



Investigator Manual

August 1, 2015



Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	08/01/15	2 of 43

Table of Contents

Scope	3
What is the purpose of this manual?	3
Definitions	3
What is Human Research?	3
Who may be a principal investigator?	3
What training do my staff and I need to conduct Human Research?	4
What financial interests do my staff and I need to disclose to conduct Human Research?.....	5
What other approvals are required before initiating Human Research?.....	5
How do I submit new Human Research to the IRB?.....	6
How do I submit a grant-only submission to the IRB?	6
Does the IRB charge to review research?.....	6
When can I submit to an external IRB?.....	7
How do I write an Investigator Protocol?.....	7
How do I store Human Research data to protect confidentiality?.....	8
Should I obtain a Certificate of Confidentiality for my research?	8
Am I a mandated reporter of child abuse?.....	8
How do I conduct research using genetic information?	9
How do I obtain Institutional Certification for submission of genomic data to an NIH-designated data repository?.....	9
What if I hold the IND for an investigational drug or an IDE for an investigational device?.....	9
When should I register my research with ClinicalTrials.gov?	9
What is an appropriate recruitment method?.....	9
Do I need IRB review for classroom-based research projects conducted by students?	10
Can I recruit my own students or people in my employ to participate my research?.....	10
How do I obtain a waiver or alteration of informed consent?.....	10
How do I obtain informed consent from participants?.....	11
Do research participants have to sign a consent document?	11
How do I create consent or assent documents?.....	11
How do I document consent or assent?	11
When am I required to obtain a HIPAA Authorization?.....	12
What if I want to enroll participants with limited English proficiency?	14
What supporting documents must I include with my IRB submission?.....	15
What are the different regulatory classifications that research activities may fall under?	15
What are the decisions the IRB can make when reviewing proposed research?.....	16
How does the IRB decide whether to approve Human Research?.....	16
What other state or federal requirements must be met?	16
What will happen after IRB review?.....	17
What are my obligations as Investigator in order to conduct Human Research?.....	17
How do I submit a modification?	18
How do I submit continuing review?	19
How do I close out a study?	19
How do I report new information to the IRB?	19
How long do I keep records?.....	21
What should I do if I leave Northwestern University?.....	21
What if I need to use an unapproved drug, biologic, or device and there is no time for IRB review?.....	21
How do I get additional information and answers to questions?.....	22

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	08/01/15	3 of 43

Scope

Throughout this document “institution” refers to Northwestern University.

What is the purpose of this manual?

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

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

Definitions

Although some terms are defined in this document, a comprehensive set of definitions relevant for Human Research can be found in “SOP: Definitions (HRP-001)”. Please refer to that SOP for clarification of certain terms employed throughout this document.

What is Human Research?

An algorithm for determining whether an activity is Human Research can be found in the “WORKSHEET: Human Research (HRP-310),” located in the Templates, Forms and SOP page of the IRB web site. Use this document for guidance as to whether an activity meets either the DHHS or USFDA definition of Human Research, keeping in mind that the IRB or IRB Office makes the ultimate determination in questionable cases as to whether an activity constitutes Human Research participant to IRB oversight.

- You are responsible not to conduct Human Research without prior IRB review and approval. The IRB will not review or approve research activity that has already occurred.
- If you have questions about whether an activity is Human Research, contact the IRB Office, who will provide you with a determination. If you wish to have a written determination, submit a new study in eIRB+ using the “Human Research Determination Form (HRP-503)” in lieu of a protocol.
- See “WORKSHEET: Exempt Determination (HRP-312)” for activities that are exempt from IRB regulatory requirements. Note that you must still submit exempt Human Research for IRB Office 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 one of the institution’s IRBs.

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 list of who may and may not serve as PI, though unique circumstances (e.g., requests from staff) may be given special consideration.

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	08/01/15	4 of 43

PI Eligible	Case-by-case	Not PI Eligible
<ul style="list-style-type: none"> • Curators; • Instructors; • Librarians; • Non-tenure-track research and/or clinical faculty (full, associate, and assistant professors); • Tenure-track faculty (full, associate, and assistant professors); and • Senior research investigators (Faculty with emeritus status or who are tenured and retired but wish to continue as PI). 	<ul style="list-style-type: none"> • Adjuncts; • Lecturers; • Contributed Services Faculty; • Health System Clinicians; • Visiting faculty; and • Visiting scholars. <p>Contact the Associate Vice President for Research via email to request permission for such faculty. Please include your CV, a copy of your protocol, and a letter of support from your Department Chair/Division Chief.</p> <p>If approval is granted, upload the confirmation email into the “Supporting Documents” section in your eIRB+ submission.</p>	<ul style="list-style-type: none"> • Postdoctoral fellows and research assistants (graduate students); • Research associates; and • Undergraduate students

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 institutional policies.

PIs, Co-investigators (Co-Is), and other staff conducting Human Research must complete one of the following training programs:

- The Collaborative Institutional Training Initiative (CITI) human subjects online training program. The [CITI site](http://www.citiprogram.org/) can be accessed at <http://www.citiprogram.org/>.
- The National Institutes of Health (NIH) Protection Human Research Participants Course (PHRP). The [NIH PHRP](http://phrp.nihtraining.com/users/login.php) site can be accessed at <http://phrp.nihtraining.com/users/login.php>.
- In-Person Training conducted by the IRB Office. More information can be found at <http://irb.northwestern.edu/training/in-person>.
- Additional training may be required for individuals when conducting research funded by certain federal agencies (e.g. Department of Defense, Department of Navy).

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

All members of the research team involved in the conduct of Human Research 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 participants.

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	08/01/15	5 of 43

For each new submission received in eIRB+, the IRB Office will verify that training requirements have been met. If they have not been met, the IRB Office will return that submission to the research team. You may re-submit for review only after all training requirements have been met or after removing individuals who have not met requirements from your research team as appropriate.

Individuals from outside of the institution with whom you are collaborating and for whom the institution's IRB has taken oversight through an Institutional Agreement for IRB Review should provide you with evidence of appropriate training completion. You are to include that information in your eIRB+ submission. Generally, evidence of training similar to the options described above will be accepted.

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

You are responsible for following all Northwestern University Conflict of Interest policies and procedures, which can be found at <http://www.northwestern.edu/coi/policy/>.

What other approvals are required before initiating Human Research?

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

- Childhood Educational Settings. If you are conducting research within childhood educational settings, e.g., pre-school, primary school, or secondary school, you are required to obtain permission from an educational official at your research site prior to initiating research. You may use "Template Letter - School Permission to Conduct Research (HRP-504)" if the research site does not already have a standard letter it issues to investigators. See, Additional Requirements for Department of Education (USED) Research (Appendix A-7) for more information about research using educational records.
- Clinical Affiliates. If you are conducting research at one of the institution's clinical affiliates, additional approvals may be required. For instance, you are required to submit the Research Protocol Review Form for review and approval for research conducted at Northwestern Memorial Healthcare Corporation site. See also the "When am I required to obtain HIPAA Authorization?" section below for more information about research using Protected Health Information.
- Nursing Home Research in the State of Illinois. Research in nursing homes in the State of Illinois requires additional state approvals. Please note if you are conducting nursing home research outside the State of Illinois you may need additional approvals. Please contact the IRB Office for assistance.
- International Research. If you are conducting research outside of the United States, you are required to follow local regulations governing Human Research for your host country in addition to the requirements described in this document. The IRB Office may request evidence of local Human Research review by an official review body. Please consult the

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	08/01/15	6 of 43

latest [Edition of the International Compilation of Human Research Standards](#), and the [International Projects Section](#) of the NU IRB website for guidance.

