the IRB decide whether to approve Human Research?

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

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

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

What will happen after IRB review?

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

- If the IRB has approved the Human Research: The Human Research may commence once all other organizational approvals have been met. IRB approval usually applies for a limited period of time which is noted in the approval letter.
- If the IRB requires modifications to secure approval and you accept the modifications: Make the requested modifications and submit them to the IRB. If all requested modifications are made, the IRB will issue a final approval letter. Research cannot



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commence until this final approval letter is received. If you do not accept the IRB's modifications, submit a written response detailing your reasons for disagreement to the IRB.

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

In all cases, you have the right to address your concerns to the IRB directly at an IRB meeting.

What are my obligations after IRB approval?

- 1) Do not start Human Research activities until you have the final IRB approval letter.
- 2) Do not start Human Research activities until you have obtained all other required institutional approvals, including approvals of departments or divisions that require approval prior to commencing research that involves their resources.
 - a) If study-related activities will occur at JHS (JHS is listed as a performance site), you must ensure that you have been granted permission by the JHS Clinical Research Review Committee prior to commencing study activities at JHS. **If you have any questions regarding this process, please contact the JHS Clinical Trials Office at 305-585-7596.** Note that the JHS informed consent document can only be used at Jackson Health System.
 - b) If study-related activities will occur at UMH (UMH is listed as a performance site), you must ensure that you have been granted permission by the UMH Research Review Committee prior to commencing study activities at UMH. **If you have any questions regarding this process, please contact the UMH Research Review Committee at 305-689-5410.**

If a study is a clinical trial, you must comply with UM's [Clinical Research Participant Enrollment and Tracking Policy](#). All human participants (inpatient and outpatient) enrolled in clinical research protocols conducted at the University of Miami or Jackson Health Systems must be registered in the Velos clinical trial management system based on applicable criteria.

- 3) If a study is an "applicable clinical trial" as defined at 42 U.S.C. 282(j)(1)(a), you must comply with UM's Clinical Trial Disclosure: Protocol Registration Policy for registration on ClinicalTrials.gov.
- 4) Ensure that there are adequate resources to carry out the research safely. This includes, but is not limited to, sufficient investigator time, appropriately qualified research team members, equipment, and space.
- 5) Ensure that Research Staff are qualified (e.g., including but not limited to appropriate training, education, expertise, credentials, protocol requirements and, when relevant, privileges) to perform procedures and duties assigned to them during the study.



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- 6) Update the IRB office with any changes to the list of study personnel.
- 7) Personally conduct or supervise the Human Research.
 - a) Conduct the Human Research in accordance with the relevant current protocol as approved by the IRB.
 - b) If approved for chart review and it will occur at UM, you must submit your IRB approval letter and watermarked data collection sheet to the Office of HIPAA Privacy & Security, PAC 409, Locator M-879, telephone: 305-243-5000. If chart review will occur at Jackson Health Systems, please contact the Jackson Privacy Office at 305-585-6854 for further information.
 - c) If a waiver or alteration (partial waiver) of HIPAA authorization is granted, you must prepare and submit to the Office of HIPAA Privacy & Security a record of disclosure for each disclosure of patient information by using the HIPAA Accounting for Disclosures form (HIPAA Attachment 45) located on the HSRO HIPAA page.
 - d) If a Limited Data Set is granted, you must provide your IRB approval letter, Business Associate or other Agreement(s) and watermarked data collection sheet to the Office of HIPAA Privacy & Security, PAC 409, Locator M-879, telephone: 305-243-5000.
 - e) If you will obtain HIPAA authorization (Form B), you must send a copy of each signed authorization form to the Office of HIPAA Privacy & Security, PAC 409, Locator M-879, telephone: 305-243-5000.
 - f) When required by the IRB, ensure that consent or permission is obtained in accordance with the relevant current protocol as approved by the IRB.
 - g) Do not modify the Human Research without prior IRB review and approval unless necessary to eliminate apparent immediate hazards to subjects.
 - h) Protect the rights, safety, and welfare of subjects involved in the research.
- 8) Submit to the IRB:
 - a) Proposed modifications as described in this manual. (See “How do I submit a modification?”)
 - b) A continuing review application as requested in the approval letter. (See “How do I submit continuing review?”)
 - c) A continuing review application when the Human Research is closed. (See “How Do I Close Out a Study?”)
- 9) Report any of the information items listed in **HRP-214 FORM: Reportable New Information** (*implemented electronically as the RNI SmartForm*)” to the IRB within ten business days of knowledge.
 - a) Non-compliance (i.e. protocol deviation) must be reported via the RNI form if it may:
 - i) impact subject safety, condition or status;
 - ii) affect the integrity of study data;
 - iii) pose a significant risk of harm and thereby change the risk/benefit ratio; and/or
 - iv) affect a subject's willingness to participate in the study.
 - b) Non-compliance (i.e. protocol deviations) not meeting the above criteria must be reported in summary format at the time of continuing review.



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- c) Unanticipated Problems Involving Risks to Subjects or Others (UPIRTSO), which may include adverse events or new risks, must be reported via the RNI form if they are:
 - i) unexpected
 - ii) related or probably related
 - iii) indicate that there is greater risk than previously described
- 10) Principal investigators are required to promptly (within 10 business days of the investigator becoming aware of the event) report to the IRB any information including unanticipated problems and adverse events as follows (more than one may apply):

| Type of Event | Selection on RNI Form |
|--|-------------------------------------|
| Interim analysis, safety monitoring report, publication in a peer-reviewed journal, or other finding that indicates that there are new or increased risks to subjects or others or that subjects are less likely to receive any direct benefits from the research | Risk |
| Internal adverse events that are unexpected, and related or possibly related to the research and that indicate there are new or increased risks to subjects | Harm |
| Unanticipated adverse device effects that are serious and caused by, or associated with, the device | Unanticipated adverse device effect |
| Deviation from the approved research protocol or plan that placed subjects or others at an increased risk of harm regardless of whether there was actual harm to subjects or others | Risk |
| Deviation from the approved research protocol or plan without IRB approval in order to eliminate apparent immediate hazard to subjects or harm to others (NOTE: Unreviewed changes are reviewed by the IRB to determine whether each change was consistent with ensuring the participants' continued welfare.) | Unreviewed change |
| Noncompliance with applicable regulations or requirements or determinations of the IRB identified by the research team or others (e.g., FDA Form 483 or Warning Letter) that indicates that the rights, welfare, or safety of subjects have been adversely affected. | Non-compliance |
| Any event that requires prompt reporting according to the research protocol or investigational plan or the sponsor | Risk or Harm |
| Medication, procedural or laboratory error (e.g., errors in drug administration or dosing, surgical or other procedure, or testing of samples or test results) regardless of whether subjects experienced any harm | Researcher Error |
| Audit, inspection or inquiry by a federal agency | Audit |
| Change in FDA labeling (e.g., black box warning), withdrawal from market, manufacturer alert from the sponsor, or recall of an FDA-approved drug, device, or biologic used in the research | Risk |



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| Breach of confidentiality or violation of HIPAA (e.g., lost or stolen laptop) | Confidentiality |
| Complaint by/on behalf of a research subject that indicates that the rights, welfare, or safety of the subject have been adversely affected or that cannot be resolved by the investigator | Complaint |
| Incarceration of a research subject during participation in research that is not approved for involvement of prisoners as subjects | Incarceration |
| Suspension or termination of the research, in whole or in part, based on information that indicates that the research places subjects at an increased risk of harm than previously known or recognized (e.g., FDA clinical hold) | Suspension |
| Suspension or disqualification of an investigator by FDA, sponsor, or others | Suspension |
| Scientific misconduct | Non-compliance |
| Any report of study monitors (DSMB, DMC, etc.) that indicates the research places subjects at an increased risk of harm than previously known or recognized | Report |
| Any other problem that indicates that the research places subjects or others at an increased risk of harm or otherwise adversely affect the rights, welfare or safety of subjects or others | Harm |

11) The reporting mechanism for other information is as follows:

| Type of Information | Mechanism to Report |
|--|---------------------|
| Modification to IRB-approved protocol or research plan for one or a few subjects | Modification |
| Updated Investigator Brochure/Packet Insert | Modification |
| DSMB, Sponsor or Other Reports | RNI or CR |
| Certificate of Confidentiality | Modification |
| Translated Consent Forms | Modification |
| External SAE/IND Safety Report | DO NOT REPORT |
| Executed Clinical Trial Agreement | DO NOT REPORT |
| Form 1572 | DONOT REPORT |
| Notice of Grant Award | Modification |

- 12) Submit an updated disclosure of financial interests within thirty days of discovering or acquiring (e.g., through purchase, marriage, or inheritance) a new financial interest.
- 13) Do not accept or provide payments to professionals in exchange for referrals of potential subjects (“finder’s fees.”)



