



**WISCONSIN**  
UNIVERSITY OF WISCONSIN-MADISON

**INVESTIGATOR MANUAL**

**DRAFT March 2021**

## TABLE OF CONTENTS

### INTRODUCTION

[Scope](#)

[Purpose of This Manual](#)

[IRB Toolkit Library](#)

[Defining Human Participant Research](#)

[Human Research Protection Program](#)

[Getting Help and Answers to Questions](#)

### RESEARCHER REQUIREMENTS

[Who Can Serve as a Principal Investigator](#)

[Principal Investigator Responsibilities](#)

[Change in Principal Investigator](#)

[Study Team Member Responsibilities](#)

[Student Research](#)

[Course Instructor and Advisor Responsibilities](#)

[Training Required to Conduct Human Participant Research](#)

[Financial Interests Disclosure \(Outside Activity Reporting\)](#)

### IRB REVIEW REQUIREMENTS AND APPLICATION TYPES

[When IRB Review May Not Be Required](#)

- [Program Evaluation and Quality Improvement Projects](#)
- [Case Reports](#)
- [Oral History](#)
- [Analysis of Publicly Available Datasets](#)

[Human Research Requiring a Protocol](#)

- [Clinical Trial and More Than Minimal Risk Applications](#)
- [Registry and Repository Applications](#)
- [Studies Requiring Review by the ICTR Scientific Review Committee \(SRC\)](#)
- [Non-Exempt Studies for Which UW-Madison Will Serve as the Reviewing IRB for Other Sites](#)

[Protocol Guidelines](#)

[Human Research Not Requiring a Protocol](#)

- [Exempt Projects \(including health care records research and not human research\)](#)
- [Non-exempt minimal risk research \(including community-based participatory research\)](#)
- [International Research](#)

[Other Types of Applications](#)

- [Umbrella Protocols, Training Grants, and Core Grants](#)
- [Analysis Center Applications](#)
- [Emergency/One-Time/Compassionate Use](#)
- [Expanded Access of Investigational Medical Products \(non-emergency\)](#)
- [Humanitarian Use Device \(HUD/HDE\)](#)
- [Proposal Lacking Definite Plans for Human Participant Research \(Requests from Funders for IRB Review; Just-In-Time Notifications\)](#)

[Institutional Requirements](#)

## **PREPARING SUPPORTING DOCUMENTS**

[Writing a Consent Document](#)

[Writing a HIPAA Authorization Form](#)

[Preparing Recruitment Materials](#)

[Other Subject-Facing Materials Requiring IRB Review](#)

[Supporting Documents That Do NOT Require IRB Review](#)

## **SUBMITTING IRB APPLICATIONS**

[Scientific Review Requirements](#)

[How to Submit a New Study Application](#)

[How to Submit a Continuing Review](#)

[How to Submit a Change of Protocol](#)

[How to Submit a Reportable Event](#)

[How to Update Personnel](#)

[How and When to Close a Study](#)

## **IRB REVIEW PROCESS**

[Regulatory Classifications for Human Participant Research](#)

- Including exempt and expedited review

[Changes to Research Determined to Be Exempt](#)

[IRB Approval Criteria](#)

[IRB Review Decisions](#)

[Communication of IRB Decisions](#)

[Disagreeing with IRB Decisions](#)

[Accessing IRB Records and Rosters](#)

## **CONDUCTING HUMAN PARTICIPANT RESEARCH**

[General Recruitment Guidelines](#)

- Including email, social media, snowball, screening, etc.

[Participant Remuneration and Compensation](#)

[Informed Consent Process and Documentation](#)

[Assent Process and Documentation](#)

[Remote Consent Processes](#)

[Documenting Consent Electronically](#)

[Enrolling Participants with Limited English Proficiency](#)

- Including use of the short form

[Translation and Interpreter Requirements](#)

[Research Involving Participants with Impaired Decision-Making](#)

[Research with Prisoners](#)

[Research with Children](#)

[Research with Pregnant Women and/or Neonates](#)

[Research with Other Vulnerable Populations](#)

- Including status relationships

[Protecting Participant Privacy and Confidentiality](#)

[Certificates of Confidentiality](#)

[Communicating with Participants](#)

## [HIPAA Privacy and Security Rules](#)

- Including prep to research

## [Federal Educational Privacy Act \(FERPA\)](#)

## [Research in K-12 Settings](#)

## [Use of Video or Audio Recording](#)

## [Biospecimen and Data Research](#)

- Including identifiability (coded, indirect, etc.)

## [Analysis Center Projects](#)

## [Research Registries and Repositories](#)

## [Sharing Data, Specimens, or Images](#)

## [Deception](#)

## [Technology and New Media Research](#)

## [Biomedical Interventions Conducted in Non-Clinical Settings](#)

## [FDA Regulations and IRB Review](#)

## [Investigator's Drug Brochure \(IDB\) and Package Inserts](#)

## [Radiation](#)

## [Controlled Substances](#)

## **POST-APPROVAL RESPONSIBILITIES**

## [Researcher Responsibilities After IRB Approval](#)

## [Clinicaltrials.gov](#)

## [Change of Protocol Requirements](#)

## [Continuing Review Requirements](#)

## [Reportable Event Reporting Requirements](#)

## [Reportable Event Reporting Requirement for VA Studies](#)

## [Protocol Exceptions and Deviations](#)

## [Changes to eliminate an apparent immediate hazard to subjects](#)

## [Corrective Action Plans](#)

## [Study Suspension or Termination](#)

## [Complaints or Concerns About a Study](#)

## [Reporting Clinically Relevant Information to Participants](#)

## [Communicable Disease Testing \(Including HIV\)](#)

## [IRB Reporting Obligations](#)

## [Record Retention](#)

## [Principal Investigator Responsibilities When Leaving UW-Madison](#)

## **OTHER ISSUES**

## [Conducting Research at the VA](#)

## [Fetal Tissue Research](#)

## [Institutional Certification for NIH Genomic Data Sharing](#)

## [General Data Privacy Rule \(GDPR\)](#)

## **APPENDICES**

## [Appendix A-1 Additional Requirements for DHHS-Regulated Research](#)

## [Appendix A-2 Additional Requirements for FDA-Regulated Research](#)

## [Appendix A-3 Additional Requirements for Clinical Trials obligated to follow ICH-GCP through contract/funding agreement commitments](#)

[Appendix A-4 Additional Requirements for Department of Defense \(DOD\) research](#)

[Appendix A-5 Additional Requirements for Department of Energy \(DOE\) Research](#)

[Appendix A-6 Additional Requirements for Department of Justice \(DOJ\) Research](#)

- [Additional Requirements for DOJ Research conducted in the Federal Bureau of Prisons](#)
- [Additional Requirements for DOJ Research Funded by the National Institute of Justice](#)

[Appendix A-8 Additional Requirements for Environmental Protection Agency \(EPA\) Research](#)

[Appendix A-9 Additional Requirements for Veterans Administration \(VA\) Research](#)

[Appendix A-10 Single IRB Studies](#)

[Appendix A-11 Additional Requirements for Research Subject to EU General Data Protection Regulations \(GDPR\)](#)

[Appendix B-1 Request to Serve as Principal Investigator form](#)

[Appendix B-2 Quality Improvement/Program Evaluation Self-Certification Tool](#)

[Appendix B-3 Exemption Category Tool](#)

[Appendix B-4 Exemption Change Table](#)

[Appendix B-5 Consent Form Wizard](#)

[Appendix B-6 IDB and Package Insert Log](#)

## **INTRODUCTION**

### **Scope**

Throughout this document “institution” refers to the University of Wisconsin-Madison.

### **Purpose of This Manual**

This document, HRP-103 - INVESTIGATOR MANUAL, 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: [“Training Required to Conduct Human Participant Research.”](#)

### **IRB Toolkit Library**

Along with this manual, current Human Research-related policies, SOPs, Worksheets, Checklists and templates may be found in the HRPP Toolkit Library.

- SOPs describe HRPP processes
- Worksheets are reference documents outlining regulatory and institutional criteria for specific items (e.g., FERPA, criteria for approval, assessing recruitment materials)
- Checklists are used by HRPP staff and the IRB to document regulatory determinations. Checklists do NOT need to be completed by study teams.

Collectively, these documents comprise the Toolkit Library and create a complete picture of Human Research Protection Program (“HRPP”) and Institutional Review Board (“IRB”) expectations and a guide to seeking IRB review and approval. All documents in the Toolkit Library are used by HRPP staff and IRB members to enhance compliance with federal, state and local requirements for conducting research and protecting human participants.

We encourage you to use all of these resources to assist in you in preparing your application and conducting your research study.

To ensure you are always referencing the most current version of Toolkit and related documents, please access them in real time from the IRB website rather than downloading and storing them on your computer.

### **Defining Human Participant Research**

HRP-101 - HUMAN RESEARCH PROTECTION PROGRAM PLAN defines the activities that this institution considers to be “Human Research.” A decision tree for determining whether an activity is Human Research can be found in HRP-310 - WORKSHEET - Human Research Determination, located in the IRB Policies & Procedures section of the IRB Web site. Use this document for guidance as to whether an activity meets either the DHHS or FDA definition of Human Research, keeping in mind that the IRB makes the ultimate determination in questionable cases as to whether an activity constitutes Human Research subject to IRB oversight.

You are responsible not to conduct Human Research without prior IRB review and approval (or an institutional review and determination of exempt Human Research). If you have questions about

whether an activity is Human Research, contact the IRB Office who will assist you in determining whether an activity is Human Research. Additionally, you can use the Quality Improvement/Program Evaluation Tool to self-certify whether your project constitutes Human Research. See Quality Improvement Projects below for more information.

### **Human Research Protection Program**

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

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

### **Getting Help and Answers to Questions**

This document and the policies and procedures for the Human Research Protection Program are available on the UW IRBs website ([www.irb.wisc.edu](http://www.irb.wisc.edu)).

- If you have questions about the IRB process and IRB review, email [asktheirb@hsirb.wisc.edu](mailto:asktheirb@hsirb.wisc.edu) or call 608.263.2362.
- If you have technical questions about ARROW, email [askarrow@hsirb.wisc.edu](mailto:askarrow@hsirb.wisc.edu).
- If you have questions about single IRB review and reliance agreements, email [irbreliance@wisc.edu](mailto:irbreliance@wisc.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 contacting the IRB Office, follow the directions in HRP-101 - HUMAN RESEARCH PROTECTION PROGRAM PLAN under "Reporting and Management of Concerns."

## **RESEARCHER REQUIREMENTS**

### **Who Can Serve as a Principal Investigator**

Every research study requires a Principal Investigator (PI). This person takes full responsibility for the conduct of the study. To be able to serve as a PI, individuals must meet certain criteria. For more details, see the [Principal Investigator Status for UW-Madison Studies Involving Human Participants policy](#).

### **Principal Investigator Responsibilities**

A PI is responsible for the overall conduct of a study. Some of these responsibilities include, but are not limited to, the following:

1. Conducting the study in compliance with relevant regulations (e.g., 45 CFR 46/the Common Rule, FDA, other federal agencies, state law) as well as ethical principles described in the Belmont Report.
2. Completing required human subjects research trainings.
3. Providing adequate training to and oversight of study personnel and, in the case of clinical research, ensuring the protocol complies with Good Clinical Practice requirements.
4. Obtaining legally effective informed consent, when required.
5. Obtaining permission for the use and disclosure of protected health information in compliance with the HIPAA Privacy Rule, as applicable.
6. Comparing contracts with consent documents.
7. Submitting follow-on applications as required for approved or exempt studies, including changes, continuing reviews, and reportable events.
8. Submitting a closure report when a study is completed.
9. Complying with all institutional requirements related to human subjects research, including conflict of interest.
10. Assuring participant privacy and confidentiality according to institutional and regulatory requirements including HIPAA and FERPA (as applicable).

### **Change in Principal Investigator**

If a PI is leaving UW-Madison, changes in the PI should be reported to the IRB prior to the former PI leaving the research study, if possible. In all cases, a PI change should be submitted within 14 business days after the departure of the former PI per [Study Closure Policy](#). A change in PI cannot be addressed via the Update Personnel function, but rather requires a Change of Protocol application.

If the former PI is leaving the institution but will remain a study team member, please contact the Reliance and Navigation Team ([irbreliance@wisc.edu](mailto:irbreliance@wisc.edu)) to discuss what additional steps may need to be taken to ensure appropriate IRB oversight is in place.

Temporary changes in PI may be needed if the PI cannot provide oversight of a research study for a planned period of time (e.g., parental leave, sabbatical) or unplanned leave for a substantial period of time. For federally funded research, it is the responsibility of the PI to ensure that funding agencies are notified of any temporary changes.

In cases where the leave will be less than 6 weeks, but is assumed to be temporary, the PI is responsible either for ceasing study activities or ensuring oversight of these activities is delegated to a qualified member of the study team. The study team does not need to inform the IRB in these cases.

In cases where the leave will be 6 weeks or longer, but is assumed to be temporary, the study team should submit a New Information Report to the IRB confirming one of the following:

1. Specifies the anticipated length of absence,
2. No study activities will occur during the PI's leave,
3. Only activities involving data analysis will occur, or
4. Identify who will assume PI responsibilities and/or how oversight of study teams will be ensured during the leave



The New Information Report should be provided to the IRB as soon as possible, preferably before the PI takes leave. If the PI cannot return from leave as planned or changes their role after the leave ends (e.g., becomes a sub-investigator), a change of protocol to formally update the PI for the study would be required.

If a change of PI is necessary, carefully review the approved file and ALL supporting documents (recruitment, consent, etc.) to ensure that updates are made to reflect the change in PI.

### **Study Team Member Responsibilities**

While the PI bears overall responsibility for the conduct of a study, study team responsibilities include, but are not limited to:

1. Completing of required human subjects research trainings.
2. Complying with all institutional requirements related to human subjects research, including conflict of interest.
3. Adhering to the federal regulations, state and local laws, institutional policies and procedures surrounding the safety and protection of human participants.
4. Assuring participant privacy and confidentiality according to institutional and regulatory requirements including HIPAA and FERPA (as applicable).

### **Student Research**

Depending on the nature and purpose of the project, student research may require IRB review as described below.

- All UW–Madison undergraduate and graduate students engaged in human participants research must obtain UW-Madison IRB approval or exemption before beginning the research (except for some class-related projects; see below). The research of a graduate student involving human participants for inclusion in a master's thesis or doctoral dissertation must be approved or determined to be exempt by a UW-Madison IRB before beginning the research.
- Student projects conducted within an academic course involving data, samples, or images collected from or about people may meet the federal definition of human participants research if the project is systematic and develops or contributes to generalizable knowledge.
- If the data, sample, or image collection and interpretation are for pedagogical purposes only and gathered without the intention of dissemination beyond the scope of the course, the student project should be categorized as a course assignment rather than human participants research and thus IRB review is not required. For example, IRB review is not required when course work may be presented to a group beyond the course as part of the pedagogical process, such as an event showcasing the work of students in the class. In these situations, this limited dissemination is not considered to constitute developing or contributing to generalizable knowledge and thus the requirement for IRB review is not triggered.

### **Course Instructor and Advisor Responsibilities**

Course instructors and faculty/staff members who serve as the formal advisor to a student on a project are responsible for the following:

1. Ensuring that the student is aware of the requirement to obtain IRB approval or exemption prior to any engagement in human participants research.
2. Determining prior to assigning a project, whether the project is a course assignment or constitutes human participants research and ensure that any students engaged in human participants research obtain IRB approval or exemption prior to commencing that project.
  - a. If a student research project is originally conducted as a course assignment, but develops into human participants research, the faculty member or instructor overseeing the course or project must ensure IRB approval or exemption is obtained before the project can continue.
3. Monitoring student projects conducted as part of coursework for the impact on human participants, especially maintaining participant confidentiality, assuring freedom of participants to withdraw from the project without penalty, and obtaining consent for participation in the project when reasonable.
4. Ensuring student researchers give due consideration of the University's ethical and legal responsibility to protect participants and their data, especially when participants are exposed to more than a minimal risk or participants include those who are considered a vulnerable population.
5. Ensuring any changes in the research project, adverse events, or incidents which may affect the conduct of research will be reported to the IRB.
6. Reviewing the proposed research study, including assessing whether the topic and design are appropriate for student research.
7. Ensuring the student researcher has the necessary experience and training to conduct the research.
8. Meeting with the student researcher on a regular basis to monitor study progress.
  - a. If the study procedures are carried out in a location away from the University or regular channels of communication are not feasible, you will make alternate arrangements to continue communication with the student-investigator;
9. If you will be unavailable, you will arrange for an alternate faculty advisor to assume the above responsibilities and will advise the IRB of this change.

### **Training Required to Conduct Human Participant Research**

Training requirements are described in HRP 066-SOP-Human Research Education and Training. All members of the research team listed on an IRB submission classified as exempt or non-exempt research, must complete the required training. Although recommended, research team members listed on submissions determined "Not Human Research" will not be required to complete the IRB training requirements.

All members of the research team involved in the design, conduct, or reporting of the research must complete training. Members of the research team who have not completed human research protections training may not take part in aspects of the research that involve human subjects. All required training must be completed before IRB final approval can be granted. Instructions on how to complete the training requirements can be found on the Training section of the HRPP website.

## **Financial Interests Disclosure (Outside Activity Reporting)**

All faculty, regardless of appointment, all academic staff with 50% or greater appointment, and all individuals listed as participants on human subject protocols or on federal grants are required to fill out an annual Outside Activities Report (OAR) and update whenever new outside activities are undertaken. This includes any financial interests related to the research in accordance with University of Wisconsin policies on Conflicts of Interest and Institutional Conflict of Interest.

In the event a study team member (including the PI) has a conflict of interest management plan for a specific study, the IRB will consider this as part of its review process and, if deemed necessary to protect the rights and welfare of study participants, may require additional measures be implemented (e.g., consent monitoring) beyond those included in the management plan.

We recommend reaching out [the Conflict of Interest office](#) directly for assistance with questions regarding the OAR process, potential conflicts of interest, and conflict of interest training requirements. See HRP 055-SOP-IRB Review of Financial Conflicts of Interest.