- **Radiation Safety.** If your research involves radiation that would not otherwise be administered as part of a participant’s standard medical treatment, you must obtain approval from the Northwestern Memorial Healthcare (NMH) Radiation Safety Officer. [The Radiation Dosimetry Form](#) can be found at <http://irb.northwestern.edu/sites/default/files/template/radiation-dosimetry-form-1336593471.doc>.
- Please consult the following webpage for additional information: <http://irb.northwestern.edu/process/new-study/additional-committee-review-approval>.

How do I submit new Human Research to the IRB?

Log in to eIRB+ using your NU NetID and password. Click “Create New Study” under my current activities. Complete each section of the online IRB Application and associated Research Supplemental Submission. Please reference Help Text for additional information. eIRB+ maintains 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.

Once you complete your eIRB+ submission, you will be required also to complete a Research Supplemental Submission (RSS) before submitting your research for review. Note that although RSS information is collected in tandem with IRB information, RSS information is not considered to be a component of your IRB submission and is, therefore, not reviewed by the IRB. RSS information is collected for institutional operating and reporting purposes. Any questions regarding RSS information should be directed to the appropriate institutional office managing that information, as indicated in the RSS submission form.

How do I submit a grant project to the IRB?

Umbrella grants (used to fund other IRB approved projects), as well as some development and training grants are not considered Human Research as defined above. Use Section 3.0 of “Human Research Determination Form (HRP-503)” to submit a grant-only application in eIRB+ in order to receive an acknowledgement letter from the IRB Office.

If your grant application is a Just in Time (JIT) submission, you need to submit an IRB protocol with as much detail as you have at the time of submission. Include at the top of the protocol document that the submission is JIT and that before you engage participants, you will submit a modification to upload the necessary participant facing documents such as the recruitment material, consents, and data collection instruments.

Does the IRB charge to review research?

Yes, the IRB does charge a fee for review of industry-sponsored research including use of an external IRB. Please see the following webpage on [Fees](#) for more information: <http://irb.northwestern.edu/about/fees>.

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	08/01/15	7 of 43

When can I submit to an external IRB?

You can submit to an external IRB only if your research fits into one of the scenarios described in “Standard Operating Procedure for Utilizing Central IRBs (HRP-092)”.

How do I write an Investigator Protocol?

If you received an Investigator Protocol from your study sponsor or lead study investigator for multi-site research, use “Template Local Protocol Addendum (HRP-508)” to document relevant local information not included in the sponsor or multi-site protocol. Upload both the received protocol and the local protocol addendum in eIRB+. This applies to Biomedical and Social Behavioral research.

Use the “Biomedical Template Protocol (HRP-593)” for Biomedical research or “Social Behavioral Template Protocol (HRP-583)” for Social Behavioral research as a starting point for drafting a new Investigator Protocol, and reference the instructions in italic text for the information the IRB looks for when reviewing research. Here are some key points to remember when developing an Investigator Protocol:

- You are required to use one of the template protocols listed above for new Human Research where the local protocol addendum alone will not suffice to describe all of your research activities, unless your department or division already has a template protocol in use that substantially addresses all of the items in the templates above. If your research was approved prior to the implementation of eIRB+, you will generally not be required to use one of the templates above. The IRB Office may ask for additional information from you in case your converted eIRB+ record is incomplete.
- Bullet points in the protocol templates serve as guidance to investigators when developing an Investigator Protocol for submission to the IRB. All comments are meant to be deleted prior to submission.
- When writing an Investigator Protocol, always keep an electronic copy. You will need to modify this copy when making changes to the Investigator Protocol. Electronic copies are also stored in eIRB+.
- 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 participants in your research unless you indicate this in your inclusion criteria as the inclusion of participants in these populations has regulatory implications.
 - Adults unable to provide legally effective consent
 - Individuals who are not yet adults (infants, children, teenagers)
 - Pregnant women
 - Prisoners
- If you are conducting community-based participatory research, you may contact the IRB Office for information about:
 - Research studies using a community-based participatory research design
 - Use of community advisory boards
 - Use of participant advocates

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	08/01/15	8 of 43

- Partnerships with community-based organizations

How do I store Human Research data to protect confidentiality?

You must have reasonable plans and procedures in place to maintain the confidentiality of the research records. You must include a description of your data storage methods in the protocol, or in the local protocol addendum to the received protocol, you upload in eIRB+.

- Your electronic data storage plan must be consistent with any of NUIT Policies, Guidelines, and Practices, which can be found at <http://www.it.northwestern.edu/policies/index.html>.
- If you are conducting Human Research under the auspices of Feinberg School of Medicine, you must follow Feinberg data security policies, which can be found at <http://www.feinberg.northwestern.edu/it/standards-policies/index.html>.

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. Note that a Certificate of Confidentiality does not protect information as it relates to the State mandate and University policy to report child abuse and neglect.

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

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

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

Am I a mandated reporter of child abuse?

All University employees (including all faculty, staff, and student employees) regardless of their position or assignment, are required by law (under the Abused and Neglected Child Reporting Act (ANCRA), 325 ILCS 5/1 et seq.) and by University policy (http://policies.northwestern.edu/docs/Reporting_Child_Abuse_and_Neglect.pdf) to report suspected cases of child abuse and/or neglect. All students, volunteers, and third-party contractors who are engaged in research activities are required by University policy to report suspected cases of child abuse and/or neglect.

University employees are not mandated reporters in Illinois of elderly abuse, neglect, or exploitation. However, it is possible that during the conduct of research you will encounter a circumstance in which an elderly participant in your research reports abuse, neglect, or exploitation. While there is no University policy that requires reporting, you may decide it is your professional duty to make a report in good faith to the Illinois Department of Aging. By law, anyone making an elder abuse report in good faith has civil and criminal immunity from liability and professional disciplinary action.

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	08/01/15	9 of 43

How do I conduct research using genetic information?

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

Recommended GINA language is provided in “Biomedical Template Consent Document (HRP-592)” for you to include for participants.

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

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

What if I hold the IND for an investigational drug or an IDE for an investigational device?

Research involving investigational drugs, biologics, or devices where the investigator holds the IND or IDE is participant to additional regulatory oversight that is generally outside of the IRB’s purview. The institution has resources available to investigators who wish to conduct such research. Please see the following [webpage](#) for more information:

<http://www.nucats.northwestern.edu/resources-services/research-study-support/center-clinical-research/index.html>.

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 the “Biomedical Template Consent Document (HRP-592)”.