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- 14) Do not accept payments designed to accelerate recruitment that were tied to the rate or timing of enrollment (“bonus payments.”)
- 15) See additional requirements of various federal agencies in Appendix A. These represent additional requirements and do not override the baseline requirements of this section.

How do I document consent?

Use the signature block approved by the IRB. Complete all items in the signature block, including dates.

The following are the requirements for long form consent documents:

- The subject or Legally Authorized Representative (LAR) signs and dates the consent document.
- The individual obtaining consent signs and dates the consent document.
- Whenever the IRB or the sponsor require a witness to the oral presentation, the witness signs and dates the consent document.
- For subjects who cannot read, and whenever required by the IRB or the sponsor, a witness to the oral presentation signs and dates the consent document.
- A copy of the signed and dated consent document is to be provided to the subject or LAR.

The following are the requirements for short form consent documents:

- The subject or Legally Authorized Representative (LAR) signs and dates the short form consent document.
- The individual obtaining consent signs and dates the summary.
- The witness to the oral presentation signs and dates the short form consent document and the summary.
- Copies of the signed and dated short form consent document and summary are provided to the subject or LAR.

For Additional details on the consent process, please refer to the “Guidance on Informed Consent” document located at Appendix 10 in this document.

How do I submit a modification to the study protocol?

Complete and submit **HRP-213 FORM: Modification** (*implemented electronically as part of the Mod/CR SmartForm*), attaching all requested supplements (e.g. summary of changes, revised consent forms, etc.). Please note that research cannot be conducted with inclusion of the modification until IRB approval is received. Updates to the list of study personnel will be acknowledged by HSRO staff. If a personnel update represents a modification to the research, IRB review will be required.



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How do I submit an application for continuing review?

Complete and submit **HRP-212 FORM: Continuing Review** (*implemented electronically as part of the Mod/CR SmartForm*), attaching all requested supplements (e.g. summary of reportable events, Velos enrollment report, etc.). Before submitting the research for continuing review, you must:

- Determine whether any member of the research staff has a change in financial interest related to the research. A “yes” or “no” answer is sufficient. There is no need to obtain additional details.
- Obtain the verbal or written agreement of each member of the research staff to his/her continuing role in the research.

If the continuing review application is not received by the date requested in the approval letter, you may be restricted from submitting new Human Research until the completed application has been received.

If the IRB approval of Human Research expires, all Human Research procedures related to the protocol under review must cease, including recruitment, advertisement, screening, enrollment, consent, interventions, interactions, and collection or analysis of private identifiable information. Continuing Human Research procedures is a violation of federal regulations. If current subjects will be harmed by stopping Human Research procedures that are available outside the Human Research context, provide these on a clinical basis as needed to protect current subjects. If current subjects will be harmed by stopping Human Research procedures that are not available outside the Human Research context, immediately contact the IRB chair and provide a written list of the currently enrolled subjects and why they will be harmed by stopping Human Research procedures.

How do I close out a study?

Complete and submit **HRP-212 FORM: Continuing Review** (*implemented electronically as part of the Mod/CR Form*), attaching all requested supplements (e.g. sponsor closure letter, etc.).

If you fail to submit a continuing review form to close out Human Research, you will be restricted from submitting new Human Research until the completed application has been received.

If the continuing review application for closing out a Human Research study is not received by the date requested in the approval letter, you will be restricted from submitting new Human Research until the completed application is received.

How long do I keep research records?

All records and documents relating to research studies and participants must be kept confidential to the extent permitted by law; however, records and documents shall be available in a timely manner to University authorized employees or other agents authorized by the University



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including IRB members and HSRO staff and appropriate governmental agencies including but not limited to the DHHS, OHRP and the FDA.

Although principal investigators are responsible 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 or others may not remove or destroy research records or documents (or copies of such records or documents) without written permission from the Vice Provost of Research. This permission requirement extends to investigators leaving the University even if they plan to continue the research at another institution.

With certain exceptions, investigators must retain complete records and documents (including the consent documents) from their study for the duration of that study and for a minimum period of three (3) years following closure of a study. Exceptions to this 3-year minimum retention period are:

- a) HIPAA REQUIREMENTS: if a study involves the collection of identifiable health information, records must be retained for a minimum of six (6) years following study closure. This retention period is consistent with the HIPAA Privacy Rule under which subjects may ask investigators for an accounting of all uses and disclosures of their study information for a period of 6 years after their participation is completed (c.f. *45 CFR 164.528*).
- b) FDA REQUIREMENTS FOR A STUDY INVOLVING AN INVESTIGATIONAL DRUG UNDER AN IND (c.f. *21 CFR 312.62*): if a study involves the use of an investigational drug under an IND, principal investigators must retain study records and documents until at least the later of the following dates:
 - a. 2-years following the date a marketing application is approved for the drug for the indication for which it was being investigated; or
 - b. 2-years after the investigation is discontinued and the FDA is notified if no marketing application is to be filed or, if the application is not approved for such indication; or
 - c. 3-years after IRB approval of the closure of the study
- c) FDA REQUIREMENTS FOR A STUDY INVOLVING AN INVESTIGATIONAL DEVICE UNDER AN IDE (c.f. *21 CFR 812.140*): if a study involves an investigational device under an IDE, principal investigators must retain study records and documents until at least the later of the following dates:
 - a. 2-years following the date on which the investigation is terminated or completed;
 or



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- b. 2-years following the date that the records are no longer required for purposes of supporting a premarket approval application or a notice of completion of a product development protocol; or
- c. 3—years after IRB approval of the closure of the study

NOTE – The FDA two-year requirements may occur during the applicable retention period or it may occur afterward and be additional to that period.

- d) VA REQUIREMENTS: if a study engages the VA, investigators must retain research records and documents for a minimum of five (5) years after IRB approval of study closure. This retention period is consistent with the VA’s Records Control Schedule (RCS 10-1).
- e) ICH-GCP REQUIREMENTS: trial documents must be retained as specified in Essential Documents for the Conduct of a Clinical Trial (see section 8) and as required by the applicable regulatory requirement(s). Measures must be taken to prevent accidental or premature destruction of these documents.

Records must be retained longer than the times specified above as other requirements may apply such as may be forthcoming from sponsors in executed contracts, institutional entities or extramural funding agencies.

If your Human Research is sponsored, contact the sponsor before disposing of Human Research records. The protocol and clinical trial agreement/contract will also contain terms for record retention.

What should I do if I leave University of Miami?

If you are planning to leave University of Miami, you must notify the Human Subject Research Office. You may decide to transfer responsibility of your research to another University of Miami researcher, close your research at University of Miami prior to your move, or transfer IRB oversight of your research to another IRB. Regardless of which option you choose, you will need to develop a plan for transfer, de-identification, or destruction of your research data and a plan for informing research participants of your move and how it affects them. Your department head and the Human Subject Research Office will be able to advise you on what actions you will need to take.