## **IRB REVIEW REQUIREMENTS AND APPLICATION TYPES**

### **When IRB Review May Not Be Required**

The IRB reviews all activities that meet the federal definitions of human research and federal guidelines for engagement. Some activities involving human subjects or their data may not fall under these definitions and do not require IRB review. If you are unsure if your proposed project meets the federal definitions of human research, refer to the HRP 310 -WORKSHEET - Human Research for guidance. If you are unsure whether your project will engage you in human subjects research, refer to the HRP 311- WORKSHEET – Engagement Determination for guidance. The following are examples of activities that are likely not human research:

- Program Evaluation/Quality Assurance Review/Quality Improvement Projects
- Case Reports
- Course-Related Activity (Please see the Student Research section above for a description of when course-related activities do not require IRB review.)
- Oral History
- Analysis of Publicly Available Datasets

The information below provides you with more details about these activities and when IRB input may be needed to assess whether IRB oversight is required. If you are unsure whether your project engages you in human subjects research or meets the criteria for not requiring IRB review, please contact the IRB office for assistance. Note that even if your study does not constitute human research, you must still comply with relevant regulatory (e.g., HIPAA) and institutional requirements. For more information, see HRP 309-WORKSHEET-Ancillary Review Matrix.

- **Program Evaluation/Quality Improvement Projects**
  - Determining whether a project constitutes human subjects research rather than quality improvement or program evaluation involves multiple factors. The federal definition of research is “a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which

meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes.” This is an important distinction to make because it determines whether IRB review and oversight of a project is needed.

- Often, determining whether a project constitutes research under federal and institutional regulations can be a complex process that involves assessing the project intent, design, mandates, expected outcomes, and dissemination of results. The QI/Program Evaluation Self-Certification Tool is designed to assist study teams in determining whether a project requires submission to the IRB. If the project involves some characteristics of a research project, the Tool will let you know that IRB review is required. If the project does qualify as program evaluation/QI, the Tool will provide you with a certification confirming this. This certification can be printed off and used as documentation that the project does not constitute research and further IRB review is not required
- NOTE: This tool is not designed to determine all cases when a project falls outside of the IRB's purview. This tool is only for determining if a project is QI/Program Evaluation, rather than research. The tool should not be used for public health surveillance projects.
- A journal or conference may not accept the certification as proof your project does not require IRB approval. In such cases, you will need to submit an application in ARROW to obtain a formal IRB determination.
- **Case Reports**
  - Case reports of 3 or fewer individuals generally do not meet the regulatory definition of research because they would not qualify as a systematic investigation that contributes to generalizable knowledge. IRB review of such case reports is therefore not required. Some journal editors do require documentation from the IRB indicating that IRB review is not necessary to publish the case report. In such cases, you may submit an IRB application requesting a not research determination.
  - Even if IRB review is not required, case reports for publication must be prepared in accordance with the requirements of the HIPAA privacy regulations. This means that the case reports must be de-identified, i.e., the presentation or article must not contain **any** of the 18 identifiers for an individual that are described in the HIPAA Privacy Rule. For case reports that disclose PHI or where the health information described in conjunction with other characteristics could reasonably be used to identify the patient (e.g., a rare injury, disease or diagnosis in combination with age, gender, geographic region), patients (or their legally authorized representatives, e.g., parents, guardians, etc.) will need to sign a HIPAA-compliant authorization form.
  - Case reports involving more than three patients are more likely to meet the criteria for research and require IRB Review. In addition, testing of a patient's biospecimen (e.g., special stain, immunohistochemistry, molecular studies) is not typically permissible as part of a case report.
- **Oral History**
  - While oral history is typically not considered human research, the prospective intent of the investigator and the definition of "research" under the federal regulations needs to be taken into account. Per federal regulation, research is defined as "a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge."
  - Specifically, the consideration of human research and the requirement for IRB review hinges upon whether:

- a) The activity involves a prospective research plan which incorporates data collection, including qualitative data, and data analysis to answer a research question; AND
  - b) The activity is designed to draw general conclusions (i.e., knowledge gained from a study may be applied to populations outside of the specific study population), inform policy, or generalize findings.
- General principles for evaluating whether oral history type activities are human research and require IRB review:
  - a) Oral history activities, such as open-ended interviews, that ONLY document a specific historical event or the experiences of individuals without intent to draw conclusions or generalize findings would NOT constitute "research" as defined by federal regulation.
  - b) Systematic investigations involving open-ended interviews that are designed to develop or contribute to generalizable knowledge (e.g., designed to draw conclusions, inform policy, or generalize findings) WOULD constitute "research" as defined by federal regulation.
  - c) Oral historians and qualitative investigators may want to create archives for the purpose of providing a resource for others to do research. Since the intent of the archive is to create a repository of information for other investigators to conduct research as defined by 45 CFR part 46, the creation of such an archive WOULD constitute research under federal regulation.
- **Analysis of Publicly Available Datasets**
  - Research projects involving analysis of secondary data will NOT require prior IRB approval in the following situations:
    - The data set(s) is (are) published and publicly available without restriction (e.g., data are published by a reputable source in a publicly-available journal, textbook or web-site) and neither the UW researcher nor any collaborating researcher on the project(s) has access to links that would connect the data to the individuals from whom they were derived.
    - The data set(s) are publicly available to researchers and others, but the data holder requires a “responsible use statement” or similar attestation to ensure appropriate use and protection of the data. Such an agreement or attestation may be automated. In this case, neither the UW researcher nor any collaborating researcher on the project can have access to any links that would connect the data to the individuals from whom they were derived, nor may any researcher on the project attempt to re-identify any person from whom the data were derived. The researcher will obtain a data set available from a Federal or State agency and will enter into an agreement with the data provider that includes language that
      - a) the data provided to the researcher does not contain any identifiers, including those specified under the HIPAA Privacy Rule; b) if the data are coded, the data provider will not release a link to the code to the researcher; and c) the researcher receiving the data set must agree to not attempt to re-identify any person from whom the data were derived.

### **Human Research Requiring a Protocol**

Studies that do meet the federal definitions of human research require IRB review. For some of these studies, the IRB requires a standalone protocol that you will upload in the IRB application. These studies include, but may not be limited to, the following:

- Clinical trials and/or more than minimal risk studies or those that involve multiple physical interventions
- Registry and repository studies
- Studies requiring review by the ICTR Scientific Review Committee
- Non-exempt studies where UW-Madison will serve as the reviewing IRB for multiple sites (excepting UnityPoint Health Meriter)

The IRB has protocol templates that can be used for these types of studies, as described in the sections below. You are not required to use these templates if you already have a protocol that addresses the same elements found in the templates. All studies requiring a protocol should be submitted using the protocol-based application (for studies likely to be single site) or the single IRB application (for studies where the UW will be serving as the single IRB for multiple sites) in ARROW.

- **Clinical Trials and More Than Minimal Risk Studies**
  - The following protocol templates are available to assist you in developing a standalone protocol:
    - a) For clinical trials and more than minimal risk studies evaluating drugs and/or devices:
      - i. ICTR therapeutic clinical trial template
      - ii. NIH protocol template
      - iii. NCI protocol template
    - b) For biomedical studies NOT evaluating a drug and/or device, see HRP-502-TEMPLATE PROTOCOL -Biomedical
    - c) For registry and/or repository studies, see HRP-503a-PROTOCOL TEMPLATE-Registries and Repositories.
  - If you have a protocol document that includes the relevant sections of the protocol template most appropriate for your study, you are not required to use the IRB-provided protocol template.
  - If you are designing an investigator-initiated study and do not have an existing protocol template, you are encouraged to use the IRB-provided protocol template.
- **Registry and Repository Studies**
  - While these studies are likely to be minimal risk, the registry and repository protocol-template is the most efficient way for you to provide the information the IRB needs to make the relevant regulatory determinations. See HRP 503a-PROTOCOL TEMPLATE-Registries and Repositories.
- **Studies Requiring Review by the ICTR Scientific Review Committee (SRC)**
  - Per institutional policy, Non-oncology-related applications for full initial IRB review require ICTR SRC unless they a) are otherwise reviewed and determined to be highly meritorious by an alternate internal or external scientific review or b) solely involve these procedures:
    - a) Collection of blood samples by finger stick, heel stick, ear stick or venipuncture, unless the purpose of the biospecimen collection is to perform large scale genetic analyses such as whole genome or whole exome sequencing
    - b) Prospective collection of biological specimens for research purposes by noninvasive means unless the purpose of the biospecimen collection is to perform large scale genetic analyses such as whole genome or whole exome sequencing

- c) Use of materials (data, documents, records, images, or specimens) that have been collected, or will be collected solely for non-research purposes (such as medical treatment or diagnosis)
- d) Collection of data from voice, video, digital, or image recordings made for research purposes
- e) Surveys
- f) Interviews, including focus groups
- g) Wearable devices, such as accelerometers and fitbits, or tests that use external sensors that do not otherwise result in physical stimulation (e.g., EEGs)
- h) Walking tests
- i) Imaging (MRIs, ultrasounds) with FDA-approved devices (hardware and software) when the imaging is performed within the FDA indications and evaluation of the device is not the focus of the research. This does not include PET-MRI.
  - If you are designing an investigator-initiated study and do not have an existing protocol template, you are encouraged to use the IRB-provided protocol template.
  - See below for more information on scientific review requirements.
- **Non-Exempt Studies for Which UW-Madison Will Serve as the Reviewing IRB for Other Sites**
  - If UW-Madison will serve as the reviewing IRB for other sites, a standalone protocol is typically required.
  - Exceptions include minimal risk studies involving only one other site that do not involve interventions with subjects or subject interventions are limited in nature.
  - Projects jointly conducted at UW-Madison and UnityPoint Health Meriter do not typically require a standalone protocol.
  - The IRB-provided protocol template includes instructions for sections specifically addressing single IRB review requirement as well as the reliance and navigation manual. You may also contact the Reliance and Navigation Team (RELIANT) for assistance ([irbreliance@wisc.edu](mailto:irbreliance@wisc.edu)).

## Protocol Guidelines

If you do not already have a protocol that addresses the relevant elements included in the protocol templates, use the appropriate protocol templates as a starting point. 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 a protocol:

- In the protocol templates, the italicized bullet points serve as guidance to study teams. All italicized comments should be deleted prior to submission.
- When writing a protocol, always keep your own electronic copy. You will need to modify this copy when making changes to the protocol.
- Note that, depending on the nature of your research, certain sections of the template may not be applicable to your study. Indicate this as appropriate.
- If you plan to involve any individuals who are members of the populations listed below as participants in your research, you must indicate this in your protocol and address the regulatory requirements that need to be met for including these populations. You are encouraged to consult the checklists referenced below to assist you in addressing these regulatory requirements.

- Adults unable to provide legally effective consent (HRP 417 – CHECKLIST - Adults with Impaired Decision-Making Capacity)
- Individuals who are not yet adults (infants, children, teenagers) (HRP 416 – CHECKLIST – Children)
- Pregnant women (HRP 412 – CHECKLIST - Pregnant Women)
- Prisoners (HRP 415–CHECKLIST-Prisoners)

### **Human Research Not Requiring a Protocol**

The IRB does not typically require a standalone protocol for the following types of studies:

- Exempt projects, including health care records research and not human research determinations
- Community-based Participatory Research
- Most minimal risk research, including most international research

For minimal risk studies, the IRB may determine that a protocol is necessary if the study involves multiple physical interventions, drugs, biological products, nutritional supplements, or devices. Non-exempt international research studies also may require a protocol depending on the complexity of the study. Studies not requiring a protocol should be submitted using the regular IRB application option in ARROW.

- **Exempt Projects (including health care records research and not human research)**
  - The federal Common Rule identifies eight categories of research that may be eligible for exemption from IRB review (45 CFR 46.104(d) (1-8)). UW-Madison currently allows projects that fall into exemption categories 1-6 and are no more than minimal risk to qualify for an exempt determination. Exemptions do not apply to FDA-regulated research or research involving prisoners (45 CFR 46, Subpart C).
  - Research that qualifies as exempt must satisfy UW-Madison's ethical standards for the protection of human research participants.
  - The HIPAA Privacy Rule (45 CFR Parts 160 and 164) applies to all exempt research that uses protected health information (PHI).
  - Before preparing your application, refer to HRP 312 – WORKSHEET – Exemption Determination and Limited IRB Review to help you determine whether your project may qualify for an exempt determination. The [Exemption Category Tool](#) also can assist you in assessing what exemption category may apply to your study.
  - If you believe your project falls into one of these exemption categories, you must submit an application to the IRB since only the IRB can determine whether the research is exempt from review.
- **Non-exempt minimal risk research (including community-based participatory research)**
  - Minimal risk studies that do not qualify for exemption may qualify for expedited review. To determine whether your study may qualify for expedited review, refer to HRP 313 – WORKSHEET – Expedited Review. Even if the study falls into an expedited review category(ies), the IRB reserves the right to refer such applications for review by the convened IRB.
  - Additional requirements may apply to community-based participatory research projects, such as the need for site permissions and IRB of record arrangements.
  - For sites engaged in human research that do not have their own IRB and for which the UW is not serving as the IRB of record, a letter of cooperation from the community



partner is required. This letter ensures the IRB that the site is aware of and supports the study.

- Even if a letter of cooperation is not required, you should still obtain permission from external sites at which study activities such as recruitment and consenting will be conducted to be sure that the site is aware and supportive of the research.
- **International Research**
  - Your application or protocol must include a description of the international research location and the levels of protection appropriate for the location (i.e., appropriate access, consent options, etc.). The IRB prefers that a local ethics committee or similar review board oversee the research in addition to the UW-Madison IRB to help ensure that the research is culturally acceptable. Please refer to HRP 336 – WORKSHEET – International Research for specific considerations that need to be addressed in your application or protocol.
  - The convened IRB or designated reviewer may review and/or consult with other UW-Madison departments/offices and local or national experts to determine if the research is appropriate based on the laws and knowledge of the location in which the research will take place. Given that review by the full IRB and consultation with experts may be required, international research projects should be submitted 2-3 months before the research is planned to begin.

### Other Types of IRB Applications

- **Umbrella Protocols, Training Grants, and Core Grants**
  - While umbrella protocols and training or core grants do not themselves constitute human research, funding agencies may require IRB review, nonetheless. These applications can only be used for approval of a grant itself and cannot be used to cover any human research activities, which must be submitted as separate IRB applications. Study teams should use the regular initial review application in ARROW and select the umbrella protocol application type option when seeking IRB review.
- **Analysis Center Applications**
  - Analysis center studies apply to situations where the UW's role is limited to analysis of data, samples, or images on behalf of a multi-site study. These are applications that do not qualify for an exempt or not human research determination. Analysis centers do not cover establishment of tissue banks or databases at the UW. Analysis center applications should be submitted using the regular application even if they have a standalone protocol.
- **Emergency/One-Time/Compassionate Use**
  - **Emergency Use of an Investigational Medical Product (insufficient time to obtain IRB approval prior to the proposed date of use)** Clinicians should notify the IRB of the proposed use prior to the actual use or, if not feasible because of an emergent situation, within five days of the use. Please notify the IRB as follows:
    - a) During business hours (Monday-Friday, 8AM-5PM), notify the IRB of the proposed emergency use by email ([irbdirector@hsirb.wisc.edu](mailto:irbdirector@hsirb.wisc.edu) and [csrogers@wisc.edu](mailto:csrogers@wisc.edu)) and include the following information:
    - b) Description of how the use meets the criteria outlined in HRP-322 - WORKSHEET - Emergency Use.

- i. Summary of the patient’s diagnosis and treatment history; and
    - ii. Date and/or timing of the proposed use; and
  - c) Attach the following as appropriate:
    - i. Draft consent document. Use HRP-506 - TEMPLATE CONSENT DOCUMENT - Emergency or Compassionate Device Use to prepare your consent document.
    - ii. For drugs or biologics only, documentation of approval of the use from the FDA (or include in the email the date when the request was submitted to the FDA).
    - iii. For devices only, a concurrence letter from an independent physician that states that use of device is warranted and no other reasonable alternative treatments are/were available.
  - d) If the IRB chair concurs with the request and agrees it meets applicable IRB requirements, the treating physician will receive an acknowledgement via email.
  - e) If the IRB chair determines that sufficient time exists for the convened IRB to review the request, the treating physician will need to submit an expanded access application in ARROW and treatment will be allowed to begin following IRB approval of the application.
  - f) Outside business hours, clinical judgement prevails over the need for administrative procedures. Emergency use of an investigational medical product in one patient outside IRB business hours may proceed as follows:
    - i. For a drug or biologic, notify the [PRC](#) (Pharmaceutical Research Center).
    - ii. Notify the IRB of the use by voicemail (608.263.2362) and email ([irbdirector@hsirb.wisc.edu](mailto:irbdirector@hsirb.wisc.edu)).
    - iii. The application will then be reviewed by the convened IRB to determine
      - a) whether the use met the criteria for emergency use of an investigational medical product per the FDA and b) that informed consent was obtained or met the criteria for exception to the requirements for informed consent.
  - g) If not completed before use, a treatment use application must be submitted in ARROW within 5 days of the emergency use. This application will be reviewed by the convened IRB to determine whether the convened board agreed with the IRB Chair’s assessment or additional information should be provided to the patient (or their representatives).
- **Expanded Access of Investigational Medical Products (non-emergency)**
  - Once the appropriate expanded access route has been identified and the FDA and drug/biologic/device manufacturer contacted, treating teams will need to submit an application through ARROW for prospective IRB approval, just as they would for research studies. This application will be reviewed by the convened IRB and approval granted before the use can proceed.
  - See HRP-325 - WORKSHEET – Device Compassionate Use and HRP 023-SOP-Emergency and Device Compassionate Use and HRP 027-SOP- All Emergency Use, Compassionate

Use (Device Only) and IRB Waiver for Individual Patient Expanded Access (Drug Only) Review

- **Humanitarian Use Device (HUD/HDE)**
  - IRB review and approval is required before a HUD can be used for clinical care. You can refer to HRP-323 - WORKSHEET - Criteria for Approval HUD for additional information regarding the criteria that the IRB uses to review and approve HUD uses. This worksheet also includes criteria for informed consent. The clinical use of a HUD is not considered Human Research but must still be submitted for review and approval by the IRB prior to clinical use (with the exception of emergency use, which should follow the emergency use process).
- **Proposal Development Activities (Requests from Funders for IRB Review, Just-In-Time Notifications)**
  - If you receive a request from a funder for IRB approval or review of a grant and human research will not be conducted immediately under the grant, you should use the Protocol Development Activities (PDA) form in ARROW. The PDA can be used when 1) research activities involving human subjects are planned for the future but have not been finalized (e.g., the grant incorporates a planning stage); 2) when an agency or organization requires IRB approval of the study in concept; and 3) when you have received a "just-in-time" requesting documentation of IRB approval. Only planning activities that do not involve human subjects can be covered by this administrative approval.
  - Not all funders will accept PDA approval in lieu of IRB approval for a human research study, so you are encouraged to consult with your funder before submitting a PDA application in ARROW.