Please also see the following webpage for more information:

<http://www.nucats.northwestern.edu/resources-services/research-study-support/center-clinical-research/#CTG>.

What is an appropriate recruitment method?

You must include a description of your recruitment methods in the protocol, or in the local protocol addendum to the received protocol, you upload in eIRB+. Additional considerations or requirements for recruitment can be found at <http://www.irb.northwestern.edu/process/new->

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	08/01/15	10 of 43

[study/requirements/recruitment-materials-guidelines](#). That webpage will be updated periodically, so please refer to it for each new study you submit.

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

The University recognizes that some student projects conducted to fulfill course requirements involve activities which, in a different context, might meet the definition of human subjects research. It is the policy of the University to not require IRB review of classroom research projects that are designed to teach students research methods. In the circumstance of a classroom assignment that might otherwise constitute human subjects research but which does not require IRB review because it is a classroom assignment, the individual faculty members and departments are responsible for overseeing the activities as defined in the Classroom-Based Research Projects guidance. See <http://www.irb.northwestern.edu/sbs/classroom-based-projects> for additional guidance.

However, there are some student human research projects that will always require IRB review: Doctoral dissertations; funded research; research conducted through collaborations external to NU, Master's theses, and honors theses. All of these must be reviewed and approved by the IRB before students may begin their research. If you have any questions about whether student projects need IRB review, contact the IRB Office.

Can I recruit my own students or people in my employ to participate my research?

An Investigator's use of students, employees or other subordinates as research participants presents the possibility for undue influence or even coercion. The regulatory requirements for IRB review and approval provide that when some or all of the participants are likely to be vulnerable because of a power differential, additional safeguards are needed to protect the rights and welfare of these participants. (See 45 CFR 46.111(b)). Although it is possible to recruit students and others with less power to your projects, in such situations, the IRB will review the protocol and research procedures to ensure that participation is voluntary, private and confidential, and that the decision to participate or not participate will not affect grades, class standing or employment in anyway. If you have any questions about how to build in the necessary protections into your research process, contact the IRB office.

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

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

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	08/01/15	11 of 43

How do I obtain informed consent from participants?

You must describe your process for obtaining informed consent from participants for participation in Human Research. The process you employ for obtaining informed consent will depend on the research setting and your participant population. The consent *process* is distinct from the consent *document*. When written documentation of consent is a requirement for IRB approval, a participant or Legally Authorized Representative (LAR) must sign a consent document, but only after you have led participants through your approved consent process. See the “Consent Process” section of “WORKSHEET: Criteria for Approval (HRP-314)” for elements to include in your consent process. See also [Process for Obtaining Consent](#) on the IRB’s website.

Do research participants have to sign a consent document?

The IRB may waive the requirement to obtain written documentation of informed consent if certain conditions are met. See “CHECKLIST: Waiver of Written Documentation of Consent (HRP-411)” for the criteria the IRB uses to determine whether a waiver of written documentation of consent is acceptable. Include information in your protocol that will help the IRB make a determination. A participant or Legally Authorized Representative must sign a consent document if the IRB has not waived the requirement to obtain written documentation of informed consent.

How do I create consent or assent documents?

Use the “Biomedical Template Consent Document (HRP-592)” for Biomedical Research or “Social Behavioral Template Consent Document (HRP-582)” for Social Behavioral research to create a consent document. Each template contains information that is *generally* relevant for each type of research. You may ultimately need to use sections from both templates for your consent document

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 the IRB’s “WORKSHEET: Criteria for Approval (HRP-314)” to ensure that these elements are addressed. When using the short form of consent documentation the appropriate signature block from one of the template consent documents above 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 Office will also watermark consent documents with IRB approval and expiration dates.

The IRB allows the person obtaining assent to document assent on the consent document and does not routinely require a separate assent form for adults incapable of providing consent or for children. Include the appropriate signature block from the consent document template for the consent document you submit for review. Study teams are encouraged to develop a separate assent document when appropriate, considering the research context, to support the informed consent process.

How do I document consent or assent?

Use the signature sections on the consent approved by the IRB. Complete all items, including dates and optional elements.

The following are the requirements for long form consent documents:

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	08/01/15	12 of 43

- The participant or representative 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 participants 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 participant.

The following are the requirements for short form consent documents:

- The participant or representative signs and dates the short form consent document and the summary.
- The individual obtaining consent signs and dates the short form consent document and 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 consent document and summary are provided to the participant or representative.

The IRB may require separate signatures for the assent of adults incapable of providing consent or for children, although such option is available in the template consent document. If adults incapable of providing consent or children do not sign the consent document, then note assent in the signature section of the consent you include in the consent document you submit for review.

When am I required to obtain a HIPAA Authorization?

If you plan to use or share protected health information (PHI) when conducting your research, you must conduct your study in accordance with the Privacy Rule of the [Health Insurance Portability and Accountability Act](#) (HIPAA). Review [Northwestern University's HIPAA policy](#) and the guidelines below to determine your need for a valid HIPAA Authorization.

A HIPAA Authorization is an individual's signed permission to allow a covered entity to use or disclose the individual's protected health information (PHI) as described in the Authorization. In contrast, an Informed Consent Document is an individual's agreement to participate in the research study and includes, among other things, a description of the study, anticipated risks and benefits, and how the confidentiality of records will be protected. A HIPAA Authorization is part of the Informed Consent Document or other permission to participate in research.

The Authorization must be written in plain language. A copy of the signed Authorization must be provided to the individual signing it if the covered entity itself is seeking the Authorization.

A research participant may revoke his/her Authorization at any time. However, a covered entity may continue to use and disclose PHI that was obtained before the participant revoked Authorization to the extent that the entity has taken action in reliance on the Authorization. This would permit the covered entity to continue using or disclosing the PHI as necessary to maintain the integrity of the research, as, for example, to account for a participant's withdrawal from the research study, to conduct investigations of scientific misconduct, or to report adverse events.

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	08/01/15	13 of 43

The Privacy Rule does not specify who must draft the Authorization, so it may be drafted by a researcher. However, the Privacy Rule does specify core elements and required statements that must be included in an Authorization. An Authorization form may also, but is not required to, include additional, optional elements provided the elements are not inconsistent with the required elements and statements and are not otherwise contrary to the Authorization requirements of the Privacy Rule.

An Authorization, whether prepared by a covered entity or by a person requesting PHI from a covered entity, must include the following core elements and required statements:

Authorization Core Elements (see Privacy Rule, 45 C.F.R. §164.508(c)(1))

- Description of the PHI to be used or disclosed (identifying the information in a specific and meaningful manner).
- The name(s) or other specific identification of person(s) or class of persons authorized to make the requested use or disclosure.
- The name(s) or other specific identification of the person(s) or class of persons who may use the PHI or to whom the covered entity may make the requested disclosure.
- Description of each purpose of the requested use or disclosure. Researchers should note that this element must be research study specific, not for future unspecified research.
- Authorization expiration date or event that relates to the individual or to the purpose of the use or disclosure (the terms "end of the research study" or "none" may be used for research, including for the creation and maintenance of a research database or repository).
- Signature of the individual and date. If the Authorization is signed by an individual's personal representative, a description of the representative's authority to act for the individual.