What if I need to use an unapproved drug, biologic, or device and there is no time for IRB review?

Contact the Human Subject Research Office or IRB chair immediately to discuss the situation. If there is no time to make this contact, see **HRP-322 WORKSHEET: Emergency Use** for the



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regulatory criteria allowing such a use and make sure these are followed. Use **HRP-506 TEMPLATE EMERGENCY USE CONSENT DOCUMENT** to prepare your consent document. You will need to submit a report of the use to the IRB within five days of the use and for drugs and biologics, submit an IRB application for initial review within 30 days if additional uses of the unapproved drug or biologic is anticipated.

If you fail to submit the report within five days or the IRB application for initial review within 30 days, you will be restricted from submitting new Human Research until the report and IRB application for initial review have been received.

Emergency use of an unapproved drug or biologic in a life-threatening situation without prior IRB review is “research” as defined by FDA, the individual getting the test article is a “subject” as defined by FDA, and therefore is governed by FDA regulations for IRB review and informed consent. Emergency use of an unapproved device without prior IRB review is not “research” as defined by FDA and the individual getting the test article is not a “subject” as defined by FDA. However, FDA guidance recommends following similar rules as for emergency use of an unapproved drug or biologic.

Individuals getting an unapproved drug, biologic, or device without prior IRB review cannot be considered a “subject” as defined by DHHS and their results cannot be included in prospective “research” as that term is defined by DHHS.

How do I get additional information and answers to questions?

This document and the policies and procedures for the Human Research Protection Program are available on the IRB Web Site at www.hsro.miami.edu.

| | |
|--|--|
| <p>If you have a concern, complaints, allegations of undue influence, allegations or findings of non-compliance about the Human Research Protection Program, please contact the Human Subject Research Office Quality Assurance at:</p> | <p>Saloni Vahia, MPH, MHSA Quality Assurance Auditor sxv297@miami.edu 305-243-1599</p> |
| <p>If you have any questions about the Human Research Protection Program, its procedures and policies, please contact the Education Lead of Human Subject Research Office at:</p> | <p>Joey Casanova, BBA, CIP Associate Director for Regulatory Initiatives and Education jcasanova@med.miami.edu 305-243-9232</p> |
| <p>For general questions or queries, you may</p> | <p>Human Subject Research Office 1400 NW 10th Avenue, Suite 1200A</p> |



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| also reach us at | Miami, Florida 33136 T: 305-243-3195 F: 305-243-3328 |
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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 Human Subject Research Office, follow the directions in **HRP-101 HUMAN RESEARCH PROTECTION PROGRAM PLAN** under “Reporting and Management of Concerns.”



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Appendix A-1 *Additional Requirements for DHHS-Regulated Research*¹

1. When a subject decides to withdraw from a clinical trial, the investigator conducting the clinical trial should ask the subject to clarify whether the subject wishes to withdraw from all components of the trial or only from the primary interventional component of the trial. If the latter, research activities involving other components of the clinical trial, such as follow-up data collection activities, for which the subject previously gave consent may continue. The investigator should explain to the subject who wishes to withdraw the importance of obtaining follow-up safety data about the subject.
2. Investigators are allowed to retain and analyze already collected data relating to any subject who chooses to withdraw from a research study or whose participation is terminated by an investigator without regard to the subject's consent, provided such analysis falls within the scope of the analysis described in the IRB-approved protocol. This is the case even if that data includes identifiable private information about the subject.
3. For research not subject to regulation and review by FDA, investigators, in consultation with the funding agency, can choose to honor a research subject's request that the investigator destroy the subject's data or that the investigator exclude the subject's data from any analysis.
4. When seeking the informed consent of subjects, investigators should explain whether already collected data about the subjects will be retained and analyzed even if the subjects choose to withdraw from the research.

¹ <http://www.hhs.gov/ohrp/policy/subjectwithdrawal.html>



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

1. When a subject withdraws from a study:²
 - a. The data collected on the subject to the point of withdrawal remains part of the study database and may not be removed.
 - b. An investigator may ask a subject who is withdrawing whether the subject wishes to provide continued follow-up and further data collection subsequent to their withdrawal from the interventional portion of the study. Under this circumstance, the discussion with the subject would distinguish between study-related interventions and continued follow-up of associated clinical outcome information, such as medical course or laboratory results obtained through non-invasive chart review, and address the maintenance of privacy and confidentiality of the subject's information.
 - c. If a subject withdraws from the interventional portion of the study, but agrees to continued follow-up of associated clinical outcome information as described in the previous bullet, the investigator must obtain the subject's informed consent for this limited participation in the study (assuming such a situation was not described in the original informed consent form). IRB approval of informed consent documents is required.
 - d. If a subject withdraws from the interventional portion of a study and does not consent to continued follow-up of associated clinical outcome information, the investigator must not access for purposes related to the study the subject's medical record or other confidential records requiring the subject's consent.
 - e. An investigator may review study data related to the subject collected prior to the subject's withdrawal from the study, and may consult public records, such as those establishing survival status.
2. For FDA-regulated research involving investigational drugs:
 - a. Investigators must abide by FDA restrictions on promotion of investigational drugs:³
 - i. An investigator, or any person acting on behalf of an investigator, must not represent in a promotional context that an investigational new drug is safe or effective for the purposes for which it is under investigation or otherwise promote the drug.
 - ii. This provision is not intended to restrict the full exchange of scientific information concerning the drug, including dissemination of scientific findings in scientific or lay media. Rather, its intent is to restrict promotional claims of safety or effectiveness of the drug for a use for which it is under investigation and to preclude commercialization of the drug before it is approved for commercial distribution.

² <http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126489.pdf>

³ <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.7>



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- iii. An investigator must not commercially distribute or test market an investigational new drug.
- b. Follow FDA requirements for general responsibilities of investigators⁴
 - i. An investigator is responsible for ensuring that an investigation is conducted according to the signed investigator statement, the investigational plan, and applicable regulations; for protecting the rights, safety, and welfare of subjects under the investigator's care; and for the control of drugs under investigation.
 - ii. An investigator must, in accordance with the provisions of 21 CFR §50, obtain the informed consent of each human subject to whom the drug is administered, except as provided in 21 CFR §50.23 or §50.24 of this chapter.
 - iii. Additional specific responsibilities of clinical investigators are set forth in this part and in 21 CFR §50 and 21 CFR §56.
- c. Follow FDA requirements for control of the investigational drug⁵
 - i. An investigator must administer the drug only to subjects under the investigator's personal supervision or under the supervision of a sub-investigator responsible to the investigator.
 - ii. The investigator must not supply the investigational drug to any person not authorized under this part to receive it.
- d. Follow FDA requirements for investigator recordkeeping and record retention⁶
 - i. Disposition of drug:
 - 1. An investigator is required to maintain adequate records of the disposition of the drug, including dates, quantity, and use by subjects.
 - 2. If the investigation is terminated, suspended, discontinued, or completed, the investigator must return the unused supplies of the drug to the sponsor, or otherwise provide for disposition of the unused supplies of the drug under 21 CFR §312.59.
 - ii. Case histories.
 - 1. An investigator is required to prepare and maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual administered the investigational drug or employed as a control in the investigation.
 - 2. Case histories include the case report forms and supporting data including, for example, signed and dated consent forms and medical records including, for example, progress notes of the physician, the individual's hospital charts, and the nurses' notes.

⁴ <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.60>

⁵ <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.61>

⁶ <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.62>



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The case history for each individual must document that informed consent was obtained prior to participation in the study.