### **Institutional Requirements**

In addition to IRB review and approval, your study may require review by other entities separate from the IRB (e.g., HIPAA security review, radiation safety). Some of these reviews should be started before you submit an IRB application. See HRP 309-WORKSHEET – Ancillary Review Matrix for more information about the non-IRB requirements that may apply to your study. You may also contact the Reliance and Navigation Team (RELIANT) for assistance. ([irbreliance@wisc.edu](mailto:irbreliance@wisc.edu)).

## **PREPARING SUPPORTING MATERIALS**

### **Writing a Consent Document**

- For new, non-exempt studies and those that do not already have an IRB approved consent document, you should use the appropriate consent template below to create your consent document(s):
  - HRP 502-TEMPLATE CONSENT DOCUMENT-Biomedical
  - HRP 507-TEMPLATE CONSENT DOCUMENT-Short Form

Note that all long form consent documents and all summaries for short form consent documents must contain all the required and any additional appropriate elements of informed consent. Review the “Long Form of Consent Documentation” section in HRP-314 - WORKSHEET - Criteria for Approval, to ensure that these elements are addressed. When using the short form

of consent documentation, the appropriate signature block from HRP-507 - TEMPLATE CONSENT DOCUMENT – Short Form should be used on the short form.

- For exempt projects that will involve interactions with subjects, you may use an abbreviated process for obtaining consent. Consent can be verbal, but you must provide the following information to participants through an information sheet or written script:
  - The participant is being asked to participate in a research study;
  - A description of the procedure(s) the participant will be asked to complete;
  - Participation is voluntary; and
  - The investigator’s name and contact information.
  - For an exempt consent template, see HRP502a-TEMPLATE CONSENT DOCUMENT-Exempt.
- For educational and social-behavioral studies, a [consent wizard](#) is available.
- For studies using a consent template provided by a sponsor that conforms to the requirements of HRP 502, you do not need to revise the consent document other than to ensure required institutional language is included. For details, see HRP 502c-STANDARD CONSENT LANGUAGE.
  - HRP 502c should also be used when creating consent documents for ceded studies. For details, see the Reliance Manual.
- For VA studies, HRP 502 includes instructions for creating VA consent documents. For details on VA requirements, see Appendix A-9 below.
- For emergency or compassionate use, see HRP 506-TEMPLATE CONSENT

We recommend that you date the revisions of your consent documents to ensure that you use the most recent version approved by the IRB.

### **Writing a HIPAA Authorization Form**

The HIPAA Privacy Rule is a set of federal regulations providing protections for the confidentiality of health information used in clinical practice, research, and the operations of health care facilities. The intended purpose of the Privacy Rule is to ensure that health information confidentiality risks are minimized.

Studies using or disclosing protected health information (PHI) subject to HIPAA requirements may need to obtain authorization from participants in addition to informed consent. IRB template consent documents include template authorization language. You are encouraged to use a combined consent and authorization form. In the event you need a separate authorization form, refer to the Office of Compliance for those templates.

### **Preparing Recruitment Materials**

All documents that will be used to recruit participants must be reviewed by the IRB. These materials include but are not limited to:

- Advertisements
- Website posting
- Letters and emails
- Social media posts
- Scripts for television or radio ads

When preparing your materials, refer to HPR 315 – WORKSHEET – Advertisements to ensure your documents meet IRB requirements.

### **Other Subject-Facing Materials Requiring IRB Review**

In addition to the documents noted elsewhere in this manual, the following documents require IRB review and must be uploaded in the ARROW application:

- Study instruments, including:
  - Questionnaires
  - Interview questions
  - Assessments specific to the study
  - Investigator's Drug Brochures
  - Device specifications
- Communications to subjects that:
  - Disclose the study condition/treatment/arm to which they were assigned when a study has been unblinded
  - Describe new information about study progress or study procedures

Depending on the study, the IRB may request additional documents required to make regulatory determinations.

### **Supporting Documents That Do NOT Require IRB Review**

Some subject-facing documents do not require IRB review as long as they contain information that is consistent with the protocol or other IRB reviewed documents and do not include new information that would affect subjects' willingness to take part in the study. These include:

- Appointment reminders
- Case report forms
- Course curriculum content
  - When content of the course is established and will not be altered for the research study
- Data collection forms
  - This does NOT include survey and other instruments used to collect data directly from subjects.
  - The data collected on these forms needs to be described in the application/protocol.
- Eligibility determination sheets/forms
  - Note this does not include telephone screening scripts.
- Instructional materials for subjects
  - If the materials are limited to the technical description of procedures or medications described in the study protocol and do not contain information about study risks
- Manuals of Procedures
- Medication or pill diaries, study diaries
- Newsletters
  - When content does not include recruitment information or describe study results or progress (other than number of subjects enrolled or study status)

## SUBMITTING IRB APPLICATIONS

### Scientific Review Requirements

Institutional policy requires that some studies undergo review by the ICTR scientific review committee (SRC) prior to being forwarded to the IRB. The SRC review process is separate from the IRB's. The [SRC website](#) has more information about its processes.

Studies submitted for full IRB review that are not oncology-related typically require SRC review unless they a) are otherwise reviewed and determined to be highly meritorious by an alternate internal or external scientific review process or b) solely involve a range of minimal risk procedures.

All oncology-related studies must undergo review by the UWCCC's protocol review and monitoring committee (PRMC) before the application is forwarded to the IRB for review. The PRMC has its own application process separate from the IRB's. For more information, contact the PRMC directly ([prmc@uwcarbone.wisc.edu](mailto:prmc@uwcarbone.wisc.edu)).

### How to Submit a New Study Application

New applications must be submitted through ARROW. The IRB application wizard offers several options and it is important to choose the right option for your study. Not choosing the correct option may require you to start your application over. The current application options are:

- Initial review application:
  - You should choose this option if you:
    - Do NOT have a standalone protocol.
    - Are not asking UW-Madison to serve as the reviewing IRB for more than one site or are not ceding IRB review.
    - Are not asking UW-Madison to rely on an external IRB.
    - Are submitting an application for all other types of studies including:
      - Exempt research
      - Studies that qualify for expedited review
      - Full review of single site studies
      - Statistical Data Analysis Center (SDAC) studies
      - Emergency Use/Expanded Access Requests
- Protocol-based application:
  - You should choose this option if your study has a standalone protocol. Additionally, you should use this application for the following:
    - Biomedical studies with multiple interventions
    - Biomedical studies of more than minimal risk
    - Clinical trials
    - Studies investigating a drug or device
    - Registry and repository studies
- Single IRB (sIRB) review application:

- You should choose this option if you are asking UW-Madison to serve as the reviewing IRB for multiple sites. (Single IRB review requirements do not apply to exempt studies.)

### **How to Submit a Continuing Review**

If your study requires continuing review, complete a continuing review application by selecting the “Continuing Review” option in the study workspace. Continuing review applications should be submitted 45 days prior to the study expiration date to ensure sufficient time for processing. No changes can be made as part of continuing review application, but changes can be submitted separately and concurrently via a change application.

If you do not submit a continuing review application and receive approval prior to the expiration date listed on your approval letter, you must cease all study activities until the continuing review is approved (except for those related to ensuring participant safety).

See “Post-Approval Responsibilities” below for details about continuing review requirements.

### **How to Submit a Change of Protocol**

To submit a change, click the “New Change” button in the study workspace. You will need to complete both a change form and modify the application to reflect the changes you are proposing, including uploading any revised documents.

You must submit planned changes to a study and receive IRB approval for those changes prior to implementing them. Changes may only be implemented without prior IRB approval where necessary to eliminate apparent immediate hazards to the subjects. In the case of changes implemented to eliminate immediate hazards to the subjects, these must be reported to the IRB using a Reportable Event submission. See “How to Submit a Reportable Event” below.

See “Post-Approval Responsibilities” below for details about change requirements.

For changes to exempt research, refer to the “IRB Review Process” section below for information regarding requirements for changes to exempt research.

### **How to Submit a Reportable Event**

To submit a reportable event, click the “Reportable Event” button in the study workspace. Reportable events must be submitted to report potential noncompliance, an unanticipated problem, or new information. Some events must be submitted within a specific timeframe. See “Post-Approval Responsibilities” below for details about reportable event requirements, including reporting timeframes.

### **How to Update Personnel**

Study team personnel except the PI and external personnel for whom UW-Madison is serving as the reviewing IRB can be made using the Update Personnel activity in ARROW. Updates to personnel can also be made with changes, if needed.

- Study team members who will no longer be working on a study must be removed within 6 weeks of their departure.
- New study team members must be added before they can begin study activities and must meet all the requirements noted above in the “Researcher Requirements” section.
- Please consult with the Reliance and Navigation Team (RELIANT; [irbreliance@wisc.edu](mailto:irbreliance@wisc.edu)) when study team members leaving the institution will still be involved in the study or if you wish to add external personnel.

See “Change in Principal Investigator” above for details on changing the PI.

### **How and When to Close a Study**

To submit a study closure report, select the “Closure Report” activity in the study workspace and complete the form as directed.

A final report (i.e., closure report) is required within 30 days of study close out or approval of a replacement application for all non-exempt research, including for studies that are not subject to continuing review. Studies can be closed when all study activities are completed; data analysis may continue only if all data is de-identified. If UW-Madison is a participating site in a multisite study, the UW-Madison may be closed with the permission of the coordinating center even if the overarching study remains open.

The IRB may require closure and re-submission of any study under the following circumstances: no research activities have begun, or no participants have been enrolled within 3 calendar years from the date of the IRB approval of an initial review application; the IRB application and/or protocol needs to be updated to meet current IRB and regulatory standards; or a study or protocol appears to have changed substantially from the IRB’s original assessment of it.

## **IRB REVIEW PROCESS**

### **Regulatory Classifications for Human Participant Research**

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

- **Non-Committee Review Processes** (three categories of research do not require review by the convened IRB):
  - **Not “Human Research”**: Activities must meet the institutional definition of “human research” to fall under IRB oversight. Activities that do not meet this definition are not subject to IRB oversight or review. Refer to the HRP 310 – WORKSHEET - Human Research for guidance. If you are unsure whether your project meets the definition of human research, contact the IRB office for assistance before beginning work on your project.
    - If you need a formal IRB determination of not research (e.g., if requested by publishers or sponsors), you can submit an ARROW application to obtain this



documentation.

- Exempt: Certain categories of human research may be exempt from certain regulations, but still require IRB review to confirm this. Per institutional policy, the IRB and not the investigator determines whether human research qualifies for exemption. Refer to HRP 312 – WORKSHEET - Exemption Determination for guidance on the categories of research that may be exempt. See also the [Exemption Categories Tool](#).
  - Review Using the Expedited Procedure: Certain categories of non-exempt Human Research may qualify for review using the expedited procedure, meaning that the project may be approved by a single designated IRB reviewer, rather than the convened board. Review *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 IRB Committee**
    - Human Research that does not qualify for review using one of the three non-committee procedures must be reviewed by the convened IRB.

### **Changes to Research Determined to Be Exempt**

Since some changes to research previously determined to be exempt may alter either the category(ies) under which the exemption was granted or require that the project be reviewed under a different review process, certain modifications to these applications need to be submitted as changes. For information on what types of changes need to be submitted for exempt studies, see [Exemption Change Table](#).

### **IRB Approval Criteria**

The criteria for IRB approval can be found in HRP-312 - WORKSHEET - Exemption Determination and Limited IRB Review for exempt Human Research and HRP-314 - WORKSHEET - Criteria for Approval for non-exempt Human Research. The latter worksheet references other checklists that might be relevant to your study. All checklists and worksheets can be found on the IRB web site.

These checklists are used for initial review, continuing review, and review of changes to previously approved human research. You are encouraged to use the checklists to write your protocol or application in a way that addresses the criteria for approval.

### **IRB Review Decisions**

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

- Approve: Made when all criteria for approval are met. See “IRB Approval Criteria” above.
- Modifications Required to Secure Approval: Made when IRB members require specific modifications to the research before approval can be finalized.
- Tabled: Made when the IRB cannot approve the research at a meeting for reasons unrelated to the research, such as loss of quorum. When taking this action, the IRB automatically schedules the research for review at the next meeting.

- Deferred: Made when the IRB determines that the board is unable to approve research and the IRB suggests modifications that 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.
- Disapproval: Made when the IRB determines that it is unable to approve research and the IRB cannot describe modifications that 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.

### **Communication of IRB Decisions**

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

- If the IRB has approved the human research: The human research may commence once all other institutional approvals have been met. IRB approval is usually good for a limited period of time which is noted in the approval letter. If no continuing review for your study is required, this also will be 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 via ARROW. 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 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.

### **Disagreeing with IRB Decisions**

Researchers may request that the IRB reconsider a decision by submitting a written response to the IRB. When submitting a request to reconsider, the researcher must provide rationale for the request, including any additional supporting documents.

Grounds for a request are limited to:

- New information not reasonably available during the IRB review/investigation
- Material failure by the IRB to follow IRB policies and procedures
- The sanction exceeds the severity of the non-compliance violations, if applicable
- The action is disproportionate to the risks to subjects safety/welfare

These considerations also apply to all other submissions, including changes, continuing reviews, reportable events, and also where the IRB has suspended or terminated the research.

## **Accessing IRB Records and Rosters**

Investigators are responsible for maintaining complete study files. All IRB related study documents are located in ARROW, and if needed, can be requested. Information from the IRB Roster, HRP-601, is available upon request.

## **CONDUCTING HUMAN PARTICIPANT RESEARCH**

The IRB reviews study recruitment methods (including advertisements and payments) to evaluate whether they will affect the equitable selection of participants, and to ensure that the proposed methods adequately protect the rights and welfare of participants.

The protocol document or application must include a description of the following: (1) the source of subjects for all study groups (intervention/case and control); (2) when, where, how, and by whom these potential subjects will be recruited; (3) the methods employed to identify potential subjects; and (4) the materials used to recruit subjects, including the use of email and text messaging. If this is a multi-center study in which subjects are recruited by methods not under the control of the local site, e.g., call center or national advertisements, describe those methods.

The IRB must review and approve the content of all recruitment and advertisement materials, including oral communications, before implementation. For guidance on what to include in an advertisement, refer to the “How to Prepare Recruitment Materials” section above as well as HRP 315-WORKSHEET-Advertisements.

### **General Recruitment Guidelines**

These guidelines apply to all research studies that will identify and recruit participants. For guidelines specific to recruiting in a clinical health care setting, refer to the “Clinical Recruitment Guidelines” section below.

- Advertising and recruiting procedures must protect potential participants' confidentiality. In particular, names and contact information for potential participants must be collected and maintained in a confidential manner.
- When obtaining the names of potential participants from third parties, you must consider whether any breach of confidentiality or privacy laws has occurred. For example, doctors must contact their patients for written permission before releasing their names to a third party.
- You are responsible for ensuring that approved procedures are followed by any third parties (e.g., therapists, teachers, or social-service providers) who may be aiding in the recruitment and/or advertising process. Payment in exchange for referral of potential participants (“finder’s fees”) and payment tied to the rate or timing of enrollment (“bonus payments”) is prohibited.
- You may not share names of previous research participants with other researchers

without permission from the participants.

### Initial Contact Guidelines

- Letter
  - *Mailed recruitment letters:* Letters, whether or not they precede a phone call, should be clear regarding why the potential subjects are being contacted and how the individual(s) sending the letter have identified the potential subjects.
  - *Recruitment of subjects from a previous study for a follow-up or other related study:* Letters should refer to the study in which the individual has already participated and state how the new study is related to it.
  - *Recruitment of children through their school:* Letters should be addressed to parents/guardians; it can be provided in a packet that children take home with them.
- Phone
  - If you plan to recruit or screen potential participants by phone, the IRB requires you to use a script to ensure consistency and completeness in the information that potential participants are given about the study or screening questions. You will need to upload these scripts as part of the IRB application.

### Email Recruitment Guidelines

- Only secure, university-issued or approved email accounts should be used, such as @wisc.edu, @medicine.wisc.edu or @uwhealth.org accounts. Personal email accounts, such as @gmail.com, may not be used. Use encrypted email if possible.
- Email addresses must not include references to health information or other potentially sensitive, private information (e.g., parkinsonsresearch@wisc.edu).
- Protocols or applications must describe how email will be used, including the source of email lists, targeted populations, frequency of emails, and methods for potential participants to remove themselves from the email list.
- You will need to provide email templates used for recruitment purposes. The subject line and content of these emails should not contain any references to health information or request health information from the subject through email.
- The University of Wisconsin-Madison allows researchers to use email to send its faculty, staff, and students information about research opportunities. Information about the campus mass email service is available at: [Mass Email - Getting Started](#).

### Clinical Recruitment Guidelines

In addition to the above general recruitment guidelines, these guidelines apply to research studies that will identify and recruit participants in a clinical health care setting (i.e., patients).

- Initial contact by letter, phone, and email
  - “Cold calling” of potential participants by phone is generally not permitted. “Cold calling” is a planned communication with a potential participant by the study team when not known to the potential participant or not expected to have access to their protected health information.
  - Phone calls for studies that fall under VA purview must be preceded by a recruitment letter because VA regulations do not permit cold calling, unless there is prior written documentation that the potential subject is willing to be contacted by phone.