Authorization Required Statements (see Privacy Rule, 45 C.F.R. § 164.508(c)(2))

- The individual's right to revoke his/her Authorization in writing and either (1) the exceptions to the right to revoke and a description of how the individual may revoke Authorization or (2) reference to the corresponding section(s) of the covered entity's Notice of Privacy Practices.
- Notice of the covered entity's ability or inability to condition treatment, payment, enrollment, or eligibility for benefits on the Authorization, including research-related treatment, and, if applicable, consequences of refusing to sign the Authorization.
- The potential for the PHI to be re-disclosed by the recipient and no longer protected by the Privacy Rule. This statement does not require an analysis of risk for re-disclosure but may be a general statement that the Privacy Rule may no longer protect health information.*

If you need to include a HIPAA Authorization, the Biomedical and Social Behavioral Consent Document Templates (HRP-592 and HRP-582) already include all of the required HIPAA Authorization elements. Therefore, you do not need to submit a separate HIPAA Authorization form for IRB review. One signature block will suffice for both informed consent and HIPAA Authorization.

Under certain conditions, the IRB may waive the requirement for a HIPAA Authorization or alter the authorization process. See "CHECKLIST: HIPAA Waiver of Authorization (HRP-441)" for the

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	08/01/15	14 of 43

criteria the IRB uses to determine whether a waiver of HIPAA Authorization is acceptable. Including this information in your protocol will help the IRB make a determination.

You must request a waiver or alteration of HIPAA Authorization when applying for a waiver of documentation of consent. The IRB can grant the waiver if it deems the following criteria are met:

1. An adequate plan to destroy identifiers at the earliest opportunity absent a health or research justification or legal requirement to retain them, and
 - a. An adequate plan to protect health information identifiers from improper use or disclosure,
 - b. An adequate plan to destroy identifiers at the earliest opportunity absent a health or research justification or legal requirement to retain them, and
 - c. Adequate written assurances that the PHI will not be used or disclosed to a third party except as required by law, for authorized oversight of the research study, or for other research uses and disclosures permitted by the Privacy Rule;
2. Research could not practicably be conducted without the waiver or alteration; and
3. Research could not practicably be conducted without access to and use of PHI.

If the IRB has not waived the requirement to obtain HIPAA authorization, you must obtain HIPAA authorization prior to accessing or using Protected Health Information.

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

What 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 participants during recruitment, while obtaining consent, and for the duration of the research. You may use a short form as described above in the “How do I document consent or assent?” section above to document consent. Consult “WORKSHEET: Short Form of Consent Documentation (HRP-317)” 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://irb.northwestern.edu/templates-forms#short-form>.

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 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 your receive approval, translate your document, and submit that document in eIRB+ with a modification, including also a Certificate of Translation. That certificate can be found at the following link:

<http://irb.northwestern.edu/sites/default/files/templates/certificate-translation-template-non-english-documents-1336592393.doc>.

Please consult the following webpage for a non-exclusive list of translation services: <http://irb.northwestern.edu/templates-forms/consent-translation>.

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	08/01/15	15 of 43

What supporting documents must I include with my IRB submission?

The eIRB+ will prompt you to upload documents throughout the submission form, including protocol(s), consent document(s), recruitment material(s), etc. Any other study-specific documents should be uploaded in the “Supporting Documents” section of the submission form. Examples of supporting documents include (but are not limited to):

- Childhood educational permission letters
- CITI Training Documents for external research team members
- Evidence of international Human Research review
- Radiation Safety Office approval documentation
- Data collection instruments, including diaries, surveys, questionnaires, or interview scripts
- Certificates of Confidentiality from a federal agency
- Recruitment materials

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 institutional definition of “Human Research” to fall under IRB oversight. Activities that do not meet this definition of are not participant to IRB oversight or review. Review the IRB Office’s “WORKSHEET: Human Research (HRP-310)” for reference. Contact the IRB Office in cases where it is unclear whether an activity is Human Research.
- Exempt: Certain categories of Human Research may be exempt from the regulations but are still human subject research and therefore, subject to IRB review under the ethical principles of Belmont. Projects that are determined to be exempt will not require annual review by the IRB. It is the responsibility of the institution, not the investigator, to determine whether Human Research is exempt from IRB review. Review the IRB Office’s “WORKSHEET: Exemption (HRP-312)” for reference on the categories of research that may be exempt. Once exempt review is completed, the researcher does not need to submit anything additional to the IRB unless the project changes in risk or in scope such that the project is no longer exempt.
- Review Using the Expedited Procedure: Certain categories of non-exempt Human Research may qualify for review using the expedited procedure, meaning that a single designated IRB reviewer, rather than the convened board may approve the project. Review the IRB Administration’s “WORKSHEET: Eligibility for Review Using the Expedited Procedure (HRP-313)” for reference on the categories of research that may be reviewed using the expedited procedure.
- Review by the Convened IRB: Non-Exempt Human Research that does not qualify for review using the expedited procedure must be reviewed by the convened IRB.

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	08/01/15	16 of 43

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:

- Approval: Made when all criteria for approval are met. See “How does the IRB decide whether to approve Human Research?” below.
- Modifications Required to Secure Approval: Made when IRB members require specific modifications to the research before approval can be finalized.
- Tabled (No Action): 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 available meeting.
- Deferred: Made when the IRB determines that the board is unable to approve research and the IRB suggests modifications the might make the research approvable. When making this motion, the IRB describes its reasons for this decision, describes modifications that might make the research approvable, and gives the investigator an opportunity to respond to the IRB in person or in writing.
- Disapproval: Made when the IRB determines that it is unable to approve research and the IRB cannot describe modifications the might make the research approvable. When making this motion, the IRB describes its reasons for this decision and gives the investigator an opportunity to respond to the IRB in person or in writing.

How does the IRB decide whether to approve Human Research?

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

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

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

What other state or federal requirements must be met?

In addition to the criteria for IRB approval mentioned above, other state or federal laws or regulations may apply to your research, such as, but not limited to:

- The Illinois Medical Studies Act:
<http://www.ilga.gov/legislation/ilcs/ilcs4.asp?DocName=073500050HArt.+VIII+Pt.+21&ActID=2017&ChapterID=56&SeqStart=64300000&SeqEnd=64900000>.
- The Illinois Mental Health and Developmental Disabilities Confidentiality Act:
<http://www.ilga.gov/legislation/ilcs/ilcs3.asp?ActID=2043&ChapterID=57>.

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	08/01/15	17 of 43

- The Illinois Nursing Home Act:
<http://www.ilga.gov/legislation/ilcs/fulltext.asp?DocName=021000450K2-104>
- See HRP-103 APPENDICES for additional federal regulatory criteria for approval of Human Research.

What will happen after IRB review?

The IRB Office 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 institutional approvals have been met. The period of time for which the IRB approval is valid 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 within 21 calendar days after receiving your determination letter. If all requested modifications are made, the IRB will issue a final approval. Research cannot commence until this final approval is received. If you do not accept the modifications, write up your response and submit it to the IRB. If you submit the requested modifications to the IRB after 21 calendar days, it will be evaluated on a case-by-case basis.
- 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 as Investigator in order to conduct Human Research?