- iii. Record retention: An investigator must retain required records for a period of 2 years following the date a marketing application is approved for the drug for the indication for which it is being investigated; or, if no application is to be filed or if the application is not approved for such indication, until 2 years after the investigation is discontinued and FDA is notified.
- e. Follow FDA requirements for investigator reports⁷
 - i. Progress reports: The investigator must furnish all reports to the sponsor of the drug who is responsible for collecting and evaluating the results obtained.
 - ii. Safety reports: An investigator must promptly report to the sponsor any adverse effect that may reasonably be regarded as caused by, or probably caused by, the drug. If the adverse effect is alarming, the investigator must report the adverse effect immediately.
 - iii. Final report: An investigator must provide the sponsor with an adequate report shortly after completion of the investigator's participation in the investigation.
 - iv. Financial disclosure reports:
 1. The clinical investigator must provide the sponsor with sufficient accurate financial information to allow an applicant to submit complete and accurate certification or disclosure statements as required under 21 CFR §54.
 2. The clinical investigator must promptly update this information if any relevant changes occur during the course of the investigation and for 1 year following the completion of the study.
- f. Follow FDA requirements for assurance of IRB review⁸
 - i. An investigator must assure that an IRB that complies with the requirements set forth in 21 CFR §56 will be responsible for the initial and continuing review and approval of the proposed clinical study.
 - ii. The investigator must also assure that he or she will promptly report to the IRB all changes in the research activity and all unanticipated problems involving risk to human subjects or others, and that he or she will not make any changes in the research without IRB approval, except where necessary to eliminate apparent immediate hazards to human subjects.
- g. Follow FDA requirements for inspection of investigator's records and reports⁹

⁷ <http://www.accessdata.fda.gov/SCRIPTS/cdrh/cfdocs/cfcr/CFRSearch.cfm?fr=312.64>

⁸ <http://www.accessdata.fda.gov/SCRIPTS/cdrh/cfdocs/cfcr/CFRSearch.cfm?fr=312.66>

⁹ <http://www.accessdata.fda.gov/SCRIPTS/cdrh/cfdocs/cfcr/CFRSearch.cfm?fr=312.68>



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- i. An investigator must upon request from any properly authorized officer or employee of FDA, at reasonable times, permit such officer or employee to have access to, and copy and verify any records or reports made by the investigator pursuant to 312.62.
- ii. The investigator is not required to divulge subject names unless the records of particular individuals require a more detailed study of the cases, or unless there is reason to believe that the records do not represent actual case studies, or do not represent actual results obtained.
- h. Follow FDA requirements for handling of controlled substances¹⁰
 - i. If the investigational drug is subject to the Controlled Substances Act, the investigator must take adequate precautions, including storage of the investigational drug in a securely locked, substantially constructed cabinet, or other securely locked, substantially constructed enclosure, access to which is limited, to prevent theft or diversion of the substance into illegal channels of distribution.
3. For FDA-regulated research involving investigational devices:
 - a. General responsibilities of investigators.¹¹
 - i. An investigator is responsible for ensuring that an investigation is conducted according to the signed agreement, the investigational plan and applicable FDA regulations, for protecting the rights, safety, and welfare of subjects under the investigator's care, and for the control of devices under investigation. An investigator also is responsible for ensuring that informed consent is obtained in accordance with 21 CFR §50.
 - b. Specific responsibilities of investigators¹²
 - i. Awaiting approval: An investigator may determine whether potential subjects would be interested in participating in an investigation, but must not request the written informed consent of any subject to participate, and must not allow any subject to participate before obtaining IRB and FDA approval.
 - ii. Compliance: An investigator must conduct an investigation in accordance with the signed agreement with the sponsor, the investigational plan, and other applicable FDA regulations, and any conditions of approval imposed by an IRB or FDA.
 - iii. Supervising device use: An investigator must permit an investigational device to be used only with subjects under the investigator's supervision. An investigator must not supply an investigational device to any person not authorized to receive it.
 - iv. Financial disclosure:

¹⁰ <http://www.accessdata.fda.gov/SCRIPTS/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.69>

¹¹ <http://www.accessdata.fda.gov/SCRIPTS/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=812.100>

¹² <http://www.accessdata.fda.gov/SCRIPTS/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=812.110>



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1. A clinical investigator must disclose to the sponsor sufficient accurate financial information to allow the applicant to submit complete and accurate certification or disclosure statements required under 21 CFR §54.
 2. The investigator must promptly update this information if any relevant changes occur during the course of the investigation and for 1 year following completion of the study.
- v. Disposing of device: Upon completion or termination of a clinical investigation or the investigator's part of an investigation, or at the sponsor's request, an investigator must return to the sponsor any remaining supply of the device or otherwise dispose of the device as the sponsor directs.
- c. Maintain the following accurate, complete, and current records relating to the investigator's participation in an investigation:¹³
- i. All correspondence with another investigator, an IRB, the sponsor, a monitor, or FDA, including required reports.
 - ii. Records of receipt, use or disposition of a device that relate to:
 1. The type and quantity of the device, the dates of its receipt, and the batch number or code mark.
 2. The names of all persons who received, used, or disposed of each device.
 3. Why and how many units of the device have been returned to the sponsor, repaired, or otherwise disposed of.
 - iii. Records of each subject's case history and exposure to the device. Case histories include the case report forms and supporting data including, for example, signed and dated consent forms and medical records including, for example, progress notes of the physician, the individual's hospital charts, and the nurses' notes. Such records must include:
 1. Documents evidencing informed consent and, for any use of a device by the investigator without informed consent, any written concurrence of a licensed physician and a brief description of the circumstances justifying the failure to obtain informed consent.
 2. Documentation that informed consent was obtained prior to participation in the study.
 3. All relevant observations, including records concerning adverse device effects (whether anticipated or unanticipated), information and data on the condition of each subject upon entering, and during the course of, the investigation, including information about relevant previous medical history and the results of all diagnostic tests.

¹³ <http://www.accessdata.fda.gov/SCRIPTS/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=812.140>



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4. A record of the exposure of each subject to the investigational device, including the date and time of each use, and any other therapy.
- iv. The protocol, with documents showing the dates of and reasons for each deviation from the protocol.
- v. Any other records that FDA requires to be maintained by regulation or by specific requirement for a category of investigations or a particular investigation.
- d. Inspections¹⁴
 - i. Entry and inspection: A sponsor or an investigator who has authority to grant access must permit authorized FDA employees, at reasonable times and in a reasonable manner, to enter and inspect any establishment where devices are held (including any establishment where devices are manufactured, processed, packed, installed, used, or implanted or where records of results from use of devices are kept).
 - ii. Records inspection: A sponsor, IRB, or investigator, or any other person acting on behalf of such a person with respect to an investigation, must permit authorized FDA employees, at reasonable times and in a reasonable manner, to inspect and copy all records relating to an investigation.
 - iii. Records identifying subjects: An investigator must permit authorized FDA employees to inspect and copy records that identify subjects, upon notice that FDA has reason to suspect that adequate informed consent was not obtained, or that reports required to be submitted by the investigator to the sponsor or IRB have not been submitted or are incomplete, inaccurate, false, or misleading.
- e. Prepare and submit the following complete, accurate, and timely reports¹⁵
 - i. Unanticipated adverse device effects. An investigator must submit to the sponsor and to the reviewing IRB a report of any unanticipated adverse device effect occurring during an investigation as soon as possible, but in no event later than 10 working days after the investigator first learns of the effect.
 - ii. Withdrawal of IRB approval. An investigator must report to the sponsor, within 5 working days, a withdrawal of approval by the reviewing IRB of the investigator's part of an investigation.
 - iii. Progress. An investigator must submit progress reports on the investigation to the sponsor, the monitor, and the reviewing IRB at regular intervals, but in no event less often than yearly.
 - iv. Deviations from the investigational plan:

¹⁴ <http://www.accessdata.fda.gov/SCRIPTS/cdrh/cfdocs/cfcr/CFRSearch.cfm?fr=812.145>

¹⁵ <http://www.accessdata.fda.gov/SCRIPTS/cdrh/cfdocs/cfcr/CFRSearch.cfm?fr=812.150>



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1. An investigator must notify the sponsor and the reviewing IRB of any deviation from the investigational plan to protect the life or physical well-being of a subject in an emergency.
 2. Such notice must be given as soon as possible, but in no event later than 5 working days after the emergency occurred.
 3. Except in such an emergency, prior approval by the sponsor is required for changes in or deviations from a plan, and if these changes or deviations may affect the scientific soundness of the plan or the rights, safety, or welfare of human subjects, FDA and IRB also is required.
- v. Informed consent. If an investigator uses a device without obtaining informed consent, the investigator must report such use to the sponsor and the reviewing IRB within 5 working days after the use occurs.
 - vi. Final report. An investigator must, within 3 months after termination or completion of the investigation or the investigator's part of the investigation, submit a final report to the sponsor and the reviewing IRB.
 - vii. Other. An investigator must, upon request by a reviewing IRB or FDA, provide accurate, complete, and current information about any aspect of the investigation.