- Mailed letters should come from someone who, by virtue of his/her position, would have access to the potential subject's confidential health-related information.
- Use of patient email addresses in HealthLink for recruitment purposes is not permitted. Use of MyChart for recruitment purposes is also not permitted unless approval from UW Health has been obtained.
- *In Person Contact*
  - How and who initiates contact with patients in a clinical setting depends on the circumstance. Any patients in private clinic rooms or hospital rooms should first be approached by someone who is part of their care team or a study team member or administrator who is part of the clinic or department in which the study is being conducted.
  - Unless a member of the care team is also a member of the study team, potential patient-subjects should provide permission to be approached by researchers in this private setting. Written permission is required if the research team is not part of the [Health Care Component](#) or [Affiliated Covered Entity](#).
  - Recruitment of potential participants in waiting areas or other similar space requires permission from the institution or clinic to ensure minimal interruption of workflow.
- *Eligibility Screening*
  - Collection of identifiable private information to determine study eligibility is considered a research procedure. Obtaining oral consent prior to the research screening interview is usually acceptable.
  - For HIPAA Privacy Rule purposes, telephone screening generally constitutes a preparatory to research activity. However, the VA interprets preparatory to research differently than the UW-Madison. Telephone screening for VA research studies requires a partial waiver or alteration of authorization.
  - In most cases, screening information from individuals who take part in the study is kept as part of study records, while screening information from individuals who are not eligible or choose not to participate is destroyed. Researchers proposing to retain contact information and/or identifiable data collected during telephone screening for future recruitment or other purposes outside the scope of the research study should specify what information will be retained, and how long, how the information will be stored, how the information will be used, and who will have access to the information.
  - Retention of sensitive screening information from subjects who are ineligible (e.g., data about illicit or stigmatizing behavior; social security numbers) is discouraged.

#### Social Media Recruitment Guidelines

- It is the responsibility of the research team, when designing a protocol, to understand the social media site terms of use (TOU). In addition, study teams should be aware of any research or recruitment-related restrictions on the social media sites through which they intend to conduct their recruitment activities. This includes a site's advertising, privacy and prohibited content policies.

- It is the responsibility of the research team, when designing a protocol, to understand the various privacy and data security provisions of social media sites and ensure that these provisions are consistent with the IRB's privacy and confidentiality guidelines.
- In social media or other Internet-based research settings, recruitment information can be forwarded or otherwise accessible to other individuals who may not be part of the intended participant pool. Research teams, therefore, must exercise caution to appropriately identify the targeted participant population and to ensure the equitable selection of participants.
- The IRB will review the content of social media recruitment materials according to existing IRB guidelines for traditional media recruitment such as flyers and news ads.
- Recruiting via public and private groups is permitted. Study teams must be aware of any site restrictions or group-specific rules or restrictions on recruiting participants via groups.
- Study teams are discouraged from using their personal social media accounts to purchase or place initial recruitment materials for studies.

### **Participant Remuneration and Compensation**

The IRB is responsible for ensuring that any payment or remuneration offered to participants in human subject research is fair and not an undue inducement to participate. Remuneration for participation in research should be reasonable and the amount paid should be comparable to other research projects involving similar time, effort, and inconvenience. Payment amounts should not be large enough to constitute an undue inducement to participate in a risky or uncomfortable procedure. Additional guidelines for specific situations:

- Short research studies involving one visit: Participants may be provided payment contingent upon completion of the study. Participants who are disqualified through no fault of their own must be paid for the time and effort they expended prior to their termination from the study.
- Research studies involving multiple visits or lengthy or repeated participation: Partial payment should be provided to participants who withdraw, are discharged early from the study by the investigator, or otherwise fail to complete the study as agreed. The amount of partial payment should relate to the amount of time, effort, or discomfort involved. Payment schedules may be designed on a per-day, per-visit, or per-procedure rate, or some combination thereof. The terms for partial payment must be described in the application and in the consent form.
- Completion bonuses: Such remuneration may be acceptable to encourage the completion of all study procedures/visits. The amount of such incentives depends on the risk and duration of the study interventions. For additional information on payment requirements, see HRP 316-WORKSHEET-Payment. For information on the campus policy for payments, see [Payments to Research Participants](#).

### **Informed Consent Process and Documentation**

Use HRP-502 - TEMPLATE CONSENT DOCUMENT to create a consent document. You may continue to use your own consent template if it includes the elements found in HRP-502.

Note that all long form consent documents and all summaries for short form consent documents must contain all of the required and all additional appropriate elements of informed consent disclosure. Review the "Long Form of Consent Documentation" section in HRP 314 - WORKSHEET - Criteria for Approval, to ensure that these elements are addressed. When using the short form of consent

documentation, the appropriate signature block from HRP-502 - TEMPLATE CONSENT DOCUMENT should be used on the short form.

If your research study meets the requirements for an exemption and there are interactions with subjects, you may use an abbreviated process for obtaining consent. Consent can be verbal, but you must provide the following information to participants through an information sheet or written script:

- The subject is being asked to participate in a research study;
- A description of the procedure(s) the participant will be asked to complete;
- Participation is voluntary; and
- The investigator's name and contact information.

We recommend that you date the revisions of your consent documents to ensure that you use the most recent version approved by the IRB.

### **Assent Process and Documentation**

Assent is defined as "a child's affirmative agreement to participate in research." Passive resignation to submit to an intervention or procedure is not considered assent. Federal regulations do not specify any of the elements of informed assent and do not provide an age at which assent ought to be possible. In determining whether children are capable of assenting, the IRB takes into account the ages, maturity, and psychological state of the children involved. The IRB determines whether all or some of the children are capable of assenting. The IRB also assess when parental permission is required, whether by one or both parents.

The assent of the children is not a necessary condition for proceeding with the research if the IRB determines that the intervention or procedure involved in the clinical investigation holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the clinical investigation. For more information on requirements for assent for children, see HRP 416 – CHECKLIST – Children and the "Research with Children" section below.

As a general rule, all adults, regardless of their diagnosis or condition, are presumed competent to consent to participate in research unless there is evidence of a serious disability that would impair reasoning or judgment. When investigators propose to include individuals with questionable capacity, you must provide a plan for assessing the participants' decision-making capacity. Assessment is done on an individual basis and should determine the potential participants' ability to understand and express a reasoned choice based on:

- The voluntary nature of research participation and the information relevant to their participation (research procedures);
- Consequences of participation for the participant's own situation, especially with regard to the participant's health condition;
- Consequences of the alternatives to participation;
- Potential risks and benefits involved in the study; and
- Procedures to follow if the participant experiences discomfort or wishes to withdraw.

If the assessment shows evidence that the participant is competent to consent, you must obtain valid informed consent directly from the participant. If the assessment determines that the potential participant does not have sufficient capacity to consent, you must do the following:

- Document the participant is incapable of understanding the information presented regarding the research in the participant's research record;
- Document the information provided to the participant's legally authorized representative regarding the cognitive and health status of the participant, the risks and benefits of the research, and the role of the legally authorized representative in the research record;
- Obtain the consent and signature of the participant's legally authorized representative; and
- Obtain and document the participant's assent if the person with decisional impairment is capable of exercising some judgment concerning the nature of the research.

The verbal objection of an adult with decisional impairment is binding. If the participant, at any time, objects to continuing in the research study, they cannot participate in the research study. Situations may arise in which you could legitimately return to the participant at a later point to ascertain whether the previous objection still stands. The only exception will be research providing direct benefit only available in the context of the research, in which case you must submit a request to the IRB to enroll or continue the participant and provide written documentation of the agreement of the participant's legally authorized representative. In this instance, the IRB may solicit advice of experts.

When appropriate, the consent process may be altered to allow for non-verbal or other alternative consent methods. Proposed alterations to the consent process are submitted for IRB review and approval.

For more information on consent and related requirements for enrolling adults with impaired decision-making, see HRP 013 – SOP – Legally Authorized Representatives, Children, and Guardians and HRP 417 – CHECKLIST – Adults with Impaired Decision-Making Capacity.

### **Remote Consent Processes**

Any method of obtaining informed consent other than a face-to-face consent interview must allow for an adequate exchange of information and documentation, and a method to ensure that the signer of the consent form is the person who plans to enroll as a subject in the clinical investigation or is the legally authorized representative of the subject.:

- A consent form may be sent to the subject or the subject's legally authorized representative by mail, facsimile or e-mail, and the consent interview may then be conducted by telephone or via a UW-approved videoconferencing platform (i.e., WebEx). This process allows the subject or subject's legally authorized representative to read the consent form before or during the consent discussion. After the consent discussion, the subject or the subject's legally authorized representative can sign and date the consent form. If the signed informed consent document cannot be mailed or collected from the participant's location and included in the study records, subjects or their LAR may scan the document or take a picture of each page via a smartphone or camera and send the document back to the study team via a UW approved document sharing option (e.g., uploads to Secure Box Folder, WebEx) or via email or fax. If a picture is used, the subject should email a picture of the entire consent form so you have a record of what information the subject received, and the full document that was signed. If the entire form cannot be sent back, the subject should email the signature page(s) as well as any pages



requiring subject responses, such as checkboxes or initials. In cases where the entire form is not provided, you should confirm that the version date and IRB stamp is visible on the page(s) received, to document that the subject signed the correct version. The email from the subject can also provide documentation of timing of receipt and should be retained in the research records.

- Finally, the person signing the consent form must receive a copy of the consent form. Although FDA regulations do not require the subject's copy to be a signed copy, FDA recommends that a copy of the signed consent form be provided.

Research records should clearly document what method was used to conduct the consent process and document that informed consent was obtained prior to beginning study procedures.

### **Documenting Consent Electronically**

"Digital signatures" may be acceptable forms of documentation of written informed consent. Electronic, computer, or tablet-based consent documents may facilitate record keeping even when an individual is present and could sign a paper form. Digital signatures may be considered for face-to-face and remote consent, but the technologies and processes used must be described in the protocol or application.

Digital signature generally take three forms: (1) actual signatures on tablets or computers (where an individual uses a stylus or finger to make a representation of their signature, as available in many retail stores) , (2) validated electronic signatures on platforms with password entry (such as those used to sign medical notes or electronically write prescriptions) or 3) typing one's name with an accompanying check box and statement noting an intent to affix a legal signature (e.g., "By checking this box and typing my name below, I am electronically signing this consent form"); this method is not allowable for FDA-regulated research. Validated electronic signatures typically require one to "set up" an identity and password within an electronic system and may not be easily and rapidly activated. All forms of digital signature may be used in research in certain settings, but because of tracking, privacy, and identity validation issues, this may be more challenging than it initially appears.

'Digital signature' methodologies, if used entirely remotely, are generally approved only for low risk research or other circumstances (i.e., time of national emergencies, pandemics, natural disasters) because it is not always possible to validate the identity of the individual. When a stylus is used to collect a signature in person, the usual methods of identity validation should be used (typically patient is asked to provide a picture identification card when they check in at the clinic).

For FDA-regulated research, the digital signature platform and process must be [21 CFR part 11 compliant](#). In addition, the research team must verify the participant's identity.

See HRP314-WORKSHEET- Criteria for Approval; HRP 090-SOP-Informed Process for Research, and HRP091 – SOP-Written Documentation Consent.

### **Enrolling Participants with Limited English Proficiency**

Subjects who have limited English proficiency should be presented with informed consent information in a language understandable to them that includes all the required and additional elements for disclosure. Persons with limited English proficiency are individuals who do not speak

English as their primary language and/or who have a limited ability to read, speak, write or understand English.

For research involving targeted populations that have limited English proficiency, the use of a written translation of the approved long form consent document is required. With prior IRB approval, a short form consent documentation process is available for documenting consent when an individual with limited English proficiency is encountered unexpectedly and an IRB-approved translated long form consent document is not available. Review the *WORKSHEET: Short Form of Consent Documentation (HRP-317)*.

- **Written translation of long form documents** - The IRB must review and approve all foreign language versions of long form consent documents for a particular study prior to use.
  - For long form consent document translations, the investigator may wish to delay translation service until IRB approval is granted for the English version to avoid extra translation costs. The IRB must have all versions of the research materials (e.g., recruitment informed consent form(s), instruments) in both English and Non-English on file.
  - The translation of a consent document must be made by a reliable source.
  - The IRB may request verification of a back-translation process by an individual who is not associated with the research to confirm the accuracy of the translated document.
  - The investigator must provide the credentials (qualifications, skills or experience for carrying out this role) of the individual(s) or service(s) that were used to translate (and back translate, if applicable) the consent documents.
- **Written translation of short form documents**
  - If you will use the pre-translated short forms provided by UWHC, you do not need to submit these forms for IRB approval.
  - If you will not use the pre-translated UWHC forms, you must submit the short forms for IRB approval.
- **Short form consent documentation process** - The short form documentation process should be used when an individual with limited English proficiency is encountered unexpectedly and no translated long form is available. For this process the following are required:
  - Oral presentation of the research in a language understandable to the subject or the subject's Legally Authorized Representative (LAR) by an interpreter
  - A short form consent document in the subject's or LAR's language
  - A written summary of the information that is presented orally (the IRB-approved English language long form consent document may serve as a summary).
  - A witness fluent in both English and the language of the subject or subject's LAR is present for the oral presentation. The witness is someone who is not involved in the research. When the person obtaining consent is assisted by a qualified interpreter or translator, that individual may serve as the witness if they are not involved in the research.
- **Signatures required for the short form consent documents.**
  - The subject or representative signs and dates the short form consent document.
  - The individual obtaining consent signs and dates the summary.
  - The witness to the oral presentation signs and dates the short form consent

- document and the summary.
- Copies of the signed and dated consent document and summary are provided to the subject or representative.

For more information, refer to HRP 090-SOP-Informed Consent Process for Research, HRP 091-SOP-Written Documentation of Consent, and HRP-317-WORKSHEET-Short Form of Consent Documentation.

### **Translation and Interpreter Requirements**

If the subject/representative has limited English proficiency, you must obtain the services of an interpreter fluent in both English and the language understood by the subject/representative. If the study is minimal risk, the interpreter may be a member of the research team, a family member, or friend of the subject/representative. If the research involves medical care and/or is more than minimal risk, use of family or friends to interpret is discouraged. Should the individual and/or their representatives insist upon the use of a friend or family member to provide them with interpreting service, you should retain a healthcare interpreter to participate in the exchange to ensure that it represents accurate communication of information between investigators and patients.

For assistance in obtaining translation and interpreter services, contact UWHC Interpreter Services.

### **Research Involving Participants with Impaired Decision-Making**

If your research includes cognitively impaired adults, or adults with potentially absent, diminished or fluctuating capacity to consent, review the HRP 417-CHECKLIST-Cognitively Impaired Adults to see the categories of research in which those with impaired decision-making may be involved. Use this checklist to ensure you are providing sufficient justification in your protocol or application for enrollment of these individuals. See also HRP 013 -SOP-Legally Authorized Representatives, Children and Guardians, and HRP 090-SOP-Informed Consent.

Your protocol or application should specify the validated assessment tool that will be used for assessing capacity to consent to research and a copy should be provided with your application. If a standard assessment tool will not be used the IRB may require documentation to determine whether the tool is appropriate in the context of the study and population.

For studies involving non-English speaking participants, your protocol or application must describe how the assessment will be conducted. The assessment tool does not need to be translated unless the assessor will assess the participant's capacity to consent by speaking in the participant's language. For studies where the assessment will be conducted in English but will include the involvement of an interpreter, the assessment tool does not need to be translated.

Your protocol or application should be explicit regarding the use of a legally authorized representative if one may potentially be utilized to consent on behalf of a participating adult.

As a matter of subjects' protection, assent should be obtained from incompetent or incapacitated adults for research participation to the extent they are able to provide assent. Even where a legally authorized representative has consented to the research participation, an incompetent or incapacitated adult

should, except in rare cases, not be included over their objection (known as dissent). The IRB will consider instances in which superseding considerations may affect this guidance.

### **Research with Prisoners**

Review HRP 415-CHECKLIST-Prisoners to ensure that you provide sufficient information in your protocol or application to justify enrollment of prisoners in your study.

Following IRB review and approval of DHHS-supported research involving prisoners, the IRB will provide a certification letter to the Office of Human Research Protections (OHRP) as required in 45CFR46.306.

Once the research has commenced, similar considerations apply when a participant becomes a prisoner at any time during the conduct of the study, regardless of study funding. In this event:

- Report this to the IRB as a reportable event; and
- Review HRP 415-CHECKLIST-Prisoners to ensure you have provided sufficient information.

### **Research with Children**

If your research involves children under the age of 18, review the HRP 416-CHECKLIST-Children to ensure that you provide sufficient information in your protocol or application to justify enrollment of children. Consider whether parental permission and assent should be obtained (refer to HRP 416 for guidance) and incorporate this information in your protocol or application. For information on state law implications for enrolling children, see HRP 013-SOP-Legally Authorized Representatives, Children, and Guardians.

For guidance on assent, the Assent Process and Documentation section above.

### **Research with Pregnant Women and/or Neonates**

If you plan to include pregnant women and/or neonates in your study, additional regulatory requirements may apply. For details on requirements for studies involving pregnant women and/or neonates, refer to HRP 412-CHECKLIST-Pregnant Women, HRP 413-CHECKLIST-Non-Viable Neonates, and HRP 414-CHECKLIST-Neonates of Uncertain Viability.

### **Research with Other Vulnerable Populations**

In addition to the populations listed above, other groups of individuals may be considered vulnerable and require additional protections and rationale be in place to involve these groups in your study. Examples of vulnerable populations include non-English speakers, students, employees of the researchers, and active-duty military members. Examples of additional protections that may be required include having someone outside the study team observe the informed consent process, exclusion of the population if not required to achieve study objectives, and independent assessment to address consent capacity.

Under Wisconsin state law, special provisions apply to individuals receiving protective services (voluntary or involuntary) or inpatient or outpatient treatment for mental illness, developmental disabilities or drug or alcohol dependency in Wisconsin must comply with the special conditions imposed by Wisconsin law.

- Protective services: Persons who receive protective services have the right not to be subjected to experimental research without the express and informed consent of the patient and the patient's guardian and after consultation with independent specialists and the patient's legal counsel. More than minimal risk research involving this population must be approved by the IRB and the Wisconsin Department of Health Services before study activities can begin.
- Mental health treatment, et al: Persons receiving treatment for mental illness, developmental disabilities, and alcoholism or drug dependency have the right not to be subjected to experimental research without the express and informed consent of the patient and the patient's guardian (if any) and after consultation with independent specialists and the patient's legal counsel. More than minimal risk research involving this population must be approved by the IRB and the Wisconsin Department of Health Services before study activities can begin.

For a full list of vulnerable populations and protective measures, see HRP 334 – WORKSHEET-Vulnerable Populations. For assistance with Wisconsin Department of Health Services review, contact the Reliance and Navigation Team (RELIANT; [irbreliance@wisc.edu](mailto:irbreliance@wisc.edu)).

### **Protecting Participant Privacy and Confidentiality**

You are required to ensure human research includes adequate provisions to protect the privacy of participants and confidentiality of data, as required by federal regulations.