- 1) Ensure that Research Staff continue to remain qualified (e.g., including but not limited to appropriate training, education, expertise, credentials, protocol requirements and, when relevant, privileges) to perform procedures and duties assigned to them for the duration of the study.
 - a) Delegate responsibilities to Research Staff in accordance with staff experience, training, and qualifications.
 - b) Assure that all research procedures are performed with appropriate supervision and only by individuals who are licensed or otherwise qualified to perform them in the state of Illinois and according to institutional policies.
 - c) Monitor the research study and perform quality assurance activities to ensure that participants are protected and that data are reliable.
- 2) Update the IRB office with any changes to the list of study personnel.

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	08/01/15	18 of 43

- 3) Personally conduct or supervise the Human Research.
 - a) Conduct the Human Research in accordance with the relevant current protocol as approved by the IRB.
 - b) When required by the IRB ensure that consent or permission is obtained in accordance with the relevant current protocol as approved by the IRB.
 - c) Do not modify the Human Research without prior IRB review and approval unless necessary to eliminate apparent immediate hazards to participants.
 - d) Protect the rights, safety, and welfare of participants involved in the research.
 - e) Make arrangements for oversight of the research and protection of participants in the event that you become temporarily unavailable to personally conduct or oversee the research.
- 4) Obtain the legally and ethically effective informed consent of research participants according to the plan approved by the IRB.
 - a) Ensure that only qualified Research Staff obtain informed consent.
- 5) Maintain accurate and complete research records.
- 6) Submit to the IRB:
 - a) Proposed modifications as described in this manual. (See “How do I submit a modification?”)
 - b) A continuing review application as requested in the approval letter. (See “How do I submit continuing review?”)
 - c) A continuing review application when the Human Research is closed. (See “How Do I Close Out a Study?”)
 - d) Reportable New Information. Reports of new information should be submitted within five business days. (See “What new information needs to be reported to the IRB?”)
- 7) Submit an updated disclosure of financial interests within thirty days of discovering or acquiring (e.g., through purchase, marriage, or inheritance) a new financial interest.
- 8) Do not accept or provide payments to professionals in exchange for referrals of potential participants (“finder’s fees.”)
- 9) Do not accept payments designed to accelerate recruitment that were tied to the rate or timing of enrollment (“bonus payments.”)
- 10) See additional requirements of various federal agencies in Appendix A. These represent additional requirements and do not override the baseline requirements of this section.

How do I submit a modification?

Log in to eIRB+ using your NU NetID and password. Navigate to the study you wish to modify. In the left-hand side of the study workspace, click “Create Modification / CR” and select “Modification”. (Note that you may also submit a combined Modification and Continuing Review. See “How do I submit continuing review?” for additional information.) Select the Modification Scope and click “Continue”. Complete all Modification Information and then make changes to IRB Application. For changes to documents previously uploaded in to eIRB+, use the electronic copies

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	08/01/15	19 of 43

maintained by the system to ensure that you are revising the most recent versions. Please note that research must continue to be conducted without inclusion of the modification until IRB approval is received.

How do I submit continuing review?

Log in to eIRB+ using your NU NetID and password. Navigate to the study for which you wish to submit a continuing review request. In the left-hand side of the study workspace, click: Create Modification / CR” and select “Continuing Review”. (Note that you may also submit a combined Modification and Continuing Review. See “How do I submit a modification?” for additional information.) Complete all Continuing Review / Study Closure Information. You will not be able to make any changes to your study at continuing review unless you submit a combined Modification and Continuing Review. Before submitting the research for continuing review, you should verify the current list of research team personnel and whether there has been any change in financial interest related to the research.

If the approval of Human Research expires all Human Research procedures related to the protocol under review must cease, including recruitment, advertisement, screening, enrollment, consent, interventions, interactions, and collection or analysis of private identifiable information. Continuing Human Research procedures is a violation of institutional policy. If current participants 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 participants. If current participants will be harmed by stopping Human Research procedures that are not available outside the Human Research context, immediately contact the IRB Office and provide a written list of the currently enrolled participants and why they will be harmed by stopping Human Research procedures.

How do I close out a study?

Log in to eIRB+ using your NU NetID and password. Navigate to the study you wish to close. In the left-hand side of the study workspace, click “Create Modification / CR” and select “Continuing Review”. Complete all Continuing Review / Study Closure Information.

If your study has been lapsed for more than thirty (30) calendar days the IRB Office may automatically close your study.

How do I report new information to the IRB?

During the course of a research study, Unanticipated Problems Involving Risk to Subjects or Others (UPIRSOs) and Non-compliance may occur and need to be reported to the IRB. Death of an NU/NU affiliate* participant that is both Unanticipated and Related must be reported within **24 hours** of knowledge or notification. Any other information pertaining to an NU/NU affiliate* that fits into any of the categories listed below must be reported within **5 business days** of knowledge or notification.

The following information should be reported:

- **Risk:** Information that indicates a new or increased risk, or a safety issue. For example:

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	08/01/15	20 of 43

- a. New information (e.g., an interim analysis, safety monitoring report, publication in the literature, sponsor report, or investigator finding) indicates an increase in the frequency or magnitude of a previously known risk, or uncovers a new risk.
 - b. An investigator brochure, package insert, or device labeling is revised to indicate an increase in the frequency or magnitude of a previously known risk, or to describe a new risk.
 - c. Withdrawal, restriction, or modification of a marketed approval of a drug, device, or biologic used in a research protocol.
 - d. Protocol violation that harmed participants or others or that indicates participants or others might be at increased risk of harm.
 - e. Complaint of a participant that indicates participants or others might be at increased risk of harm or at risk of a new harm.
 - f. Any changes significantly affecting the conduct of the research.
- **Harm/Death:** Any harm (including death) experienced by an NU participant or other individual that, in the opinion of the investigator, is unexpected and at least probably related to the research procedures.
 - a. A harm is “unexpected” when its specificity or severity is inconsistent with risk information previously reviewed and approved by the IRB in terms of nature, severity, frequency, and characteristics of the study population.
 - b. A harm is “probably related” to the research procedures if, in the opinion of the investigator, the research procedures more likely than not caused the harm.
 - **Non-compliance:** Non-compliance with the federal regulations governing human research or with the requirements or determinations of the IRB that causes harm, adversely affects the rights or welfare of participants or undermines the scientific integrity of the data, or an allegation of such non-compliance.
 - **Audit:** Audit, inspection, or inquiry by a federal agency and any resulting reports (e.g., FDA Form 483).
 - **Reports:** Only certain written reports of study monitors must be reported. Prompt reporting (within 5 business days) is required for monitoring reports for which the industry sponsor determined the findings could affect the safety of participants or influence the conduct of the study.
 - **Researcher error:** Failure to follow the protocol due to the action or inaction of the investigator or research staff.
 - **Confidentiality:** Breach of confidentiality.
 - **Unreviewed change:** Change to the protocol taken without prior IRB review to eliminate an apparent immediate hazard to a participant.
 - **Incarceration:** Incarceration of a participant in a study not approved by the IRB to involve prisoners.
 - **Complaint:** Complaint of a participant that cannot be resolved by the research team.
 - **Suspension:** Premature suspension or termination of the research by the sponsor, investigator, or institution.