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Appendix A-3 *Additional Requirements for Clinical Trials-- International Conference on Harmonisation-Good Clinical Practice (ICH-GCP)*

1. Investigator's Qualifications and Agreements
 - a. The clinical trial should be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with good clinical practice and the applicable regulatory requirements.
 - b. The investigator should be qualified by education, training, and experience to assume responsibility for the proper conduct of the trial, should meet all the qualifications specified by the applicable regulatory requirements, and should provide evidence of such qualifications through up-to-date curriculum vitae and/or other relevant documentation requested by the sponsor, the IRB, and/or the regulatory authorities.
 - c. The investigator should be thoroughly familiar with the appropriate use of the investigational product, as described in the protocol, in the current Investigator's Brochure, in the product information and in other information sources provided by the sponsor.
 - d. The investigator should be aware of, and should comply with, GCP and the applicable regulatory requirements.
 - e. The investigator/institution should permit monitoring and auditing by the sponsor, and inspection by the appropriate regulatory authorities.
 - f. The investigator should maintain a list of appropriately qualified persons to whom the investigator has delegated significant trial-related duties.
2. Adequate Resources
 - a. The investigator should be able to demonstrate (e.g., based on retrospective data) a potential for recruiting the required number of suitable subjects within the agreed recruitment period.
 - b. The investigator should have sufficient time to properly conduct and complete the trial within the agreed trial period.
 - c. The investigator should have available an adequate number of qualified staff and adequate facilities for the foreseen duration of the trial to conduct the trial properly and safely.
 - d. The investigator should ensure that all persons assisting with the trial are adequately informed about the protocol, the investigational product, and their trial-related duties and functions.
3. Medical Care of Trial Subjects
 - a. A qualified physician (or dentist, when appropriate), who is an investigator or a sub-investigator for the trial, should be responsible for all trial-related medical (or dental) decisions.



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- b. During and following a subject's participation in a trial, the investigator/institution should ensure that adequate medical care is provided to a subject for any adverse events, including clinically significant laboratory values, related to the trial. The investigator/institution should inform a subject when medical care is needed for intercurrent illnesses of which the investigator becomes aware.
 - c. It is recommended that the investigator inform the subject's primary physician about the subject's participation in the trial if the subject has a primary physician and if the subject agrees to the primary physician being informed.
 - d. Although a subject is not obliged to give his/her reasons for withdrawing prematurely from a trial, the investigator should make a reasonable effort to ascertain the reasons, while fully respecting the subject's rights.
4. Communication with IRB
- a. Before initiating a trial, the investigator/institution should have written and dated approval opinion from the IRB for the trial protocol, written informed consent form, consent form updates, subject recruitment procedures (e.g., advertisements), and any other written information to be provided to subjects.
 - b. As part of the investigator's/institution's written application to the IRB, the investigator/institution should provide the IRB with a current copy of the Investigator's Brochure. If the Investigator's Brochure is updated during the trial, the investigator/institution should supply a copy of the updated Investigator's Brochure to the IRB.
 - c. During the trial the investigator/institution should provide to the IRB all documents subject to review.
5. Compliance with Protocol
- a. The investigator/institution should conduct the trial in compliance with the protocol agreed to by the sponsor and, if required, by the regulatory authorities and which was given approval opinion by the IRB. The investigator/institution and the sponsor should sign the protocol, or an alternative contract, to confirm agreement.
 - b. The investigator should not implement any deviation from, or changes of the protocol without agreement by the sponsor and prior review and documented approval opinion from the IRB of an amendment, except where necessary to eliminate an immediate hazards to trial subjects, or when the changes involves only logistical or administrative aspects of the trial (e.g., change in monitors, change of telephone numbers).
 - c. The investigator, or person designated by the investigator, should document and explain any deviation from the approved protocol.
 - d. The investigator may implement a deviation from, or a change of, the protocol to eliminate an immediate hazard to trial subjects without prior IRB approval opinion. As soon as possible, the implemented deviation or change, the reasons for it, and, if appropriate, the proposed protocol amendments should be submitted:



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a) to the IRB for review and approval opinion, b) to the sponsor for agreement and, if required, c) to the regulatory authorities.

6. Investigational Product

- a. Responsibility for investigational product accountability at the trial site rests with the investigator/institution.
- b. Where allowed/required, the investigator/institution may/should assign some or all of the investigator's/institution's duties for investigational product accountability at the trial site to an appropriate pharmacist or another appropriate individual who is under the supervision of the investigator/institution.
- c. The investigator/institution and/or a pharmacist or other appropriate individual, who is designated by the investigator/institution, should maintain records of the product's delivery to the trial site, the inventory at the site, the use by each subject, and the return to the sponsor or alternative disposition of unused product. These records should include dates, quantities, batch/serial numbers, expiration dates (if applicable), and the unique code numbers assigned to the investigational product and trial subjects. Investigators should maintain records that document adequately that the subjects were provided the doses specified by the protocol and reconcile all investigational product received from the sponsor.
- d. The investigational product should be stored as specified by the sponsor and in accordance with applicable regulatory requirements.
- e. The investigator should ensure that the investigational product is used only in accordance with the approved protocol.
- f. The investigator, or a person designated by the investigator/institution, should explain the correct use of the investigational product to each subject and should check, at intervals appropriate for the trial, that each subject is following the instructions properly.
- g. Randomization Procedures and Unblinding: The investigator should follow the trial's randomization procedures, if any, and should ensure that the code is broken only in accordance with the protocol. If the trial is blinded, the investigator should promptly document and explain to the sponsor any premature unblinding (e.g., accidental unblinding, unblinding due to a serious adverse event) of the investigational product.

7. Informed Consent of Trial Subjects

- a. In obtaining and documenting informed consent, the investigator should comply with the applicable regulatory requirements, and should adhere to GCP and to the ethical principles that have their origin in the Declaration of Helsinki. Prior to the beginning of the trial, the investigator should have the IRB's written approval opinion of the written informed consent form and any other written information to be provided to subjects.
- b. The written informed consent form and any other written information to be provided to subjects should be revised whenever important new information becomes available that may be relevant to the subject's consent. Any revised



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written informed consent form, and written information should receive the IRB's approval opinion in advance of use. The subject or the subject's legally acceptable representative should be informed in a timely manner if new information becomes available that may be relevant to the subject's willingness to continue participation in the trial. The communication of this information should be documented.