- Privacy refers to a person's desire to control the access of others to themselves. For example, research participants may not want to be seen entering a place that might stigmatize them, such as a pregnancy counseling center that is clearly identified as such by signs on the front of the building.
- Confidentiality refers to the researcher's agreement with the participant about how the research participant's identifiable private information will be handled, managed, and disseminated.

For the IRB to assess privacy and confidentiality protections, you must describe how you will protect participant privacy and data confidentiality in your protocol or application. The IRB will assess whether the participants' privacy interests and confidentiality of data are protected in ways commensurate with the benefits to participants and the risks of everyday life.

For more information, refer to HRP 314-WORKSHEET-Criteria for Approval.

### **Certificates of Confidentiality**

A Certificate of Confidentiality (COC) protects the privacy of research participants by prohibiting forced disclosure of their individually identifiable, sensitive research information to anyone not associated with the research, except when the participant consents to such disclosures or in other limited specific situations.

Effective October 1, 2017, all ongoing or new research as of December 13, 2016 that is

- funded wholly or in part by the NIH AND
- collects or uses identifiable, sensitive information

is automatically issued a CoC as a term and condition of the NIH grant award. Certificates will no longer be issued in a separate document. The Notice of Award and the NIH Grants Policy Statement will serve as documentation of the Certificate protection.

You are required to determine whether your research records generated with NIH funding are covered by a COC. See HRP 333-Worksheet-Certificate of Confidentiality for details on evaluating whether a NIH-funded research study is covered by a COC.

When a COC covers the research records, and informed consent will be obtained from participants, the participants must be told about the protections afforded by the COC and any limitations to those protections. Available consent form templates have been revised to include language that addresses COC protections. This language must be included in consent forms to be used in studies to which the COC policy applies.

A number of other HHS agencies also issue COCs. For information and instructions go to: <https://grants.nih.gov/policy/humansubjects/coc.htm> Information and templates for requesting a COC when the funding source is not an HHS agency, or when the funding source is not federal can also be found at the link provided above. Researchers conducting a non-federally funded study who are applying for a COC should draft the COC assurance template according to language provided at the link provided above. For assistance in obtaining the institutional officials' signature, review the [CoC Application Help guidance](#) or email [compliance@research.wisc.edu](mailto:compliance@research.wisc.edu) for signature routing.

Researchers must be aware that:

- Information protected by a COC and all copies are subject to the protections of the COC in perpetuity. If a secondary researcher receives information protected by a COC, the secondary researcher is required to uphold the protections. Researchers who provide a secondary researcher with data protected by a COC should inform the secondary researcher of the continuing obligation to protect the data
- If the study continues to enroll additional participants after your NIH funding ends, those participants will not be protected by the Certificate unless you apply for a Certificate following the process for non- federally funded research.
- Certificates will be issued for applicable research regardless of the country where the investigator or the protected information resides though a COC may not be effective for data held in foreign countries.
- Should the researcher ever receive a subpoena, or any other legal process request seeking disclosure of research records, the researcher should not release any records or information and should immediately contact the IRB office and the [Office of Legal Affairs](#).

For complete information about the policy, including FAQs, please visit:

<https://grants.nih.gov/policy/humansubjects/coc.htm>

### **Communicating with Participants**

Throughout the course of a study, researchers may wish to communicate with participants using a range of methods. Depending on the method used, you may need to follow specific guidelines, particularly if your study falls under HIPAA or FERPA.

- Using email to schedule initial study visit: Upload a copy of the email script you will use to schedule initial visits in the IRB application. You must obtain permission from participants before using email to schedule a visit. Permission may be obtained by emailing subjects to ask if they agree to set up an appointment by email before sending scheduling information. Emails scheduling an initial visit may not include information about the subject's health unless they provide permission to do so. Even with subject permission, the email should contain as little health information as is necessary to convey the intended message.
- Using email as part of study participation: The consent form must include information on how email will be used in the study and the study team must obtain permission to communicate with the subject by email. You cannot require that subjects provide an email address in order to participate in a research study unless the study cannot be carried out without access to email. Additionally, subjects may request that email no longer be used to communicate about the study, without any loss or penalty.
- Phone: Whether calling potential subjects for recruitment purposes or communicating with participants during the study, you should avoid leaving voicemail messages that include any information about the subject's health (e.g., identifying that you are calling from a specific clinic).

## **HIPAA Privacy and Security Rules**

The [HIPAA Privacy Rule](#) is a set of federal regulations providing protections for the confidentiality of health information used in clinical practice, research, and the operations of health care facilities. The purpose of the Privacy Rule is to ensure that health information confidentiality risks are minimized. If your study falls under HIPAA, you may need to obtain authorization from participants to use or access their protected health information or you may need to request a waiver. Authorization language is included in the IRB's template consent document.

While the IRB serves as the HIPAA privacy board for UW-Madison, the Office of Compliance is responsible for HIPAA policy and oversight. For comprehensive guidance on how HIPAA applies to human research – including training requirements – please review [the HIPAA website](#).

## **Federal Educational Privacy Act (FERPA)**

The Family Educational Rights and Privacy Act (FERPA) is a Federal law administered by the U.S. Department of Education; 34 CFR Part 99. FERPA applies to all educational agencies and institutions that receive federal funding. FERPA aims to protect the privacy of Student Education Records. Education records include any record containing personally identifiable information (PII) directly related to the student. PII is not limited to name but may include indirect identifiers as well. Note that student medical records from University Health Services (UHS) are considered student records and subject to FERPA regulations. To use student records for research purposes, you must first obtain informed consent from those students (with certain exceptions).

For details on FERPA requirements in human research, refer to HRP 331-WORKSHEET-FERPA Compliance. Additional information about FERPA may also be found on the <https://registrar.wisc.edu/ferpa/> Office of the Registrar's website.

## Research in K-12 Settings

If you are planning on conducting research in K-12 schools, additional requirements will apply to your research. These schools are autonomous institutions that retain the right to approve/reject any human research to be conducted on their site, in their facilities, or with their teachers, staff or students. The IRB therefore requires documentation from an appropriate authority at each school or district granting permission to conduct the human research. Permissions must include the following information:

- Protocol title/number (or name of study);
- Name(s) of the researcher(s);
- A scope of the research and/or activities to be conducted at the site;
- Name of the site;
- Person or entity providing permission (including title, contact information, and confirmation of appropriate authority to provide permission).

You are responsible for contacting each school or district to obtain this permission and meet the requirements each site may have for conducting human research (e.g., review by its own research review committee). If review by a separate committee is required, you will need to plan additional time for this approval process as well as IRB review. Since some committees meet infrequently, it is especially important that you plan accordingly.

Other important items to keep in mind:

- Often K-12 school sites will require proof of IRB review prior to their approval. If the study does not qualify for exemption, the IRB can provide conditional approval via an Administrative Hold. Your study will not be granted final approval, however, until appropriate site permission has been submitted.
- If teachers/school staff are engaged in human research for studies that do not qualify for exemption, they must complete human subjects training, and be listed in the IRB application. If UW-Madison will be serving as their reviewing IRB, an individual investigator agreement may be required. (For assistance with such agreements, contact [irbreliance@wisc.edu](mailto:irbreliance@wisc.edu))
- Some schools require research personnel to undergo background checks. If required, you are responsible for completing any background checks prior to starting your research.
- Many school districts will not allow research activities to take place during normal class time.
- Many schools place limitations on the use of video or audio recording in classrooms. The school will want to see your video/audio recording procedure, and the IRB requires that it is included as part of your description of the scope of research to potential sites.
- Parental consent is required for minors to be included as research subjects. You must provide an appropriate method to obtain consent from parents (i.e., send the study information and consent forms to parents for review, etc.). You will also need to plan for a method of collecting the forms from the parents, without engaging staff. You will need to describe these processes in your protocol or application.
- Minor assent is also required prior to including minors as research subjects. Once parental consent has been obtained, their child(ren) can be asked to provide assent. The assent process should be similar to the consent process. Assent documents should be appropriate for the subject population (reading level, assent procedures, etc.).

For more information, refer to HRP 331-WORKSHEET-FERPA, HRP 416-CHECKLIST-Children, and the Assent Process and Documentation section above.



## **Use of Video or Audio Recording**

If you plan to record subjects (audio and/or video) or take full face photographs, the consent form and, if applicable, HIPAA authorization form must include information about these procedures. In addition, the consent form should include information about how long these materials will be maintained, how they will be protected from risk of breach of confidentiality, who will have access to the recording materials (e.g., study team only) and whether they will be used for future, unspecified research.

If video recording will occur in a K-12 educational setting, all students and instructors in that class must sign consent forms, or video recording will not be allowed. Individuals may not want to be videotaped for many reasons, including cultural and religious considerations. Technical and logistical limitations make it nearly impossible to “exclude” images from those not consenting to video recording, so informed consent is required from all those within the room or other setting where recording will occur. (If students are minors, parental consent is also required.) In all cases, the preferences of students, parents, and instructors/staff must be respected.

If you will videotape in a UWHC or UWMF facility or publish full face photographs or videos of UWHC and/or UWMF patients, you are required to follow UWHC and UWMF institutional policies and procedures.

## **Biospecimen and Data Research**

Under the Common Rule and UW-Madison HRPP Policy, IRB review is required for all human subjects research, defined as:

- A systematic investigation designed to contribute to generalizable knowledge, and
- Involves obtaining information or biospecimens from a living individual through either interaction or intervention, with the individual or access to the individual's private information, including protected health information (PHI).

In addition, the FDA requires IRB review for the use of de-identified human specimens in clinical investigations of medical devices when the research may generate or collect data that may be submitted to the FDA for review.

- **IRB Review requirements for biospecimen or data research**

IRB review is required for most research studies that use data or biospecimens obtained from human subjects. These research studies may qualify for exemption, expedited review, or require full board review. Some studies may ultimately not fit the definition of research involving human subjects but the IRB must make this determination.

Examples of biospecimen and data research requiring IRB review include, but are not limited to:

- Prospective collection of data or biospecimens for a specific research study
- Prospective collection and storage of data or biospecimens for future research use, including whole genome and whole exome sequencing

- Secondary use of identifiable data or biospecimens
  - Example: Obtaining blood/tissue samples along with identifiers from a biobank or repository
  - Example: Obtaining data, including identifiers, from a health care record for research analysis
- Secondary use of coded data or biospecimens when the investigator collected the specimens him/herself for another research project
- Secondary use of coded data or biospecimens when the investigator has access to the code that would allow linkage of the data or specimens to identifiable information
- Secondary use of de-identified or coded data or biospecimens in a project that will generate or collect data that will or may be submitted to the FDA
  - Example: Testing the efficacy of a diagnostic device using de-identified biospecimens collected as standard of care and no longer needed for clinical diagnostic purposes
- Secondary use of de-identified or coded data or biospecimens in a project conducting whole genome or whole exome sequencing
- Secondary use of de-identified or coded biospecimens when the investigator will not have access to the code AND the data generated or collected will not be submitted to the FDA
- Collection and/or use of de-identified biospecimens obtained through standard of care clinical procedures and that are not required for treatment or diagnostic purposes (waste) provided the project will not generate or collect data that may be submitted to the FDA.
  - Biospecimens obtained through standard of care clinical procedures may require analysis by pathology for diagnostic purposes. During this process, pathology will assess what portion of the biospecimen is required for clinical purposes and what portion, if any, is deemed waste and/or can be used for research purposes.
  - If clinical biospecimens are being obtained from UW Health patients, investigators will need to find out whether the specimens require pathology evaluation, can be deemed waste per UW Health policies, or whether an exception to pathology evaluation can be made if the specimen is not deemed as waste.
  - Resources for information on pathology workflows and the need for sign-off to use clinical biospecimens for research include the Department of Pathology and Laboratory Medicine, the UW Carbone Cancer Center, and the Office of Clinical Trials.

Examples of research NOT requiring IRB review include, but are not limited to the following (note that a formal Not Human Subjects Research request can be made to the IRB for documentation purposes, but is not required):

- Secondary use of data from publicly available datasets (e.g., US Census data)
- Use of biological specimens from deceased individuals in a project provided the project will not generate or collect data that may be submitted to the FDA (HIPAA regulations may still apply if PHI is used along with the specimens)
- Some funding agencies may require IRB review and approval for research projects that are not regulated by the Common Rule or the FDA. In these cases, investigators are encouraged to speak directly with the IRB Office to determine the best course of action.

- **Informed consent for biospecimen and data research**

The federal regulations generally require subjects voluntarily consent to participate in research; however, the regulations also allow a waiver of this requirement for research that meets certain criteria. The decision regarding whether consent must be obtained is made on a case-by-case basis and is dependent on the type of research being conducted.

Biospecimen and data research can be categorized into three common groups:

- Prospective collection of data or biospecimens for research purposes
- Use of clinical data or samples in a research project
- Secondary use of previously collected data or biospecimens

*Prospective collection of data or biospecimens for research purposes*

Prospective studies are those that ask a question and look forward and are generally designed before any information is collected. Study subjects are identified and followed forward to see if the outcome of interest happens over time. This outcome is assessed relative to the intervention. Prospective research with data or biospecimens occurs when subjects are identified, and then data or biospecimens are collected from the subjects as part of the research interventions.

For prospective research with data or biospecimens, the IRB will generally require that consent be obtained from subjects prior to the collection of the data or biospecimen. Specifically, consent is likely to be required when the following are true:

- Subjects are identified prospectively prior to collection of the data or biospecimens
- At the time of collection, the investigators know and intend that the data or samples will be used for research purposes

*Use of clinical data or samples in a research project*

Biospecimens and data are often collected for clinical diagnostic purposes and then used for research purposes as well. Collection and use of these samples and corresponding clinical data for research purposes may not require prospective consent if the investigators can provide justification that the criteria for waiver of informed consent have been met. For more information on waiver criteria, see HRP 410-WORKSHEET-Waiver or Alteration of Consent Process.

*Secondary use of previously collected data or biospecimens*

When an investigator uses previously collected data or biospecimens for a secondary, new/different research project, it is likely that additional consent for the secondary use will not be required. Subjects may have provided consent for use of their data or biospecimens during the initial collection. The IRB may need to determine whether the data or biospecimens were collected in accordance with an IRB approval and, if the secondary investigator has access to identifiers, whether the secondary use is consistent with the subjects' original consent and HIPAA authorization.

- **Storage of biospecimens and data for research**

When reviewing a research study, the IRB will consider whether appropriate provisions are in place to protect the privacy interests of research subjects, the confidentiality of the research data, and the

security of the data and biospecimens. The IRB will consider the following when determining whether a research study has adequate provisions to protect research subjects' privacy interests, confidentiality of data, and security of data and specimens:

- Risk/Benefit assessment,
- Location of the data collection,
- Sensitivity of the data being collected,
- The identifiability of the data and biospecimens.

The IRB requires detailed information on the confidentiality and security of biospecimens and data to be used in research. The following is a list of items to describe in the submission materials for IRB review. For additional guidance, please see HRP 503a-TEMPLATE PROTOCOL-Registries and Repositories.

- Describe any procedures that will be used for quality control of collected data and/or biospecimens.
- Describe the steps that will be taken to secure the data and specimens (e.g., training, authorization of access, password protection, encryption, physical controls, and separation of identifiers and data) for storage and use.
- Describe how and where data and/or biospecimens will be stored and maintained throughout the life of the study. Reference any relevant storage standard operating procedures, including how the data and specimens will be tracked.
- Explain whether anyone, including the lead researcher, can identify the participants. Explain whether there will be a unique code on the biospecimens/dataset that can be used to link to a participant's identity, but will not, by itself, reveal who the participant is.
- Describe the procedures in place to protect participants' privacy. By privacy, this means a person's desire to place limits on with whom they interact or to whom they provide personal information.
- If you will be collecting sensitive information (e.g., sexual health information, communicable disease status, genetic test results), provide a justification for this.

### **Analysis Center Projects**

A significant number of research groups at UW-Madison serve as analysis centers for multi-site studies. Analysis centers are defined as providing core or central image reading or analysis, biospecimen analysis, or statistical data analysis for multi-site studies but are otherwise not involved in the conduct of the research. In some cases, UW-Madison researchers may not be considered engaged in human subjects research by serving as an analysis center and in these cases, IRB review and approval is not required. The following outline several analysis center scenarios and the criteria for determining whether IRB review and approval is required:

- *Research with previously collected coded data and/or specimens* - Previously collected coded data or specimens may include left-over clinical samples, medical data, research data or research samples.
  - If the research is FDA regulated, IRB review and approval IS required.
  - For research NOT regulated by the FDA, IRB review is not required if BOTH of the following conditions are true:

- The data or specimens to be studied were not collected specifically for the current research;  
AND
- Investigator(s) cannot readily ascertain the identity of the source(s) of the coded data or specimens because one or more of the following is true:
  - The investigator(s) and the holder of the key enter into an agreement prohibiting the release of the key to the investigator(s) under any circumstances
  - IRB-approved written policies and procedures for the repository or data coordinating center prohibit the release of the key to the investigator(s) under any circumstances.

Investigators that want to use research data or leftover research samples must also consult the original informed consent document signed by participants to ensure that subsequent use was specifically permitted.

- *Research with coded data or specimens obtained for the current research* – UW personnel receive coded data or specimens for analysis for the current research study.
  - If the research is FDA regulated, IRB review and approval IS required.
  - For research NOT regulated by the FDA, IRB review is not required because UW is not engaged in human subjects research if BOTH of the following conditions are met:
    - UW personnel obtain coded private information or human biological specimens from another institution involved in the research that retains a link to individually identifying information (such as name or social security number); and
    - UW personnel are unable to readily ascertain the identity of the subjects to whom the coded information or specimens pertain because, for example:
      - the institution’s employees or agents and the holder of the key enter into an agreement prohibiting the release of the key to those employees or agents under any circumstances;
      - the releasing institution has IRB-approved written policies and operating procedures applicable to the research project that prohibit the release of the key to the institution’s employees or agents under any circumstances; or
      - there are other legal requirements prohibiting the release of the key to the institution’s employees or agents.

In some circumstances, IRB review may be required by the sponsor or contract. In these cases, please consult with [irbreliance@wisc.edu](mailto:irbreliance@wisc.edu).