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	08/01/15	21 of 43

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

Information that does not fit into one of the categories above does not need to be submitted.

To report new information, log in to eIRB+ using your NU NetID and password. You may report new information in two ways.

- If the Reportable New Information is related to a particular study, navigate to the study. In the left-hand side of the study workspace, click “Report New Information”. Review the list of categories of information that should be reported to the IRB. If your new information fits into one or more of the categories on the list, then select those categories and provide other relevant information.
- If the Reportable New Information is not related to a particular study, click “Report New Information” in the upper left-hand corner of your Inbox. Review the list of categories of information that should be reported to the IRB. If your new information fits into one or more of the categories on the lists, then select those categories and provide other relevant information.

How long do I keep records?

Maintain your Human Research records, including signed and dated consent documents, in accordance with the policies on Retention of University Records

(http://policies.northwestern.edu/docs/Retention_of_University_Records_030410.pdf) and Research Data: Ownership, Retention and Access

(http://www.research.northwestern.edu/policies/documents/research_data.pdf). If your Human Research is sponsored, contact the sponsor before disposing of Human Research records.

What should I do if I leave Northwestern University?

If you are planning to leave Northwestern University, you must notify the IRB Office. You may decide to transfer responsibility of your research to another Northwestern University researcher, close your research at Northwestern University 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 and a plan for informing research participants of your move if appropriate and how it affects them. IRB Office staff will be able to advise you on what actions you will need to take. Please refer to NU Policy: Research Data: Ownership, Retention, and Access.

(http://www.research.northwestern.edu/policies/documents/research_data.pdf)

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

Contact the IRB Office or IRB chair immediately to discuss the situation. If there is no time to make this contact, see the “WORKSHEET: Emergency Use (HRP-322)” for the regulatory criteria



Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	08/01/15	22 of 43

allowing such a use and make sure these are followed. Use the “Template Emergency Use Consent Document (HRP-506)” to prepare your consent document. You will need to submit a report of the use to the IRB within five calendar days of the use and for drugs and biologics, submit an IRB application for initial review within 30 calendar days.

Emergency use of an unapproved drug or biologic in a life-threatening situation without prior IRB review is “research” as defined by USFDA, the individual getting the test article is a “participant” as defined by USFDA, and therefore is governed by USFDA regulations for IRB review and informed consent.

Emergency use of an unapproved device without prior IRB review is not “research” as defined by USFDA and the individual getting the test article is not a “participant” as defined by USFDA. However, USFDA 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 “participant” 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 Participant Protection Program are available on the IRB web Site at <http://irb.northwestern.edu>.

If you have any questions or concerns, about the Human Participant Protection Program, contact the IRB Office at:

Biomedical IRB
Arthur Rubloff Building, 7th Floor
750 N. Lake Shore Dr.
Chicago, IL 60611
Phone: (312) 503-9338
irb@northwestern.edu

Social Behavioral IRB
Chambers Hall, 2nd Floor
600 Foster Street
Evanston, IL 60201
Phone: (847) 467-1723
irb@northwestern.edu

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 contact the IRB Office, follow the directions in the “Human Participant Protection Program Plan (HRP-101)” under “Reporting and Management of Concerns.”

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	08/01/15	23 of 43

Appendix A-1

Additional Requirements for DHHS-Regulated Research¹

1. When a participant decides to withdraw from a clinical trial, the investigator conducting the clinical trial should ask the participant to clarify whether the participant 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 participant previously gave consent may continue. The investigator should explain to the participant who wishes to withdraw the importance of obtaining follow-up safety data about the participant.
2. Investigators are allowed to retain and analyze already collected data relating to any participant who chooses to withdraw from a research study or whose participation is terminated by an investigator without regard to the participant'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 participant.
3. For research not participant to regulation and review by USFDA, investigators, in consultation with the funding agency, can choose to honor a research participant's request that the investigator destroy the participant's data or that the investigator exclude the participant's data from any analysis.
4. When seeking the informed consent of participants, investigators should explain whether already collected data about the participants will be retained and analyzed even if the participants choose to withdraw from the research.

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

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	08/01/15	24 of 43

Appendix A-2

Additional Requirements for USFDA-Regulated Research

1. When a participant withdraws from a study:²
 - a. The data collected on the participant to the point of withdrawal remains part of the study database and may not be removed.
 - b. An investigator may ask a participant who is withdrawing whether the participant 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 participant 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 participant's information.
 - c. If a participant 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 participant'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 participant 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 participant's medical record or other confidential records requiring the participant's consent.
 - e. An investigator may review study data related to the participant collected prior to the participant's withdrawal from the study, and may consult public records, such as those establishing survival status.
2. For USFDA-regulated research involving investigational drugs:
 - a. Investigators must abide by USFDA 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.
 - iii. An investigator must not commercially distribute or test market an investigational new drug.
 - b. Follow USFDA requirements for general responsibilities of investigators⁴

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>

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

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	08/01/15	25 of 43

- 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 participants 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 participant 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 USFDA requirements for control of the investigational drug⁵
- i. An investigator must administer the drug only to participants 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 USFDA 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 participants.
 2. If the investigation is terminated, suspended, discontinued, or completed, the investigator must return the unused supplies of the drug to the sponsor, or otherwise provide for disposition of the unused supplies of the drug under 21 CFR §312.59.
 - ii. Case histories.
 1. An investigator is required to prepare and maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual administered the investigational drug or employed as a control in the investigation.
 2. Case histories include the case report forms and supporting data including, for example, signed and dated consent forms and medical records including, for example, progress notes of the physician, the individual's hospital charts, and the nurses' notes. The case history for each individual must document that informed consent was obtained prior to participation in the study.
 - iii. Record retention: An investigator must retain required records for a period of 2 years following the date a marketing application is approved for the drug for the indication for which it is being investigated; or, if no application is to be filed or if the application is not approved for such indication, until 2 years after the investigation is discontinued and USFDA is notified.
- e. Follow USFDA requirements for Expanded Access to Investigational Drugs for Treatment Use per 21 CFR 312.300 (Subpart I). This is often referred to as “compassionate use”. The aim of this subpart is to facilitate the availability of

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>

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	08/01/15	26 of 43

investigational new drugs and approved drugs to patients with serious diseases or conditions when there is not comparable or satisfactory alternative therapy to diagnose, monitor, or treat the patient's disease or condition. Expanded access to investigational drugs requires prior IRB review and approval (with the exception of [Emergency Use](#)).