- c. Neither the investigator, nor the trial staff, should coerce or unduly influence a subject to participate or to continue to participate in a trial.
- d. None of the oral and written information concerning the trial, including the written informed consent form, should contain any language that causes the subject or the subject's legally acceptable representative to waive or to appear to waive any legal rights, or that releases or appears to release the investigator, the institution, the sponsor, or their agents from liability for negligence.
- e. The investigator, or a person designated by the investigator, should fully inform the subject or, if the subject is unable to provide informed consent, the subject's legally acceptable representative, of all pertinent aspects of the trial including the written information and the approval opinion by the IRB.
- f. The language used in the oral and written information about the trial, including the written informed consent form, should be as non-technical as practical and should be understandable to the subject or the subject's legally acceptable representative and the impartial witness, where applicable.
- g. Before informed consent may be obtained, the investigator, or a person designated by the investigator, should provide the subject or the subject's legally acceptable representative ample time and opportunity to inquire about details of the trial and to decide whether or not to participate in the trial. All questions about the trial should be answered to the satisfaction of the subject or the subject's legally acceptable representative.
- h. Prior to a subject's participation in the trial, the written informed consent form should be signed and personally dated by the subject or by the subject's legally acceptable representative, and by the person who conducted the informed consent discussion.
- i. If a subject is unable to read or if a legally acceptable representative is unable to read, an impartial witness should be present during the entire informed consent discussion. After the written informed consent form and any other written information to be provided to subjects, is read and explained to the subject or the subject's legally acceptable representative, and after the subject or the subject's legally acceptable representative has orally consented to the subject's participation in the trial and, if capable of doing so, has signed and personally dated the informed consent form, the witness should sign and personally date the consent form. By signing the consent form, the witness attests that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the subject or the subject's legally acceptable



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representative, and that informed consent was freely given by the subject or the subject's legally acceptable representative.

- j. Both the informed consent discussion and the written informed consent form and any other written information to be provided to subjects should include explanations of the following:
- i. That the trial involves research.
 - ii. The purpose of the trial.
 - iii. The trial treatments and the probability for random assignment to each treatment.
 - iv. The trial procedures to be followed, including all invasive procedures.
 - v. The subject's responsibilities.
 - vi. Those aspects of the trial that are experimental.
 - vii. The reasonably foreseeable risks or inconveniences to the subject and, when applicable, to an embryo, fetus, or nursing infant.
 - viii. The reasonably expected benefits. When there is no intended clinical benefit to the subject, the subject should be made aware of this.
 - ix. The alternative procedures or courses of treatment that may be available to the subject, and their important potential benefits and risks.
 - x. The compensation and/or treatment available to the subject in the event of trial related injury.
 - xi. The anticipated prorated payment, if any, to the subject for participating in the trial.
 - xii. The anticipated expenses, if any, to the subject for participating in the trial.
 - xiii. That the subject's participation in the trial is voluntary and that the subject may refuse to participate or withdraw from the trial, at any time, without penalty or loss of benefits to which the subject is otherwise entitled.
 - xiv. That the monitors, the auditors, the IRB, and the regulatory authorities will be granted direct access to the subject's original medical records for verification of clinical trial procedures and/or data, without violating the confidentiality of the subject, to the extent permitted by the applicable laws and regulations and that, by signing a written informed consent form, the subject or the subject's legally acceptable representative is authorizing such access.
 - xv. That records identifying the subject will be kept confidential and, to the extent permitted by the applicable laws and/or regulations, will not be made publicly available. If the results of the trial are published, the subject's identity will remain confidential.
 - xvi. That the subject or the subject's legally acceptable representative will be informed in a timely manner if information becomes available that may be relevant to the subject's willingness to continue participation in the trial.



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- xvii. The persons to contact for further information regarding the trial and the rights of trial subjects, and whom to contact in the event of trial-related injury.
- xviii. The foreseeable circumstances and/or reasons under which the subject's participation in the trial may be terminated.
- xix. The expected duration of the subject's participation in the trial.
- xx. The approximate number of subjects involved in the trial.
- k. Prior to participation in the trial, the subject or the subject's legally acceptable representative should receive a copy of the signed and dated written informed consent form and any other written information provided to the subjects. During a subject's participation in the trial, the subject or the subject's legally acceptable representative should receive a copy of the signed and dated consent form updates and a copy of any amendments to the written information provided to subjects.
- l. When a clinical trial (therapeutic or non-therapeutic) includes subjects who can only be enrolled in the trial with the consent of the subject's legally acceptable representative (e.g., minors, or patients with severe dementia), the subject should be informed about the trial to the extent compatible with the subject's understanding and, if capable, the subject should sign and personally date the written informed consent.
- m. Except as described above, a non-therapeutic trial (i.e. a trial in which there is no anticipated direct clinical benefit to the subject), should be conducted in subjects who personally give consent and who sign and date the written informed consent form.
- n. Non-therapeutic trials may be conducted in subjects with consent of a legally acceptable representative provided the following conditions are fulfilled: a) The objectives of the trial cannot be met by means of a trial in subjects who can give informed consent personally. b) The foreseeable risks to the subjects are low. c) The negative impact on the subject's well-being is minimized and low. d) The trial is not prohibited by law. e) The approval opinion of the IRB is expressly sought on the inclusion of such subjects, and the written approval opinion covers this aspect. Such trials, unless an exception is justified, should be conducted in patients having a disease or condition for which the investigational product is intended. Subjects in these trials should be particularly closely monitored and should be withdrawn if they appear to be unduly distressed.
- o. In emergency situations, when prior consent of the subject is not possible, the consent of the subject's legally authorized representative, if present, should be requested. When prior consent of the subject is not possible, and the subject's legally authorized representative is not available, enrollment of the subject in research is not permissible pursuant to the Florida Patient Bill of Rights which states the following: "a patient has the right to know if medical treatment is for purposes of experimental research and to consent prior to participation in such experimental research."



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8. Records and Reports

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

9. Progress Reports

- a. The investigator should submit written summaries of the trial status to the IRB annually, or more frequently, if requested by the IRB.
- b. The investigator should promptly provide written reports to the sponsor, the IRB and, where applicable, the institution on any changes significantly affecting the conduct of the trial, and/or increasing the risk to subjects.

10. Safety Reporting

- a. All serious adverse events (SAEs) should be reported immediately to the sponsor except for those SAEs that the protocol or other document (e.g., Investigator's Brochure) identifies as not needing immediate reporting. The immediate reports



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

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



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

1. When appropriate, research protocols must be reviewed and approved by the IRB prior to the Department of Defense approval. Consult with the Department of Defense funding component to see whether this is a requirement.
2. Employees of the Department of Defense (including temporary, part-time, and intermittent appointments) may not be able to legally accept payments to participate in research and should check with their supervisor before accepting such payments. Employees of the Department of Defense cannot be paid for conducting research while on active duty.
3. Service members must follow their command policies regarding the requirement to obtain command permission to participate in research involving human subjects while on-duty or off-duty.
4. Components of the Department of Defense might have stricter requirements for research-related injury than the DHHS regulations.
5. There may be specific educational requirements or certification required.
 - a. Initial and continuing research ethics education is required for all personnel who conduct, review, approve, oversee, support, or manage Human Research.
 - b. The IRB staff, chair, and members; and researchers and research staff become aware of the specific requirements contained in Department of Defense regulations via the trainings conducted on the HRPP toolkit (specifically, **HRP-318 WORKSHEET: Additional Federal Agency Criteria**) and are educated about these requirements when appropriate.
6. When assessing whether to support or collaborate with this institution for research involving human subjects, the Department of Defense may evaluate this institution's education and training policies to ensure the personnel are qualified to perform the research based on the complexity and risk of the research.
7. The following shall be promptly reported (no longer than within 30 days) to the DOD human research protection officer:
 - a. results of IRB continuing review
 - b. change of reviewing IRB
 - c. when significant changes to the research protocol are approved by the IRB
 - d. when the Organization is notified by any Federal department, agency, or national organizations that any part of the HRPP is under investigation for cause involving a DoD-supported research protocol
8. When conducting multi-site research, a formal agreement between organizations is required to specify the roles and responsibilities of each party.
9. When research involves U.S. military personnel, policies and procedures require limitations on dual compensation:
 - a. Prohibit an individual from receiving pay of compensation for research during duty hours.