### **Research Registries and Repositories**

The IRB uses the terms recruitment registry, data repository, and biospecimen repository for these various research tools/resources, although terminology can vary widely across institutions. Generally, the creation and maintenance of a research registry or repository requires IRB review and approval. A protocol template for the creation and maintenance of research registries and repositories is available for researchers to use when preparing to submit to the IRB (see HRP 503a-TEMPLATE PROTOCOL-

Registries and Repositories. IRB review is not required for the development of a Quality Improvement or Quality Assurance database.

#### *Recruitment Registry*

Generally, a registry is a tool used to identify and track a group of individuals that have similar characteristics. The characteristics can vary widely (e.g., disease, genetic make-up, health behaviors, surgical procedures), but the intent of the registry is to track and classify these groups of individuals. The IRB prefers the use of the word “registry” to be used to describe lists of people along with limited personal and, when applicable, medical information. The primary use of these lists is to provide investigators with pools of potential study volunteers, as in recruitment registries. Recruitment registries generally require IRB approval, both for the creation and maintenance of the registry itself, as well as for future projects that wish to use a registry as a recruitment method.

#### *Data Repository*

A data repository is a tool used to compile a set of individual subject/patient data that will be used for analysis purposes. A data repository generally has data added to it in an on-going manner that is stored long-term. Data in the repository are intended to be distributed to multiple users and subsequently used for ongoing analysis purposes. The HS IRBs prefer use of the term ‘data repository’ over terms such as ‘databases’ and ‘registries.’ If the primary intent of the repository is for use in future research projects, IRB review and approval is required, and may be required for the subsequent use of the data from the repository.

#### *Biospecimen/Tissue Repository*

A biospecimen repository (also known as a tissue bank) is a mechanism for maintaining tissue, blood, and other biological specimens for unspecified future use. These repositories typically involve the collection and long-term storage of tissue and often corresponding data to be used primarily for future research projects. Tissue to be stored in the repository can be collected retrospectively, prospectively, or both. Tissue repositories can include tissue collected from other research protocols or clinical procedures. IRB review and approval is required for banking of biospecimens and may be required for the subsequent use of the specimens from the repository.

### **Sharing Data, Specimens, or Images**

If you plan to share or receive specimens or data to/from external entities, you will need to address the additional requirements described below. Your protocol or application must describe how you will meet these requirements. Guidance regarding what items you must address can be found in the protocol templates or via consultation with IRB staff.

Note: If the samples being shipped or received will include dates of service associated with the provision of health care or laboratory tests (such as date of collection and date of processing) the data comprises a [limited data set](#) of protected health information (PHI) and a data use agreement (DUA) is needed. The requirement for a DUA can be achieved using a [stand-alone template](#) or through incorporation of language into the Material Transfer Agreement (MTA) which meets the requirement of HIPAA at 45 CFR 164.514(e). For more information on these agreements, see this [page](#).

- Sending Specimens or Data to Other Sites

If your approved protocol or application does not already address sending specimens or data to other sites, you must submit a change to obtain IRB approval before sending the specimens or data. Guidance regarding what items you must address can be found in the protocol templates or via consultation with IRB staff. Whether the researcher receiving specimens or images must obtain IRB approval depends on several factors:

1. Will the items be analyzed solely as a professional service?
2. Will the items being sent be completely anonymized (i.e., no one can trace them back to the individual from whom they were derived) to external personnel who is not a collaborator?
3. Will the items being sent be coded and the code will not be released to the external researcher who is not a collaborator?
4. Will the items be identifiable to any personnel at any site?

In the first three cases, IRB oversight may not be required for those receiving the items. In the fourth case, IRB review is likely required. Since these can be complex determinations, we encourage you to contact the IRB office for assistance.

- Receiving Specimens or Data from Other Sites

If the currently approved IRB application does not specifically state that specimens or data will be received from a specific site or researchers, a change must be submitted to the IRB before the items can be received. Guidance regarding what items you must address can be found in the protocol templates or via consultation with IRB staff.

## **Deception**

Research which requires deception regarding the purpose of the research or any other necessary element of consent is permissible when justified by prospective scientific, educational, or applied value and when effective non-deceptive alternative procedures are not feasible. Additional consent debriefing requirements are necessary to obtain informed consent for this type of research.

You must provide a prompt opportunity for participants to obtain appropriate information about the nature, results, and conclusions of the research, and then take reasonable steps to correct any misconceptions that participants may have of which the psychologists are aware. If a participant in a study involving deception chooses to withdraw consent following the debriefing, the data collected in that case may not be included in the analysis of the study.

Deception is a form of alteration of the consent process and alteration of the consent documentation. You should review HRP 410-CHECKLIST-Waiver or Alteration of Consent Process to ensure that you have provided sufficient information regarding the need for a waiver or alteration of the consent process.

## **Technology and New Media Research**

Online research sources such as Facebook, Twitter, blogs, chat rooms, discussion forums, and other social networking sites will be treated as publicly available data by the IRB in a very broad sense, and with a number of limitations.

- **Privacy Statements & Terms of Use**

You are responsible for checking the privacy statement and terms of use of any site being used for research purposes. You must adhere to the written policies of any site used for research. The IRB expects that researchers will either: 1) obtain consent to use data from an individual's social media page or 2) make an appropriate argument as part of the application process as to why the IRB should waive consent for the purposes of the project.

- **Publicly Available**

The IRB does not consider sites that require the user to create an account, and then provide a log in and password, to be publicly available data. Therefore, participants must be consented before an investigator can observe or interact with participants in these online environments. Members of sites that require a log in have an expectation of privacy and do not expect that anything they post will be used for research purposes. In some circumstances, researchers can petition the IRB for a waiver of consent. In these situations, researchers will need to provide an appropriate argument/justification as to why a waiver of consent is appropriate.

- **Not Human Subjects Research**

Some technology-based studies may not meet the definition of human subjects research per the federal regulations, and therefore not require IRB review. An example would be if a researcher is studying how many Facebook pages include images of families; the unit of measure in this case is the page, and not a human subject.

- **Identifiable Information**

Research using public documents such as newspapers, books, or journals published online and that involve no other data source(s) is not considered human research. However, projects that combine identifiable information about individuals obtained from public documents, with identifiable information obtained from other sources, may be considered human research.

- **Data Mining**

Facebook, Twitter, and others may provide data mining services where their developers will mine data from the site, for a fee, at the researcher's request. Depending on the scope, the IRB may treat the data differently because data collection would be done by the media site and (likely) provided to the researcher without direct identifiers. The IRB deals with this type of research activity on a case-by-case basis.

## **Biomedical Interventions Conducted in Non-Clinical Settings**

- **Training and Competency:** You are responsible for ensuring that all personnel listed on an IRB application have the appropriate training and experience to perform their assigned duties. When considering whether certain biomedical procedures may be performed in an investigator's research laboratory, the IRB will take into account the risk level of the procedures as well as applicable training/licensure requirements for individuals to perform certain procedures.
  - In some cases, the IRB will allow non-therapeutic/non-diagnostic procedures to be carried out by non-medically licensed personnel provided they have sufficient training. Such procedures may include finger sticks, screening urine pregnancy tests, and pulmonary function testing.
  - For more involved and/or more than minimal risk procedures (e.g., blood draw via



venipuncture, IV drug infusion), the IRB will likely require the procedures be performed by an appropriately licensed medical professional.

- **Emergency Procedures:** Your protocol or application should include a description of emergency medical procedures that will be implemented to ensure the safety of research participants. Calling 911 may be sufficient if, for example, a participant experiences an accident during an exercise study. Calling 911 alone may not be sufficient, however, if the research procedures are more than minimal risk and the participant experiences, for example, an event that may require surgery or immediate medical intervention. The IRB will consider emergency procedures on case-by-case basis. The IRB expects that emergency procedures requiring more than a 911 call will involve medically licensed/registered personnel, as determined by the level of risk.

### **FDA Regulations and IRB Review**

The IRB reviews studies involving drugs, devices, biologics, radioactive materials, and in vitro diagnostic devices in accordance with relevant FDA regulations. In addition, some foods and dietary supplements, software, and mobile apps may need to be assessed in accordance with FDA regulations. Depending on how the test articles will be used in a study, you may be asked to consult with the FDA and provide documentation from the FDA during the IRB review process.

For studies where a UW-Madison investigator will hold an investigational new drug (IND) and/or investigational device exemption (IDE), additional institutional requirements (including training and monitoring) must be met.

- The [FDA Regulated Research Oversight Program](#) can provide you with more information about investigator-held IND/IDE requirements.
- For assistance in determining whether your study may require an IND/IDE, you should contact the [IND/IDE Consultation Service](#).

The IRB uses the following tools and policies when reviewing studies that may be regulated.

- [Control of Test Articles Used in Research Policy](#)
- HRP 306-WORKSHEET-Drugs and Biologics
- HRP 307-WORKSHEET-Devices
- HRP 418-CHECKLIST-Non-Significant Risk Device

Additional information about relevant FDA regulations can be found in Appendix A-2 in this manual. We encourage you to refer to the above resources when preparing an application that may be FDA regulated. IRB staff also are available to consult with you regarding how FDA regulations may apply to your study.

### **Investigator's Drug Brochure (IDB) and Package Inserts**

For investigational and FDA-approved drugs, you may need to submit IDBs and package inserts to provide the IRB with sufficient information to assess regulatory criteria for approval.

- **Initial review requirements**
  - If a research study involves testing or evaluating drug(s) and their use in the research is covered under an IND, an IDB should be provided to the IRB. For any drugs being tested

or evaluated as part of the research that are FDA-approved and an IND is not required for their use in the research, the study team should provide the IRB with package inserts rather than IDBs.

- Many studies involve FDA-approved drugs used within their approved indication and which are not the focus of a study (e.g., drugs to mitigate side effects, lidocaine). The IRB may request package inserts or other documentation in these cases, so that the IRB is able to assess whether there are additional risks to study participation.
- Change requirements
  - Updates to the IDBs and/or package inserts must be submitted as a change to the IRB within 60 days of receipt when the revisions will:
    - affect the risk/benefit ratio of the study (i.e., will result in a change to the study documents);
    - affect alternatives to study participation for subjects; OR
    - represent new information that should be provided to subjects.
- Continuing review requirements
  - Revised IDBs/Package Inserts may be submitted at continuing review if:
    - The revised IDBs/Package Inserts do NOT contain revisions that would require a change as describe above. Or
    - The study is permanently closed to enrollment locally, no local subjects are on treatment, and the revised IDB and/or package insert contains no new information that would affect past subjects (e.g., new latent risks).
  - In these cases, you must upload an [IDB and Package Insert Log](#) to the continuing review.
    - For IDBs: The log should include a brief summary of the revised information in the IDB as compared to the most recent version of the IDB the IRB has on file as well as an explanation why the IDB did not meet any of the criteria noted above that would require submission prior to continuing review.
    - For Package Inserts: If a summary of the changes is not available, you should confirm that the PI has reviewed the revised package insert and confirms it does not meet the criteria for reporting via a change.

## **Radiation**

If your study interventions involve the use/administration of radiation, additional state law requirements apply that are outside IRB purview. For information and assistance with these requirements, see [the Radiation Safety website](#).

## **Controlled Substances**

If you are conducting research with controlled substances, you must comply with federal and state requirements for use of these substances. These requirements are rigorous and the investigator is responsible for ensuring compliance with these requirements.

Controlled drugs fall into five different categories, from Schedule I (substances which do not have a legitimate medical use in the United States and which can be addictive i– such as LSD and heroin) to Schedule V (drugs which have a clear medical use, low potential for abuse and limited psychological and physical dependence – such as cough medications with small amounts of codeine).

Use of controlled substances for research requires registering with both the federal government (through the Drug Enforcement Agency) and the State of Wisconsin (through the Controlled Substances Board). Penalties for using such drugs without proper registration can be severe. The regulations strictly limit who can handle or administer the drugs and impose both physical security and inventory requirements. Some key points concerning the regulations:

- The permitting process is between an individual researcher, the DEA and the State of Wisconsin.
- Registrants cannot share controlled substances with non-registered users who are not under their supervision (e.g., another research laboratory in their department).
- Possession of expired drugs also poses a risk to researchers from the USDA since administration of expired controlled substances is not allowed.
- Disposal is also strictly regulated. Only the DEA Special Agent in Charge can authorize the disposal of controlled substances.

The [Research Animal Resources Center](#) has more information on the requirements regarding the use of controlled substances. This information is provided only as a reference for researchers, who are solely responsible meeting regulatory requirements. If you need assistance with these processes, contact the IRB office.

## **POST-APPROVAL RESPONSIBILITIES**

### **Researcher Responsibilities After IRB Approval**

In addition to the requirements described elsewhere in this manual and in the Toolkit library, you are responsible for the following after you receive IRB approval:

- 1) Do not start human research activities until you have the final IRB approval letter.
- 2) Do not start human research activities until you have obtained all other required institutional approvals, including approvals of departments or divisions that require approval prior to commencing research that involves their resources.
- 3) Ensure that there are adequate resources to carry out the research safely. This includes, but is not limited to, sufficient investigator time, appropriately qualified research team members, equipment, and space.
  - a) Delegate responsibility to the research staff in accordance with the staff's training and qualifications.
  - b) Assure that all procedures associated with the research are performed, with the appropriate level of supervision, only by individuals who are licensed or otherwise qualified to perform them.
  - c) Monitor the research study and perform quality management activities to ensure the protection of subjects and the quality of the research data.
- 4) Obtain the legally effective informed consent from human subjects or their representatives, using only the currently approved informed consent documents, and provide a copy to the subject, if applicable.
  - a) Ensure that only IRB-approved investigators obtain informed consent from potential subjects.
- 5) If unavailable to conduct this research personally, as when on sabbatical leave or vacation, arrange for another IRB-approved investigator on this study to assume direct responsibility, or notify the IRB of alternate arrangements

- 6) Maintain accurate and complete research records, including but not limited to, original signed informed consent and authorization documents, and retain these records according to IRB policy and the applicable regulatory retention terms.
- 7) Fully inform the IRB of all locations in which human subjects will be recruited for this project and obtain and maintain current IRB approvals/letters of agreement when applicable
- 8) Update study personnel; see “How to Update Personnel” section above.
- 9) Personally conduct or supervise the human research. Recognize that the investigator is accountable for the failures of any study team member.
  - a) Conduct the human research in accordance with the relevant current protocol as approved by the IRB, and in accordance with applicable federal regulations and local laws.
  - 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 study or project without prior IRB review and approval unless necessary to eliminate apparent immediate hazards to subject.
  - d) Protect the rights, safety, and welfare of subjects involved in the research.
- 10) Submit to the IRB:
  - a) Proposed modifications to the approved research, as described in this manual. (See “How to Submit a Change” and “Change Requirements”)
  - b) If required, a continuing review application as requested in the approval letter. (See “Continuing Review Requirements”)
- 11) Report any of the information items listed in “Reportable Event Requirements.”
- 12) Submit an updated disclosure of financial interests within thirty days of discovering or acquiring (e.g., through purchase, marriage, or inheritance) a new financial interest.
- 13) Do not accept or provide payments to professionals in exchange for referrals of potential subjects (“finder’s fees.”)
- 14) Do not accept payments designed to accelerate recruitment that were tied to the rate or timing of enrollment (“bonus payments.”)
- 15) See additional requirements of various federal agencies in this manual’s appendices. These represent additional requirements and do not override the baseline requirements of this section.
- 16) If the IRB directs or your study is selected for an onsite post-approval review, cooperate with post-approval monitoring staff to complete the onsite review.
- 17) If the study is a clinical trial and supported by a Common Rule agency, one IRB-approved version of a consent form that has been used to enroll participants must be posted on a public federal website designated for posting such consent forms. The form must be posted after recruitment closes, and no later than 60 days after the last study visit. Please contact the study sponsor with any questions.

### **Clinicaltrials.gov**

ClinicalTrials.gov is a publicly available registry and results database of federally and privately supported clinical trials, supported by the U.S. National Library of Medicine. The purpose of ClinicalTrials.gov is to disclose to the public key information about clinical trials that are currently available or that have been conducted. All UW–Madison faculty, staff, and students conducting human subjects research on University premises are expected to follow federal registration and results reporting requirements regarding ClinicalTrial.gov. This is not an IRB requirement. More information

about [clinicaltrials.gov](https://clinicaltrials.gov) requirements can be found [here](#).

### **Change of Protocol Requirements**

You must report planned changes in a study and receive approval from the IRB prior to implementing these changes, except where necessary to eliminate apparent immediate hazards to the subjects. In the case of changes implemented to eliminate immediate hazards to the subjects, the emergency protocol changes must be reported to the IRB using a reportable event submission. See “Reportable Event Requirements” below. For studies determined to be exempt, see “Changes to Studies Determined to Be Exempt” above.

When revising previously approved documents, such as protocols, consent forms, recruitment materials, etc., use a tracked changes feature to denote all revisions. Maintain electronic copies of all documents submitted to the IRB in case revisions are required. Please note that research must continue to be conducted without inclusion of proposed changes until IRB approval of the modification is received unless the changes are necessary to eliminate apparent immediate hazards to subjects.

If revisions to a consent document are needed, the revised consent incorporating the new information must be submitted. Depending on the type of new information, a consent form addendum may be appropriate for informing currently enrolled subjects of significant new findings that may have a bearing on their willingness to continue participation in the study. The addendum to consent focuses on the new information subjects need to consider when making a decision about their continued participation in the study but avoids them having to reassess the entire consent when much of it may not be relevant to the change(s).

The IRB assesses each change to determine whether convened IRB review is required or if the change can be reviewed under expedited procedures (meaning the change can be reviewed by one IRB member apart from an IRB meeting). Typically, changes that can be considered minimal risk (even if the overarching study is more than minimal risk) may be reviewed under expedited procedures. For more information, see HRP 402-CHECKLIST-Non-Committee Review and HRP 313-WORKSHEET-Expedited Review.

For studies funded by NIH, certain modifications will require prior approval by NIH as outlined in NIH’s “Guidance on Changes That Involve Human Subjects in Active Awards and That Will Require Prior NIH Approval: Updated Notice.” Investigators should review this guidance located at <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-128.html> for information on modifications that require prior approval and the process for submitting prior approval requests.

### **Continuing Review Requirements**

If your study requires continuing review, you must submit your continuing review no later than 45 days prior to the last day of approval to allow sufficient time for IRB review. When completing the continuing review form, if your study enrolls subjects, you will be required to specify enrollment totals. Enrollment is defined as eligible, appropriately informed individuals agreeing to participate in a study who have signed the informed consent. For data and/or specimen only protocols, this number should reflect the total number of data and/or specimens accessed for research purposes. This number should not exceed

the total number of subjects requested in the approved protocol. If you wish to request additional subjects, you should submit a change for review.