- f. Follow USFDA 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.
- g. Follow USFDA 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 participants 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 participants.
- h. Follow USFDA requirements for inspection of investigator's records and reports⁹
 - i. An investigator must upon request from any properly authorized officer or employee of USFDA, 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 participant 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.
- i. Follow USFDA requirements for handling of controlled substances¹⁰

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

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

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

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

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	08/01/15	27 of 43

- i. If the investigational drug is participant 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 USFDA-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 USFDA regulations, for protecting the rights, safety, and welfare of participants 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 participants would be interested in participating in an investigation, but must not request the written informed consent of any participant to participate, and must not allow any participant to participate before obtaining IRB and USFDA approval.
 - ii. Compliance: An investigator must conduct an investigation in accordance with the signed agreement with the sponsor, the investigational plan, and other applicable USFDA regulations, and any conditions of approval imposed by an IRB or USFDA.
 - iii. Supervising device use: An investigator must permit an investigational device to be used only with participants under the investigator's supervision. An investigator must not supply an investigational device to any person not authorized to receive it.
 - iv. Financial disclosure:
 1. A clinical investigator must disclose to the sponsor sufficient accurate financial information to allow the applicant to submit complete and accurate certification or disclosure statements required under 21 CFR §54.
 2. The investigator must promptly update this information if any relevant changes occur during the course of the investigation and for 1 year following completion of the study.
 - v. Disposing of device: Upon completion or termination of a clinical investigation or the investigator's part of an investigation, or at the sponsor's request, an investigator must return to the sponsor any remaining supply of the device or otherwise dispose of the device as the sponsor directs.
 - c. Maintain the following accurate, complete, and current records relating to the investigator's participation in an investigation:¹³

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>

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

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	08/01/15	28 of 43

- i. All correspondence with another investigator, an IRB, the sponsor, a monitor, or USFDA, 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 participant'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 participant upon entering, and during the course of, the investigation, including information about relevant previous medical history and the results of all diagnostic tests.
 - 4. A record of the exposure of each participant 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 USFDA 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 USFDA 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 USFDA employees, at reasonable times and in a reasonable manner, to inspect and copy all records relating to an investigation.

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

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	08/01/15	29 of 43

- iii. Records identifying participants: An investigator must permit authorized USFDA employees to inspect and copy records that identify participants, upon notice that USFDA 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:
 - 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 participant 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 participants, USFDA 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 USFDA, provide accurate, complete, and current information about any aspect of the investigation.

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

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	08/01/15	30 of 43

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

1. Investigator's Qualifications and Agreements
 - a. The clinical trial should be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with good clinical practice and the applicable regulatory requirements.
 - b. The investigator should be qualified by education, training, and experience to assume responsibility for the proper conduct of the trial, should meet all the qualifications specified by the applicable regulatory requirements, and should provide evidence of such qualifications through up-to-date curriculum vitae and/or other relevant documentation requested by the sponsor, the IRB, and/or the regulatory authorities.
 - 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 participants 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 Participants
 - a. A qualified physician (or dentist, when appropriate), who is an investigator or a sub-investigator for the trial, should be responsible for all trial-related medical (or dental) decisions.
 - b. During and following a participant's participation in a trial, the investigator/institution should ensure that adequate medical care is provided to a participant for any adverse events, including clinically significant laboratory values, related to the trial. The investigator/institution should inform a participant when medical care is needed for co-existing illnesses of which the investigator becomes aware.
 - c. It is recommended that the investigator inform the participant's primary physician about the participant's participation in the trial if the participant has a primary physician and if the participant agrees to the primary physician being informed.

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	08/01/15	31 of 43

- d. Although a participant 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 participant'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, participant recruitment procedures (e.g., advertisements), and any other written information to be provided to participants.
 - 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 participant 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 participants, 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 participants without prior IRB approval opinion. As soon as possible, the implemented deviation or change, the reasons for it, and, if appropriate, the proposed protocol amendments should be submitted: a) to the IRB for review and approval opinion, b) to the sponsor for agreement and, if required, c) to the regulatory authorities.
 6. Investigational Product
 - a. Responsibility for investigational product accountability at the trial site rests with the investigator/institution.
 - b. Where allowed/required, the investigator/institution may/should assign some or all of the investigator's/institution's duties for investigational product accountability at the trial site to an appropriate pharmacist or another appropriate individual who is under the supervision of the investigator/institution.
 - c. The investigator/institution and/or a pharmacist or other appropriate individual, who is designated by the investigator/institution, should maintain records of the product's delivery to the trial site, the inventory at the site, the use by each participant, 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

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	08/01/15	32 of 43

trial participants. Investigators should maintain records that document adequately that the participants 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 participant and should check, at intervals appropriate for the trial, that each participant 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 Participants
- 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 participants.
 - b. The written informed consent form and any other written information to be provided to participants should be revised whenever important new information becomes available that may be relevant to the participant's consent. Any revised written informed consent form, and written information should receive the IRB's approval opinion in advance of use. The participant or the participant's legally acceptable representative should be informed in a timely manner if new information becomes available that may be relevant to the participant'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 participant 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 participant or the participant'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 participant or, if the participant is unable to provide informed consent, the participant'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 participant or the participant's legally acceptable representative and the impartial witness, where applicable.

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	08/01/15	33 of 43

- g. Before informed consent may be obtained, the investigator, or a person designated by the investigator, should provide the participant or the participant'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 participant or the participant's legally acceptable representative.
- h. Prior to a participant's participation in the trial, the written informed consent form should be signed and personally dated by the participant or by the participant's legally acceptable representative, and by the person who conducted the informed consent discussion.
- i. If a participant 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 participants, is read and explained to the participant or the participant's legally acceptable representative, and after the participant or the participant's legally acceptable representative has orally consented to the participant'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 participant or the participant's legally acceptable representative, and that informed consent was freely given by the participant or the participant'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 participants 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 participant's responsibilities.
 - vi. Those aspects of the trial that are experimental.
 - vii. The reasonably foreseeable risks or inconveniences to the participant and, when applicable, to an embryo, fetus, or nursing infant.
 - viii. The reasonably expected benefits. When there is no intended clinical benefit to the participant, the participant should be made aware of this.
 - ix. The alternative procedures or courses of treatment that may be available to the participant, and their important potential benefits and risks.
 - x. The compensation and/or treatment available to the participant in the event of trial related injury.
 - xi. The anticipated prorated payment, if any, to the participant for participating in the trial.
 - xii. The anticipated expenses, if any, to the participant for participating in the trial.
 - xiii. That the participant's participation in the trial is voluntary and that the participant may refuse to participate or withdraw from the trial, at any time,

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	08/01/15	34 of 43

without penalty or loss of benefits to which the participant is otherwise entitled.