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- b. An individual may be compensated for research if the participant is involved in the research when not on duty.
 - c. Federal employees while on duty and non-Federal persons may be compensated for blood draws for research up to \$50 for each blood draw.
 - d. Non-Federal persons may be compensated for research participating other than blood draws in a reasonable amount as approved by the IRB according to local prevailing rates and the nature of the research.
10. Other specific requirements of the Department of Defense research be found in the “Additional Requirements for Department of Defense (DOD) Research” section in **HRP-318 WORKSHEET: Additional Federal Criteria.**

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

1. You must report the following within ten business days to the Department of Energy human subject research program manager
 - a. Any significant adverse events, unanticipated risks; and complaints about the research, with a description of any corrective actions taken or to be taken.
 - b. Any suspension or termination of IRB approval of research.
 - c. Any significant non-compliance with HRPP procedures or other requirements.
2. You must report the following within three business days to the Department of Energy human subject research program manager
 - a. Any compromise of personally identifiable information must be reported immediately.
3. Other specific requirements of the Department of Energy (DOE) research be found in the “Additional Requirements for Department of Energy (DOE) Research” section in **HRP-318 WORKSHEET: Additional Federal Criteria**.



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

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

1. Implementation of Bureau programmatic or operational initiatives made through pilot projects is not considered to be research.
2. The project must not involve medical experimentation, cosmetic research, or pharmaceutical testing.
3. The research design must be compatible with both the operation of prison facilities and protection of human subjects.
4. Investigators must observe the rules of the institution or office in which the research is conducted.
5. Any investigator who is a non-employee of the Bureau of Prisoners must sign a statement in which the investigator agrees to adhere to the requirements of 28 CFR §512.
6. The research must be reviewed and approved by the Bureau Research Review Board.
7. Incentives cannot be offered to help persuade inmate subjects to participate. However, soft drinks and snacks to be consumed at the test setting may be offered. Reasonable accommodations such as nominal monetary recompense for time and effort may be offered to non-confined research subjects who are both: No longer in Bureau of Prisons custody. Participating in authorized research being conducted by Bureau employees or contractors.
8. A non-employee of the Bureau may receive records in a form not individually identifiable when advance adequate written assurance that the record will be used solely as a statistical research or reporting record is provided to the agency.
9. Except as noted in the consent statement to the subject, you must not provide research information that identifies a subject to any person without that subject's prior written consent to release the information. For example, research information identifiable to a particular individual cannot be admitted as evidence or used for any purpose in any action, suit, or other judicial, administrative, or legislative proceeding without the written consent of the individual to whom the data pertain.
10. Except for computerized data records maintained at an official Department of Justice site, records that contain non-disclosable information directly traceable to a specific person may not be stored in, or introduced into, an electronic retrieval system.
11. If you are conducting a study of special interest to the Office of Research and Evaluation but the study is not a joint project involving Office of Research and Evaluation, you may be asked to provide Office of Research and Evaluation with the computerized research data, not identifiable to individual subjects, accompanied by detailed documentation. These arrangements must be negotiated prior to the beginning of the data collection phase of the project.



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12. Required elements of disclosure additionally include:
 - a. Identification of the investigators.
 - b. Anticipated uses of the results of the research.
 - c. A statement that participation is completely voluntary and that the subject may withdraw consent and end participation in the project at any time without penalty or prejudice (the inmate will be returned to regular assignment or activity by staff as soon as practicable).
 - d. A statement regarding the confidentiality of the research information and exceptions to any guarantees of confidentiality required by federal or state law. For example, an investigator may not guarantee confidentiality when the subject indicates intent to commit future criminal conduct or harm himself or herself or someone else, or, if the subject is an inmate, indicates intent to leave the facility without authorization.
 - e. A statement that participation in the research project will have no effect on the inmate subject's release date or parole eligibility.
13. You must have academic preparation or experience in the area of study of the proposed research.
14. The IRB application must include a summary statement, which includes:
 - a. Names and current affiliations of the investigators.
 - b. Title of the study.
 - c. Purpose of the study.
 - d. Location of the study.
 - e. Methods to be employed.
 - f. Anticipated results.
 - g. Duration of the study.
 - h. Number of subjects (staff or inmates) required and amount of time required from each.
 - i. Indication of risk or discomfort involved as a result of participation.
15. The IRB application must include a comprehensive statement, which includes:
 - a. Review of related literature.
 - b. Detailed description of the research method.
 - c. Significance of anticipated results and their contribution to the advancement of knowledge.
 - d. Specific resources required from the Bureau of Prisons.
 - e. Description of all possible risks, discomforts, and benefits to individual subjects or a class of subjects, and a discussion of the likelihood that the risks and discomforts will actually occur.
 - f. Description of steps taken to minimize any risks.
 - g. Description of physical or administrative procedures to be followed to: Ensure the security of any individually identifiable data that are being collected for the study.
 - h. Destroy research records or remove individual identifiers from those records when the research has been completed.



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- i. Description of any anticipated effects of the research study on organizational programs and operations.
 - j. Relevant research materials such as vitae, endorsements, sample consent statements, questionnaires, and interview schedules.
16. The IRB application must include a statement regarding assurances and certification required by federal regulations, if applicable.
17. You must assume responsibility for actions of any person engaged to participate in the research project as an associate, assistant, or subcontractor.
18. At least once a year, you must provide the Chief, Office of Research and Evaluation, with a report on the progress of the research.
19. At least 12 working days before any report of findings is to be released, you must distribute one copy of the report to each of the following: the chairperson of the Bureau Research Review Board, the regional director, and the warden of each institution that provided data or assistance.
20. You must include an abstract in the report of findings.
21. In any publication of results, you must acknowledge the Bureau's participation in the research project.
22. You must expressly disclaim approval or endorsement of the published material as an expression of the policies or views of the Bureau.
23. Prior to submitting for publication the results of a research project conducted under this subpart, You must provide two copies of the material, for informational purposes only, to the Chief, Office of Research and Evaluation, Central Office, Bureau of Prisons.
24. Other specific requirements of the Department of Justice (DOJ) Research Conducted within the Federal Bureau of Prisons (BOP) can be found in the “Additional Requirements for Department of Justice (DOJ) Research Conducted within the Federal Bureau of Prisons (BOP)” section in **HRP-318 WORKSHEET: Additional Federal Criteria**.

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

1. The project must have a privacy certificate approved by the National Institute of Justice Human Subjects Protection Officer.
2. All investigators and research staff are required to sign employee confidentiality statements, which are maintained by the responsible investigator.
3. The confidentiality statement on the consent document must state that confidentiality can only be broken if the subject reports immediate harm to subjects or others.
4. Under a privacy certificate, investigators and research staff do not have to report child abuse unless the subject signs another consent document to allow child abuse reporting.
5. A copy of all data must be de-identified and sent to the National Archive of Criminal Justice Data, including copies of the informed consent document, data collection instruments, surveys, or other relevant research materials.



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- 6. Other specific requirements of the Department of Justice (DOJ) Research Funded by the National Institute of Justice can be found in the “Additional Requirements for Department of Justice (DOJ) Research” section in **HRP-318 WORKSHEET: Additional Federal Criteria.**



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

1. Each school at which the research is conducted must provide an assurance that they comply with the Family Educational Rights and Privacy Act (FERPA) and the Protection of Pupil Rights Amendment (PPRA).
2. Provide a copy of all surveys and instructional material used in the research. Upon request parents of children¹⁶ involved in the research¹⁷ must be able to inspect these materials.
3. The school in which the research is being conducted must have policies regarding the administration of physical examinations or screenings that the school may administer to students.
4. Other specific requirements of the Department of Education (ED) Research can be found in the “Additional Requirements for Department of Education (ED) Research” section in **HRP-318 WORKSHEET: Additional Federal Criteria.**

¹⁶ Children are persons enrolled in research not above the elementary or secondary education level, who have not reached the age or majority as determined under state law.