If the approval of human research expires because you have failed to submit the continuing review application or you submitted the continuing review application without enough time for IRB review prior to expiration, all human research procedures related to the protocol or study under review must cease, including recruitment, advertisement, screening, enrollment, consent, interventions, interactions, and collection or analysis of private identifiable information.

If current subjects will be harmed by stopping human research procedures that are available outside the human research context, provide these on a clinical basis as needed to protect current subjects. If current subjects will be harmed by stopping human research procedures that are not available outside the human research context, immediately contact the IRB office and provide a written list of the currently enrolled subjects and why they will be harmed by stopping human research procedures. If current subjects will be harmed by stopping human research procedures that are not available outside the human research context, these should continue as necessary for subject safety. Any ongoing procedures that were not able to safely stop should be summarized in the continuing review application.

If the IRB reviewed your continuing review application, but requires modifications to secure approval, you should submit those modifications in a timely fashion so they can be reviewed before study approval lapses.

For more information, see “How to Submit a Continuing Review” above and HRP 314-WORKSHEET-Criteria for Approval.

### **Reportable Event Reporting Requirements**

Information items that fall into one or more of the categories listed below must be reported to the IRB. These information items will be reviewed by the IRB to determine if they represent non-compliance, unanticipated problems involving risks to subjects or others, and/or result in suspension or termination of IRB approval. For more information, see the “How to Submit a Reportable Event” section above. Do not include any identifiable information related to subjects in the submission or supporting materials. Maintain electronic copies of all information submitted to the IRB.

- **What to Report in 1 business day** (Report the information items that fall into one or more of the following categories to the via phone call to the IRB Chair and Director within 1 business day):
  - Events that occur in studies involving drugs or biologics and are:
    - Probably caused by or associated with study participation; and
    - Unexpected; and
    - Immediately life-threatening or severely debilitating to current subjects or others not participating in the study
  - Events that occur in studies involving testing of devices and are:
    - Not previously identified in nature, severity, or frequency in IRB documentation (e.g., protocol, consent documents) OR relates to subjects’ rights, welfare, or safety; and
    - Immediately life-threatening or severely debilitating to current subjects.

- **What to Report in 10 Business Days (Only for Studies Involving Testing of Investigational Device):**
  - An event must be reported within 10 business days if the event was caused by/associated with the device and not previously identified in nature, severity or frequency in any IRB documents (or relates to the rights, safety and welfare of subjects).
- **What to Report Within 14 Business Days** (Report the information items that fall into one or more of the following categories to the IRB within 14 business days):
  - Information that indicates a new or increased risk, or a new safety issue. For example:
    - 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.
    - 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 describe a new risk.
    - Note, if revised study documents will be received by the study team within 14 business days of learning of the new information, ONLY a change of protocol would need to be submitted. If revised study documents are not expected to be received in time to submit a change of protocol within 14 days, a new information report should be submitted as a placeholder.
    - Withdrawal, restriction, or modification of a marketed approval of a drug, device, or biologic used in a research protocol
    - Protocol violation that harmed subjects or others or that indicates subjects or others might be at increased risk of harm
    - Complaint of a subject that indicates subjects or others might be at increased risk of harm or at risk of a new harm
    - Any changes significantly affecting the conduct of the research
  - Harm experienced by a subject or other individual, which in the opinion of the investigator are unexpected and probably related to the research procedures.
    - A harm is “unexpected” when its specificity or severity are inconsistent with risk information previously reviewed and approved by the IRB in terms of nature, severity, frequency, and characteristics of the study population.
    - A harm is “probably related” to the research procedures if in the opinion of the investigator, the research procedures more likely than not caused the harm.
  - Non-compliance with the federal regulations governing human research or with the requirements or determinations of the IRB, or an allegation of such non-compliance.
  - Audit, inspection, or inquiry by a federal agency that result in reportable findings (e.g., FDA Form 483.)
  - Written reports of study monitors that result in reportable findings (e.g., noncompliance with the IRB approved protocol)
  - Failure to follow the protocol due to the action or inaction of the investigator or research staff.
  - Breach of confidentiality. Note that breaches that involve PHI must be reported to the HIPAA privacy officer.
  - Incarceration of a subject in a study not approved by the IRB to involve prisoners.

- Complaint of a subject that cannot be resolved by the research team.
- Premature or unexpected suspension or termination of the protocol by the sponsor, investigator, or institution.
- Unanticipated adverse device effect (any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

### **Reportable Event Reporting Requirement for VA Studies**

VA reporting requirements generally parallel reporting requirements for non-VA studies, with the timeframe for report. Any event that occurs on a study under Madison VA purview that meets UW unanticipated problem or noncompliance reporting requirements must be reported to the IRB and Associate Chief of Staff within 5 business days of the local research team becoming aware of the event.

Any local research death that is both unanticipated AND related to the research must be orally reported to the IRB immediately after the local research team becomes aware of the death. Written notification of the death must be received by the IRB within 5 business days of the local research team becoming aware of the death.

### **Protocol Exceptions and Deviations**

Described below are cases when eligibility criteria and protocol deviations generally do not need to be reported to the IRB because they are not expected to adversely affect subject safety or data integrity. Please note: The following exceptions to the noncompliance policy DO NOT apply to any study involving an Investigational Device Exemption (IDE). Any planned deviations for studies involving IDEs must be submitted as a full change of protocol and be approved by the IRB before implementation.

#### **Deviations Related to Eligibility Criteria**

A one-time deviation from a single eligibility criterion for a single study participant under UW purview may occur without prior IRB approval in a **potentially therapeutic** study that meets the ALL of the following requirements:

- The study is fully industry-sponsored or is a federally sponsored, collaborative study with a coordinating center;
- The deviation will not affect the safety of the individual participant;
- The deviation does not involve the enrollment of a vulnerable subject population (e.g., children, pregnant women, prisoners, veterans) not previously approved by the IRB for enrollment in the study; and
- The sponsor is informed and approves the deviation before it occurs.

If all of the above criteria are met, this one-time deviation from the specific protocol eligibility requirement does not need to be reported to the IRB but should be recorded in the study file. The study participant who does not meet the eligibility criteria should be informed of this deviation. Examples of



deviations in eligibility criteria that may fall under this guidance include blood pressure or a laboratory value slightly higher or lower than dictated by the protocol when all other criteria are met.

Deviations from IRB-approved eligibility criteria for studies other than those specified above (e.g., non-sponsored or non-therapeutic studies) must be approved by the IRB prior to their implementation unless the deviation is required to eliminate an apparent immediate hazard to the research participant.

### **Other Protocol Deviations That Do Not Require Reporting to the IRB**

Protocol deviations under the control of the study team (as opposed to noncompliance due to the subject's behavior) do not require reporting to the IRB unless they meet ANY of the following criteria:

- The deviation affected or had the potential to affect the subject's rights, safety or welfare\*;
- The deviation resulted in a change to the participant's clinical or emotional condition or status;
- The deviation affected the integrity, accuracy and/or reliability of the research data; and
- The deviation resulted from willful or knowing misconduct on the part of the study team.

\*The IRB considers all study drug dosing errors (under- or over-dosing) to meet this criterion; therefore, all dosing errors require reporting to the IRB.

If the protocol deviation does NOT meet any of the criteria above, the event does not require reporting to the IRB, but **should still be documented in the study records**.

If the study team has multiple (i.e., two or more) occurrences of the same kind of deviation that is not otherwise reportable to the IRB (e.g., missed questionnaire, sample collection), please consult with the HS-IRBs Office whether reporting is required.

### **Changes to eliminate an apparent immediate hazard to subjects**

Changes in approved research initiated without prior IRB review and approval are allowed under both the Common Rule and FDA regulations ONLY to eliminate apparent immediate hazards to subjects. These changes are expected to be rare. Any such changes made must be reported to the IRB within fourteen (14) business days of implementation as both an unanticipated problem and a change of protocol.

- In the unanticipated problem report, the investigator must give an overview of the situation including what changes were implemented prior to IRB approval and why these changes needed implementation prior to IRB approval to prevent immediate hazard to study subjects.
- In the change of protocol, the investigator needs to specifically explain any changes to the protocol and study documents (e.g., informed consent documents) that are required.

If a change of protocol is implemented prior to IRB approval and the IRB determines that the change was not necessary to eliminate apparent immediate hazards to a subject, the investigator's action may be considered to represent noncompliance with the regulations governing human subjects research and result in additional action by the IRB.

### **Corrective Action Plans**

When a deviation/noncompliance event is discovered, immediate measures (also referred to as corrections) to mitigate risk and protect rights, safety, and welfare of the subject(s) and others should be taken. This may be in the form of a phone call or an office/clinic visit between the subject and a member of the research team, or other tests and procedures to ensure the subject's safety. Corrections alone may resolve minor deviations, but they will not effectively resolve more significant or systematic noncompliance, which generally also require corrective and preventive action.

*Corrective and Preventive Actions (CAPA)* are developed and implemented for more significant or systematic noncompliance, once the root cause is known. CAPA are implemented to prevent the occurrence and recurrence of an event. For more information on CAPAs, see the Post-Approval Monitoring Program's website.

### **Study Suspension or Termination**

If the IRB suspends or terminates your human research, the IRB will provide a written determination that includes the reasons for suspension or termination of IRB approval.

- For suspension, the IRB will indicate whether some or all the human research activities have been suspended. If, for example, the suspension applies only to the enrollment of new subjects, the IRB will indicate this specifically.
- For terminations, you must immediately cease all research activities and work with the IRB to develop a plan for safely removing subjects from the research as applicable.

### **Complaints or Concerns About a Study**

Investigators should make a good faith effort to promptly respond to and try to resolve any study-related complaint or concern that you receive or of which you are aware.

Some complaints and concerns that an investigator may receive are relatively minor (e.g., a subject complaint about a late payment that can be quickly resolved). One-time, minor complaints that can be quickly resolved generally do not require reporting to the IRB.

Complaints or concerns may be submitted directly by anyone, including but not limited to research subjects, family members, and representatives, and study team members. Complaints may be received by the study team, UWHC Patient Relations, the IRB office, and/or the confidential human research protection reporting line (608.890.1273 or hrpp@research.wisc.edu). The IRB office is required to respond to all concerns and complaints received by the IRB office. The IRB director, IRB Chair, or designee may ask other HRPP entities (e.g., patient relations, post-approval monitors) for assistance in attempting to resolve minor concerns or complaints with the complainant, if appropriate. This may include referring the subject to the study team. If the item cannot be resolved easily, additional actions will be taken. This may include requesting that the researcher report the item to the IRB as a reportable event.

### **Reporting Clinically Relevant Information to Participants**

Research teams should identify in their IRB applications any clinically relevant results that could be produced by study tests or procedures. Clinically relevant information may arise because of radiological

examinations conducted for research purposes, physical examinations or physiologic tests, test results from samples collected from subject, or the analysis of cognitive or behavioral assessments completed by subjects. Examples include:

- MRIs of the head may identify serious medical concerns, such as brain tumors, that might not be identified if the subject had not taken part in the research
- Genetic testing may identify actual or potential conditions that may affect the health of the individual participating in the research (and their relatives) or a reproductive decision
- Validated psychological screening tests may identify potential suicidality or severe depression
- Laboratory tests that reveal severe anemia or suggest diabetes

In addition to identifying the possibility of clinically relevant results that may be discovered, you should describe whether you intend to disclose the results to subjects. The IRB would not expect (and in some cases will not allow) the dissemination of information to subjects generated from tests or procedures that are considered experimental or have not been clinically validated. This is because the clinical relevance of the results in such cases may be unclear and can create inadvertent anxiety or confusion for the participant without providing potential benefit. In addition, the IRB generally does not allow the release of laboratory analyses to subjects unless they are performed by a CLIA-approved entity. Finally, the IRB would expect that any results released to subjects from research tests should be actionable.

If the results will be disclosed to participants, the research team will be asked to identify who assesses whether the information should be reported to subjects, provide a timeframe for reporting the results to subjects, and describe the process for informing subjects of these results and whether other resources are in place to assist with the explaining the results and their consequences to research subjects (e.g., a genetic counselor, referral to a physician). If the study team plans to release results directly to a subject's health care provider, this should be with the subject's permission and a qualified member of the research team should call the health care provider to contextualize the results and highlight any that may require follow-up.

If the IRB has not previously approved the disclosure of clinically relevant findings to subjects and a special circumstance arises for a single subject, research teams may submit a reportable event to request disclosure. The following information should be included in the new information report:

- Description of the incidental finding (e.g., abnormal result of laboratory test or MRI), when it was discovered and who discovered it
- Rationale for disclosing the incidental finding (i.e., why the subject may benefit from knowing this information)
- Process for informing the subject of the incidental finding (i.e., who is going to disclose the finding, how, and who should the subject contact regarding questions)
  - Statement clarifying whether this is expected to occur again or if this is an isolated incident (if not an isolated incident, a change of protocol is required)

### **Communicable Disease (Including HIV)**

If you plan on collecting information about or testing participants for communicable disease status, additional considerations apply. The IRB generally defines a communicable disease as:

- Health conditions that must be reported to health authorities under [state and/or federal law](#), such as hepatitis, tuberculosis, or syphilis.
- Health conditions that may require health care providers to use contact precautions, such as gown and gloves or isolation, when interacting with an affected individual.

Your protocol or application should address why such information must be collected for your study as well as whether any test results will be disclosed to participants and what impact, if any, such testing will have on their clinical care. The informed consent document must include language informing potential participants about such testing and its impact on their clinical care.

For HIV testing, additional requirements apply, including those mandated by state law.

- **Informed consent**: Participants must be informed the research includes HIV testing or use of HIV test results and the associated risks, unless the criteria for the IRB to waive informed consent are met. If results will be placed in the participant’s medical record, they must be informed of this as well. Under Wisconsin law, the informed consent process for HIV testing must also include a written or oral explanation or description of:
  - HIV infection
  - HIV test results
  - Requirements for reporting to the State epidemiologist
  - Treatment options for a person who has a positive HIV test result; and
  - Services provided by AIDS service organizations and other community-based organizations.
- **Reporting HIV test results**: If a participant tests positive for HIV/AIDS, a report must be made to the state epidemiologist. If identifiable specimens are provided to the University of Wisconsin Hospital and Clinics (UWHC) laboratory or the Wisconsin State Laboratory of Hygiene (WSLH), the UWHC laboratory or WSLH will make required reports to the state epidemiologist. If only coded specimens are provided to the UWHC laboratory or WSLH, you are responsible for making all required reports.
- **Maintaining records**: State law requires that a record be maintained of the following:
  - Whether the person or their authorized representative consented to or declined the HIV test;
  - Any authorization for disclosure of HIV test results that the person or their authorized representative has made;
  - Results of an HIV test administered to the person.
  - Additionally, for purposes of verifying compliance with Wisconsin reporting laws, the study team should maintain records of any report made to local health departments or the state epidemiologist; such forms may be de-identified to protect subjects' privacy.
- **Use of test results from the medical record**: HIV test results are confidential but may be revealed without the subject's authorization for research purposes if:
  - The researcher is affiliated with a health care provider,
  - The study has IRB approval for the research,
  - The information will be used only for the approved research, and will not be released to a person not connected with the research, and
  - The final product will not include identifying information.

## **IRB Reporting Obligations**

Federal regulations (HHS and FDA) require that institutions have written procedures to ensure that the following determinations are promptly reported:

- Any unanticipated problems involving risks to subjects or others;
- Any serious or continuing noncompliance with FDA or HHS regulations or the requirements or determinations of the IRB; and
- Any suspension or termination of IRB approval.

You will be notified of these determinations in writing. In addition, the following officials and entities may be notified: funding agency, Department Head, Dean, Institutional Officials, and others. When reporting to regulatory entities (e.g., FDA and/or OHRP) is required, the IRB will make every effort to notify the study team in writing, by phone, or in person prior to forwarding the report to the regulatory entity. See HRP 052-SOP-Post Review for more information regarding the IRB's obligations to report this information to regulatory and university officials and department leadership.

### **Record Retention**

Maintain your human research records, including but not limited to signed and dated consent documents, consent documents that integrate or have stand-alone HIPAA authorization, and screening materials documenting subject eligibility for at least seven years after completion of the research.

If your human research is sponsored contact the sponsor before disposing of human research records.

### **Principal Investigator Responsibilities When Leaving UW-Madison**

If you plan to leave UW-Madison while your study is ongoing, please contact IRB office overseeing your research to discuss the transfer or closure of your study prior to your departure. You can have another UW-Madison investigator assume principal investigator responsibilities, you can transfer the study and data to another institution, or you can close the study entirely. We will advise you regarding what actions will need to be taken. To transfer the research data and specimens to the new location you will need to have a data transfer and use agreement (DTUA) [<https://research.wisc.edu/compliance-policy/human-research-protection-program/guidance-on-external-sharing-of-human-subjects-research-data/>] and/or materials transfer agreement (MTA) in place [<https://rsp.wisc.edu/contracts/mta.cfm>].

## **OTHER ISSUES**

### **Conducting Research at the VA**

The UW-Madison IRB serves as the reviewing IRB for the Madison VA. Human research at the Madison VA must also be reviewed by the Madison VA Research & Development Committee (VA R&D) before the research can begin. Additional regulatory requirements apply to VA research. These requirements are described in Appendix A-9.

Please keep in mind that if you plan to conduct the same study at both the VA and UWMC, you will need to submit separate applications to ensure that all VA regulatory requirements are met. Also note that the VA allows single IRB review in limited circumstances.

For more information on VA processes and requirements, you can contact the following:

- Research and Development Committee: 608-280-7007, [VHAMADRDCOORDINATOR@va.gov](mailto:VHAMADRDCOORDINATOR@va.gov)
- Research Service: 608-280-7007, [VHAMADRDCOORDINATOR@va.gov](mailto:VHAMADRDCOORDINATOR@va.gov)
- Research Compliance Officer: 608-256-1901, extension 17805
- HIPAA Privacy Officer: 608-256-1901, extension 11699
- Information Security Officer: 608-256-1901, extension 17282

### **Fetal Tissue Research**

Several federal, state, and local requirements apply to use of fetal tissue in research. For details, see the [Use of Human Fetal Tissue policy](#).