- xiv. That the monitors, the auditors, the IRB, and the regulatory authorities will be granted direct access to the participant's original medical records for verification of clinical trial procedures and/or data, without violating the confidentiality of the participant, to the extent permitted by the applicable laws and regulations and that, by signing a written informed consent form, the participant or the participant's legally acceptable representative is authorizing such access.
- xv. Records identifying the participant 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 participant's identity will remain confidential.
- xvi. That the participant or the participant's legally acceptable representative will be informed in a timely manner if information becomes available that may be relevant to the participant's willingness to continue participation in the trial.
- xvii. The persons to contact for further information regarding the trial and the rights of trial participants, and whom to contact in the event of trial-related injury.
- xviii. The foreseeable circumstances and/or reasons under which the participant's participation in the trial may be terminated.
 - xix. The expected duration of the participant's participation in the trial.
 - xx. The approximate number of participants involved in the trial.
- k. Prior to participation in the trial, the participant or the participant'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 participants. During a participant's participation in the trial, the participant or the participant'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 participants.
- l. When a clinical trial (therapeutic or non-therapeutic) includes participants who can only be enrolled in the trial with the consent of the participant's legally acceptable representative (e.g., minors, or patients with severe dementia), the participant should be informed about the trial to the extent compatible with the participant's understanding and, if capable, the participant 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 participant), should be conducted in participants who personally give consent and who sign and date the written informed consent form.
- n. Non-therapeutic trials may be conducted in participants 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 participants who can give informed consent personally. b) The foreseeable risks to the participants are low. c) The negative impact on the participant'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 participants, and the written approval opinion covers this

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	08/01/15	35 of 43

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. Participants 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 participant is not possible, the consent of the participant's legally acceptable representative, if present, should be requested. When prior consent of the participant is not possible, and the participant's legally acceptable representative is not available, enrolment of the participant should require measures described in the protocol and/or elsewhere, with documented approval opinion by the IRB, to protect the rights, safety and well-being of the participant and to ensure compliance with applicable regulatory requirements. The participant or the participant's legally acceptable representative should be informed about the trial as soon as possible and consent to continue and other consent as appropriate should be requested.

8. Records and Reports

- a. The investigator should ensure the accuracy, completeness, legibility, and timeliness of the data reported to the sponsor in the CRFs and in all required reports.
- b. Data reported on the CRF, that are derived from source documents, should be consistent with the source documents or the discrepancies should be explained.
- c. Any change or correction to a CRF should be dated, initialed, and explained (if necessary) and should not obscure the original entry (i.e. an audit trail should be maintained); this applies to both written and electronic changes/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.

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	08/01/15	36 of 43

- 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 participants.
10. Safety Reporting
- a. All serious adverse events (SAEs) should be reported immediately to the sponsor except for those SAEs that the protocol or other document (e.g., Investigator's Brochure) identifies as not needing immediate reporting. The immediate reports should be followed promptly by detailed, written reports. The immediate and follow-up reports should identify participants by unique code numbers assigned to the trial participants rather than by the participants' 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 participants, should assure appropriate therapy and follow-up for the participants, 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.

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	08/01/15	37 of 43

Appendix A-4

Additional Requirements for Department of Defense (USDOD) research

1. When appropriate, research protocols must be reviewed and approved by the IRB prior to the US Department of Defense approval. Consult with the US Department of Defense funding component to see whether this is a requirement.
2. Employees of the US 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 US 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 participants while on-duty or off-duty.
4. Components of the US Department of Defense might have stricter requirements for research-related injury than the DHHS regulations.
5. There may be specific educational requirements or certification required.
6. When assessing whether to support or collaborate with this institution for research involving human participants, the US Department of Defense may evaluate this institution's education and training policies to ensure the personnel are qualified to perform the research.
7. When research involves U.S. military personnel, policies and procedures require limitations on dual compensation:
 - a. Prohibit an individual from receiving pay of compensation for research during duty hours.
 - b. An individual may be compensated for research if the participant is involved in the research when not on duty.
 - c. Federal employees while on duty and non-Federal persons may be compensated for blood draws for research up to \$50 for each blood draw.
 - d. Non-Federal persons may be compensated for research participating other than blood draws in a reasonable amount as approved by the IRB according to local prevailing rates and the nature of the research.
8. Other specific requirements of the US Department of Defense research be found in the "Additional Requirements for Department of Defense (USDOD) Research" section in the IRB's "WORKSHEET: Additional Federal Criteria (HRP-318)."

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	08/01/15	38 of 43

Appendix A-5

Additional Requirements for Department of Energy (USDOE) Research

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

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

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

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	08/01/15	39 of 43

Additional Requirements for Department of Justice (USDOJ) 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 participants.
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 participants 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 participants 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 participant, you must not provide research information that identifies a participant to any person without that participant'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 participants, accompanied by detailed documentation. These arrangements must be negotiated prior to the beginning of the data collection phase of the project.
12. Required elements of disclosure additionally include:
 - a. Identification of the investigators.
 - b. Anticipated uses of the results of the research.
 - c. A statement that participation is completely voluntary and that the participant 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).

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	08/01/15	40 of 43

- 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, a investigator may not guarantee confidentiality when the participant indicates intent to commit future criminal conduct or harm himself or herself or someone else, or, if the participant 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 participant'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 participants (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 US Bureau of Prisons.
 - e. Description of all possible risks, discomforts, and benefits to individual participants or a class of participants, and a discussion of the likelihood that the risks and discomforts will actually occur.
 - f. Description of steps taken to minimize any risks.
 - g. Description of physical or administrative procedures to be followed to: Ensure the security of any individually identifiable data that are being collected for the study.
 - h. Destroy research records or remove individual identifiers from those records when the research has been completed.
 - i. Description of any anticipated effects of the research study on institutional 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

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	08/01/15	41 of 43

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 US Department of Defense Justice (USDOJ) Research Conducted within the Federal Bureau of Prisons (BOP) can be found in the “Additional Requirements for Department of Justice (USDOJ) Research Conducted within the Federal Bureau of Prisons (BOP)” section in the IRB’s “WORKSHEET: Additional Federal Criteria (HRP-318).”

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

1. The project must have a privacy certificate approved by the National Institute of Justice Human Participants 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 participant reports immediate harm to participants or others.
4. Under a privacy certificate, investigators and research staff do not have to report child abuse unless the participant signs another consent document to allow child abuse reporting.
5. A copy of all data must be de-identified and sent to the National Archive of Criminal Justice Data, including copies of the informed consent document, data collection instruments, surveys, or other relevant research materials.
6. Other specific requirements of the US Department of Defense Justice (USDOJ) Research Funded by the National Institute of Justice can be found in the “Additional Requirements for Department of Justice (USDOJ) Research” section in the IRB’s “WORKSHEET: Additional Federal Criteria (HRP-318).”



Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	08/01/15	42 of 43

Appendix A-7

Additional Requirements for Department of Education (USED) 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 US Department of Defense Education (USED) Research can be found in the “Additional Requirements for Department of Education (USED) Research” section in the IRB’s “WORKSHEET: Additional Federal Criteria (HRP-318).”

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.

Investigator Manual		
NUMBER	DATE	PAGE
HRP-103	08/01/15	43 of 43

Appendix A-8

Additional Requirements for Environmental Protection Agency (USEPA) Research

1. Research conducted, supported, or intended to be submitted to EPA is participant 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 participant 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 US Environmental Protection Agency (USEPA) Research can be found in the “Additional Requirements for Environmental Protection Agency (USEPA) Research and Research Intended to be Submitted to the US Environmental Protection Agency” section in the IRB’s “WORKSHEET: Additional Federal Criteria (HRP-318).”