¹⁷ Research or experimentation program or project means any program or project in any research that is designed to explore or develop new or unproven teaching methods or techniques.

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

1. Research conducted, supported, or intended to be submitted to EPA is subject to Environmental Protection Agency Regulations.
2. Intentional exposure of pregnant women or children to any substance is prohibited.
3. Observational research involving pregnant women and fetuses are subject to additional DHHS requirements for research involving pregnant women (45 CFR §46 Subpart B) and additional DHHS requirements for research involving children (45 CFR §46 Subpart D.)
4. Research involving children must meet category #1 or #2.
5. Other specific requirements of the Environmental Protection Agency (EPA) Research can be found in the “Additional Requirements for Environmental Protection Agency (EPA) Research and Research Intended to be Submitted to the Environmental Protection Agency” section in **HRP-318 WORKSHEET: Additional Federal Criteria**.



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Appendix A-9 University Fees and Related Financial / Billing Information

1. What HSRO/IRB Fees apply to my research study?

- a. **Research Compliance Fee** – Applicable to research protocols that are reviewed by the IRB/HSRO and are *non-government sponsored and supported by for-profit sponsors/agencies/foundations that do not otherwise cover compliance fees through indirect costs to the institution or other mechanisms and contractually allow for processing of compliance fees*. This fee of \$350 is charged to new protocols only. This fee will be collected through a journal entry using sub code 4205.
- b. **HSRO Processing Fee** – Will be applicable to all studies *supported by for-profit sponsors and/or agencies/foundations that do not otherwise cover IRB fees through indirect costs to the institution or other mechanisms and contractually allow for processing of IRB fees*.

2. How will the HSRO/IRB Fees be billed?

All applicable submissions subject to the fee schedule will require the completion of the HSRO/IRB activity entitled *Update Billing Information before the ‘Submit’* activity can be executed by the PI or PI Proxy. Upon submission, the account information provided in this *Update Billing Information* activity will be confirmation for the HSRO to process payment and journal the fee accordingly.

The HSRO will bill and automatically journal all applicable submissions, in the subsequent month from the time an IRB determination is recorded. The journals will be provided to the financial data entry custodians for review and processing. The current HSRO/IRB fee schedule can be found on our webpage:

<http://hsro.med.miami.edu/irbs/fees>.

3. What if the corresponding sponsored account has not been established at the time of submission?

If a sponsored account has not been established prior to the submission, the appropriate account to be used for payment is the corresponding Departmental IRB account number. Upon issuance of the sponsored account the Department/Study team will be responsible to do the internal journal to transfer the IRB fees that were previously recorded under the Departmental IRB account number. The PI/Study team must update the account number via the *‘Update Billing Information’* in the study workspace in the IRB7 system once



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the sponsored account is issued.

4. **What happens if I provide an incorrect account number or need to update an account number in the application?**

If the account number submitted is returned to us by the data entry custodian for being an invalid and/or frozen/closed account number, the Departmental account number for HSRO/IRB/Research fees will automatically be used. The PI/study team must update the account number via the “Update Billing Information” activity in the study workspace in the IRB7 system.

5. **Can we be provided invoices from the HSRO/IRB?**

Yes. If the financial posting and IRB determination is not sufficient for a sponsor, please invoice the sponsor directly. If an invoice is required from the HSRO/IRB, please contact our office and we can prepare and provide one from us to you. Please note we do not bill the sponsor directly as we have previously collected the fee.



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Appendix A-10 Investigator Guidance: Elements of Consent

Obtaining informed consent from a prospective research participant is essential. Unless waived by the IRB, a consent form is an integral part of the consent process through which researchers seek volunteers to participate in human research studies or clinical trials. As such, great attention must be given to the creation of these documents to ensure a prospective research participant understands and comprehends the information disclosed in consent forms so that they are able to make an informed decision about whether to participate in human research studies.

To meet federal requirements, consent forms should be written in language understandable to the participant (or authorized representative). Every effort should be made to ensure that technical and scientific terms are adequately explained or that common terms are substituted.

Standard IRB Consent Format

The HSRO/IRB has developed standard language as well as a standard format to be used in portions of all consent documents. These documents are available on the HSRO website. Each investigator should determine the IRB's requirements before submitting a study for initial review. Where changes are needed from the standard paragraphs or format, the investigator can save time by anticipating the local IRB's concerns and explaining in the submission to the IRB why the changes are necessary.

Sponsor-prepared sample consent documents

For some funded studies, sample or draft consent documents may be provided by a sponsor or cooperative study group. However, the UM IRB that reviews the study is the final authority on the content of the consent documents that is approved 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 consent document is considered 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. Any substantive changes to the document made by the UM IRB must be submitted to FDA (by the sponsor) for review and approval.



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Elements of Consent

Informed consent documents for studies that are subject to the DHHS regulations must meet requirements specified in 45 CFR 46.116. Informed consent documents for studies that are subject to the FDA regulations must meet the requirements of 21 CFR 50.25. Both sets of regulations require the same* eight (8) basic elements of consent and six (6) additional elements of consent that applies based on the study to be conducted. The IRBs have the final authority for ensuring the adequacy of the information in the informed consent document(s). All consent forms should meet the minimum requirements of the respective regulations with the expectation that a well-written document will exceed those requirements.

Required Elements of Consent

- A statement that:
 - the study involves research
 - explains the purposes of the research
 - explains the expected duration of the subject's participation
 - explains the procedures to be followed
 - identifies any procedures which 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*
- As 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

Required for More than Minimal Risk Research

- 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



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Additional Elements

- 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.
- Approximate number of subjects involved in the study.

Required for FDA-Regulated Research

- The possibility that the Food and Drug Administration may inspect the records.
- 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."
- Please note, pursuant to FDA guidance, the investigator and sponsor are responsible for determining whether a trial is an applicable clinical trial and to include the required statement in the informed consent document, as appropriate for approval by the IRB. If an error is made, the IRB should be notified as soon as possible and a revised consent form that includes the required statement should be provided to the IRB for review and approval.

-

Recommended for Clinical Trials

- The data collected on the subject to the point of withdrawal remains part of the study database and may not be removed
- The investigator will ask a subject who is withdrawing whether the subject wishes to provide further data collection from routine medical care
- The probability for random assignment to each treatment
- The subject's responsibilities
- When there is no intended clinical benefit to the subject, a statement to this effect
- The monitors, auditors, IRB, and regulatory authorities will be granted direct access to the subject's original medical records for verification of clinical trial procedures and data, without violating the confidentiality of the subject, to the extent permitted by applicable



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laws and regulations and that, by signing the consent document, the subject or LAR is authorizing such access

- If the results of the trial are published, the subject's identity will remain confidential
- Amount and schedule of all payments
- How to contact the research team for questions, concerns, or complaints about the research
- How to contact someone independent of the research team for questions, concerns, or complaints about the research; questions about the subjects' rights; to obtain information; or to offer input
- Whom to contact in the event of a research-related injury to the subject

UM-Specific Requirements

- UChart language
- IRS template language for compensation of \$600 or more per calendar year
- Category B devices – “You will not be billed for a device, a price greater than that charged to the University which should not exceed an amount necessary to recover the costs of manufacture, research development, and handling of the device”
- 24-hour contact number

References:

1. 45 CFR 46.116
2. OHRP Informed Consent Checklist – Basic and Additional Elements
3. 21 CFR 50.20
4. FDA: A Guide To Informed Consent - Information Sheet
5. UM Informed Consent Boilerplate Language

*Basic element a(5) of the DHHS regulations differ from that of the FDA regulations insofar as the FDA has an added requirement to disclose the possibility that the FDA may inspect the records.