### **Institutional Certification for NIH Genomic Data Sharing**

To request institutional certification for NIH Genomic Data Sharing (NIH GDS), submit a change to the study in ARROW. When submitting this change, submit any documentation required in the supplemental information section of the IRB application. For additional information see:

- HRP 064-SOP-NIH GDS Institutional Certification
- HRP 332-WORKSHEET-NIH GDS Institutional Certification

### **General Data Privacy Regulation (GDPR)**

The European Union has additional requirements regarding data privacy, referred to as the GDPR. Where UW-Madison is working with personal data collected in, or transferred from, any EU country, GDPR will be relevant. This includes data collected, obtained, or used for research projects. Failure to follow GDPR if it applies puts the University at risk of noncompliance, monetary fines, and reputational harm so it is critical to assess whether GDPR applies to your study. For details about GDPR, see Appendix-11 and contact the IRB office with any questions.

## Appendix A-1 ***Additional Requirements for DHHS-Regulated Research***<sup>1</sup>

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

---

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

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

1. When a subject withdraws from a study:<sup>2</sup>
  - a. The data collected on the subject to the point of withdrawal remains part of the study database and may not be removed.
  - b. An investigator may ask a subject who is withdrawing whether the subject wishes to provide continued follow-up and further data collection subsequent to their withdrawal from the interventional portion of the study. Under this circumstance, the discussion with the subject would distinguish between study-related interventions and continued follow-up of associated clinical outcome information, such as medical course or laboratory results obtained through non-invasive chart review, and address the maintenance of privacy and confidentiality of the subject's information.
  - c. If a subject withdraws from the interventional portion of the study, but agrees to continued follow-up of associated clinical outcome information as described in the previous bullet, the investigator must obtain the subject's informed consent for this limited participation in the study (assuming such a situation was not described in the original informed consent form). IRB approval of informed consent documents is required.
  - d. If a subject withdraws from the interventional portion of a study and does not consent to continued follow-up of associated clinical outcome information, the investigator must not access for purposes related to the study the subject's medical record or other confidential records requiring the subject's consent.
  - e. An investigator may review study data related to the subject collected prior to the subject's withdrawal from the study, and may consult public records, such as those establishing survival status.
2. For FDA-regulated research involving investigational drugs:
  - a. Investigators must abide by FDA restrictions on promotion of investigational drugs:<sup>3</sup>
    - i. An investigator, or any person acting on behalf of an investigator, must not represent in a promotional context that an investigational new drug is safe or effective for the purposes for which it is under investigation or otherwise promote the drug.
    - ii. This provision is not intended to restrict the full exchange of scientific information concerning the drug, including dissemination of scientific findings in scientific or lay media. Rather, its intent is to restrict promotional claims of safety or effectiveness of the drug for a use for which it is under investigation and to preclude commercialization of the drug before it is approved for commercial distribution.
    - iii. An investigator must not commercially distribute or test market an investigational new drug.
  - b. Follow FDA requirements for general responsibilities of investigators<sup>4</sup>
    - i. An investigator is responsible for ensuring that an investigation is conducted according to the signed investigator statement, the investigational plan, and applicable regulations; for protecting the rights, safety, and welfare of subjects under the investigator's care; and for the control of drugs under investigation.

---

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

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

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



- ii. An investigator must, in accordance with the provisions of 21 CFR §50, obtain the informed consent of each human subject to whom the drug is administered, except as provided in 21 CFR §50.23 or §50.24 of this chapter.
    - iii. Additional specific responsibilities of clinical investigators are set forth in this part and in 21 CFR §50 and 21 CFR §56.
  - c. Follow FDA requirements for control of the investigational drug<sup>5</sup>
    - i. An investigator must administer the drug only to subjects under the investigator's personal supervision or under the supervision of a sub-investigator responsible to the investigator.
    - ii. The investigator must not supply the investigational drug to any person not authorized under this part to receive it.
  - d. Follow FDA requirements for investigator recordkeeping and record retention<sup>6</sup>
    - i. Disposition of drug:
      - 1. An investigator is required to maintain adequate records of the disposition of the drug, including dates, quantity, and use by subjects.
      - 2. If the investigation is terminated, suspended, discontinued, or completed, the investigator must return the unused supplies of the drug to the sponsor, or otherwise provide for disposition of the unused supplies of the drug under 21 CFR §312.59.
    - ii. Case histories.
      - 1. An investigator is required to prepare and maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual administered the investigational drug or employed as a control in the investigation.
      - 2. Case histories include the case report forms and supporting data including, for example, signed and dated consent forms and medical records including, for example, progress notes of the physician, the individual's hospital charts, and the nurses' notes. The case history for each individual must document that informed consent was obtained prior to participation in the study.
    - iii. Record retention: An investigator must retain required records for a period of 2 years following the date a marketing application is approved for the drug for the indication for which it is being investigated; or, if no application is to be filed or if the application is not approved for such indication, until 2 years after the investigation is discontinued and FDA is notified.
  - e. Follow FDA requirements for investigator reports<sup>7</sup>
    - i. Progress reports: The investigator must furnish all reports to the sponsor of the drug who is responsible for collecting and evaluating the results obtained.
    - ii. Safety reports: An investigator must promptly report to the sponsor any adverse effect that may reasonably be regarded as caused by, or probably caused by, the drug. If the adverse effect is alarming, the investigator must report the adverse effect immediately.
    - iii. Final report: An investigator must provide the sponsor with an adequate report shortly after completion of the investigator's participation in the investigation.

---

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

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

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

- iv. Financial disclosure reports:
  - 1. The clinical investigator must provide the sponsor with sufficient accurate financial information to allow an applicant to submit complete and accurate certification or disclosure statements as required under 21 CFR §54.
  - 2. The clinical investigator must promptly update this information if any relevant changes occur during the course of the investigation and for 1 year following the completion of the study.
- f. Follow FDA requirements for assurance of IRB review<sup>8</sup>
  - i. An investigator must assure that an IRB that complies with the requirements set forth in 21 CFR §56 will be responsible for the initial and continuing review and approval of the proposed clinical study.
  - ii. The investigator must also assure that he or she will promptly report to the IRB all changes in the research activity and all unanticipated problems involving risk to human subjects or others, and that he or she will not make any changes in the research without IRB approval, except where necessary to eliminate apparent immediate hazards to human subjects.
- g. Follow FDA requirements for inspection of investigator's records and reports<sup>9</sup>
  - i. An investigator must upon request from any properly authorized officer or employee of FDA, at reasonable times, permit such officer or employee to have access to, and copy and verify any records or reports made by the investigator pursuant to 312.62.
  - ii. The investigator is not required to divulge subject names unless the records of particular individuals require a more detailed study of the cases, or unless there is reason to believe that the records do not represent actual case studies, or do not represent actual results obtained.
- h. Follow FDA requirements for handling of controlled substances<sup>10</sup>
  - i. If the investigational drug is subject to the Controlled Substances Act, the investigator must take adequate precautions, including storage of the investigational drug in a securely locked, substantially constructed cabinet, or other securely locked, substantially constructed enclosure, access to which is limited, to prevent theft or diversion of the substance into illegal channels of distribution.
- 3. For FDA-regulated research involving investigational devices:
  - a. General responsibilities of investigators.<sup>11</sup>
    - i. An investigator is responsible for ensuring that an investigation is conducted according to the signed agreement, the investigational plan and applicable FDA regulations, for protecting the rights, safety, and welfare of subjects under the investigator's care, and for the control of devices under investigation. An investigator also is responsible for ensuring that informed consent is obtained in accordance with 21 CFR §50.
  - b. Specific responsibilities of investigators<sup>12</sup>

---

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

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

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

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

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

- i. Awaiting approval: An investigator may determine whether potential subjects would be interested in participating in an investigation, but must not request the written informed consent of any subject to participate, and must not allow any subject to participate before obtaining IRB and FDA approval.
  - ii. Compliance: An investigator must conduct an investigation in accordance with the signed agreement with the sponsor, the investigational plan, and other applicable FDA regulations, and any conditions of approval imposed by an IRB or FDA.
  - iii. Supervising device use: An investigator must permit an investigational device to be used only with subjects under the investigator's supervision. An investigator must not supply an investigational device to any person not authorized to receive it.
  - iv. Financial disclosure:
    - 1. A clinical investigator must disclose to the sponsor sufficient accurate financial information to allow the applicant to submit complete and accurate certification or disclosure statements required under 21 CFR §54.
    - 2. The investigator must promptly update this information if any relevant changes occur during the course of the investigation and for 1 year following completion of the study.
  - v. Disposing of device: Upon completion or termination of a clinical investigation or the investigator's part of an investigation, or at the sponsor's request, an investigator must return to the sponsor any remaining supply of the device or otherwise dispose of the device as the sponsor directs.
- c. Maintain the following accurate, complete, and current records relating to the investigator's participation in an investigation:<sup>13</sup>
- i. All correspondence with another investigator, an IRB, the sponsor, a monitor, or FDA, including required reports.
  - ii. Records of receipt, use or disposition of a device that relate to:
    - 1. The type and quantity of the device, the dates of its receipt, and the batch number or code mark.
    - 2. The names of all persons who received, used, or disposed of each device.
    - 3. Why and how many units of the device have been returned to the sponsor, repaired, or otherwise disposed of.
  - iii. Records of each subject's case history and exposure to the device. Case histories include the case report forms and supporting data including, for example, signed and dated consent forms and medical records including, for example, progress notes of the physician, the individual's hospital charts, and the nurses' notes. Such records must include:
    - 1. Documents evidencing informed consent and, for any use of a device by the investigator without informed consent, any written concurrence of a licensed physician and a brief description of the circumstances justifying the failure to obtain informed consent.
    - 2. Documentation that informed consent was obtained prior to participation in the study.

---

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

3. All relevant observations, including records concerning adverse device effects (whether anticipated or unanticipated), information and data on the condition of each subject upon entering, and during the course of, the investigation, including information about relevant previous medical history and the results of all diagnostic tests.
4. A record of the exposure of each subject to the investigational device, including the date and time of each use, and any other therapy.
- iv. The protocol, with documents showing the dates of and reasons for each deviation from the protocol.
- v. Any other records that FDA requires to be maintained by regulation or by specific requirement for a category of investigations or a particular investigation.
- d. Inspections<sup>14</sup>
  - i. Entry and inspection: A sponsor or an investigator who has authority to grant access must permit authorized FDA employees, at reasonable times and in a reasonable manner, to enter and inspect any establishment where devices are held (including any establishment where devices are manufactured, processed, packed, installed, used, or implanted or where records of results from use of devices are kept).
  - ii. Records inspection: A sponsor, IRB, or investigator, or any other person acting on behalf of such a person with respect to an investigation, must permit authorized FDA employees, at reasonable times and in a reasonable manner, to inspect and copy all records relating to an investigation.
  - iii. Records identifying subjects: An investigator must permit authorized FDA employees to inspect and copy records that identify subjects, upon notice that FDA has reason to suspect that adequate informed consent was not obtained, or that reports required to be submitted by the investigator to the sponsor or IRB have not been submitted or are incomplete, inaccurate, false, or misleading.
- e. Prepare and submit the following complete, accurate, and timely reports<sup>15</sup>
  - i. Unanticipated adverse device effects. An investigator must submit to the sponsor and to the reviewing IRB a report of any unanticipated adverse device effect occurring during an investigation as soon as possible, but in no event later than 10 working days after the investigator first learns of the effect.
  - ii. Withdrawal of IRB approval. An investigator must report to the sponsor, within 5 working days, a withdrawal of approval by the reviewing IRB of the investigator's part of an investigation.
  - iii. Progress. An investigator must submit progress reports on the investigation to the sponsor, the monitor, and the reviewing IRB at regular intervals, but in no event less often than yearly.
  - iv. Deviations from the investigational plan:
    1. An investigator must notify the sponsor and the reviewing IRB of any deviation from the investigational plan to protect the life or physical well-being of a subject in an emergency.
    2. Such notice must be given as soon as possible, but in no event later than 5 working days after the emergency occurred.

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

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

3. Except in such an emergency, prior approval by the sponsor is required for changes in or deviations from a plan, and if these changes or deviations may affect the scientific soundness of the plan or the rights, safety, or welfare of human subjects, FDA and IRB also is required.
- v. Informed consent. If an investigator uses a device without obtaining informed consent, the investigator must report such use to the sponsor and the reviewing IRB within 5 working days after the use occurs.
- vi. Final report. An investigator must, within 3 months after termination or completion of the investigation or the investigator's part of the investigation, submit a final report to the sponsor and the reviewing IRB.
- vii. Other. An investigator must, upon request by a reviewing IRB or FDA, provide accurate, complete, and current information about any aspect of the investigation.

Appendix A-3      ***Additional Requirements for Clinical Trials obligated to follow ICH-GCP through contract/funding agreement commitments***

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

medical care is needed for intercurrent illnesses of which the investigator becomes aware.

- c. It is recommended that the investigator inform the subject's primary physician about the subject's participation in the trial if the subject has a primary physician and if the subject agrees to the primary physician being informed.
  - d. Although a subject is not obliged to give his/her reasons for withdrawing prematurely from a trial, the investigator should make a reasonable effort to ascertain the reasons, while fully respecting the subject's rights.
4. Communication with IRB
- a. Before initiating a trial, the investigator/institution should have written and dated approval opinion from the IRB for the trial protocol, written informed consent form, consent form updates, subject recruitment procedures (e.g., advertisements), and any other written information to be provided to subjects.
  - b. As part of the investigator's/institution's written application to the IRB, the investigator/institution should provide the IRB with a current copy of the Investigator's Brochure. If the Investigator's Brochure is updated during the trial, the investigator/institution should supply a copy of the updated Investigator's Brochure to the IRB.
  - c. During the trial the investigator/institution should provide to the IRB all documents subject to review.
5. Compliance with Protocol
- a. The investigator/institution should conduct the trial in compliance with the protocol agreed to by the sponsor and, if required, by the regulatory authorities and which was given approval opinion by the IRB. The investigator/institution and the sponsor should sign the protocol, or an alternative contract, to confirm agreement.
  - b. The investigator should not implement any deviation from, or changes of the protocol without agreement by the sponsor and prior review and documented approval opinion from the IRB of a modification, except where necessary to eliminate an immediate hazards to trial subjects, or when the changes involves only logistical or administrative aspects of the trial (e.g., change in monitors, change of telephone numbers).
  - c. The investigator, or person designated by the investigator, should document and explain any deviation from the approved protocol.
  - d. The investigator may implement a deviation from, or a change of, the protocol to eliminate an immediate hazard to trial subjects without prior IRB approval opinion. As soon as possible, the implemented deviation or change, the reasons for it, and, if appropriate, the proposed protocol modifications 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 subject, and the return to the sponsor or alternative disposition of unused product. These records should include dates, quantities, batch/serial numbers, expiration dates (if applicable), and the unique code numbers assigned to the investigational product and trial subjects. Investigators should maintain records that document adequately that the subjects were provided the doses specified by the protocol and reconcile all investigational product received from the sponsor.
  - d. The investigational product should be stored as specified by the sponsor and in accordance with applicable regulatory requirements.
  - e. The investigator should ensure that the investigational product is used only in accordance with the approved protocol.
  - f. The investigator, or a person designated by the investigator/institution, should explain the correct use of the investigational product to each subject and should check, at intervals appropriate for the trial, that each subject is following the instructions properly.
  - g. Randomization Procedures and Unblinding: The investigator should follow the trial's randomization procedures, if any, and should ensure that the code is broken only in accordance with the protocol. If the trial is blinded, the investigator should promptly document and explain to the sponsor any premature unblinding (e.g., accidental unblinding, unblinding due to a serious adverse event) of the investigational product.
7. Informed Consent of Trial Subjects
- a. In obtaining and documenting informed consent, the investigator should comply with the applicable regulatory requirements, and should adhere to GCP and to the ethical principles that have their origin in the Declaration of Helsinki. Prior to the beginning of the trial, the investigator should have the IRB's written approval opinion of the written informed consent form and any other written information to be provided to subjects.
  - b. The written informed consent form and any other written information to be provided to subjects should be revised whenever important new information becomes available that may be relevant to the subject's consent. Any revised written informed consent form, and written information should receive the IRB's approval opinion in advance of use. The subject or the subject's legally acceptable representative should be informed in a timely manner if new information becomes available that may be relevant to the subject's willingness



to continue participation in the trial. The communication of this information should be documented.

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

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

- xix. The expected duration of the subject's participation in the trial.
  - xx. The approximate number of subjects involved in the trial.
  - k. Prior to participation in the trial, the subject or the subject's legally acceptable representative should receive a copy of the signed and dated written informed consent form and any other written information provided to the subjects. During a subject's participation in the trial, the subject or the subject's legally acceptable representative should receive a copy of the signed and dated consent form updates and a copy of any modifications to the written information provided to subjects.
  - l. When a clinical trial (therapeutic or non-therapeutic) includes subjects who can only be enrolled in the trial with the consent of the subject's legally acceptable representative (e.g., minors, or patients with severe dementia), the subject should be informed about the trial to the extent compatible with the subject's understanding and, if capable, the subject should sign and personally date the written informed consent.
  - m. Except as described above, a non-therapeutic trial (i.e. a trial in which there is no anticipated direct clinical benefit to the subject), should be conducted in subjects who personally give consent and who sign and date the written informed consent form.
  - n. Non-therapeutic trials may be conducted in subjects with consent of a legally acceptable representative provided the following conditions are fulfilled: a) The objectives of the trial cannot be met by means of a trial in subjects who can give informed consent personally. b) The foreseeable risks to the subjects are low. c) The negative impact on the subject's well-being is minimized and low. d) The trial is not prohibited by law. e) The approval opinion of the IRB is expressly sought on the inclusion of such subjects, and the written approval opinion covers this aspect. Such trials, unless an exception is justified, should be conducted in patients having a disease or condition for which the investigational product is intended. Subjects in these trials should be particularly closely monitored and should be withdrawn if they appear to be unduly distressed.
  - o. In emergency situations, when prior consent of the subject is not possible, the consent of the subject's legally acceptable representative, if present, should be requested. When prior consent of the subject is not possible, and the subject's legally acceptable representative is not available, enrolment of the subject should require measures described in the protocol and/or elsewhere, with documented approval opinion by the IRB, to protect the rights, safety and well-being of the subject and to ensure compliance with applicable regulatory requirements. The subject or the subject's legally acceptable representative should be informed about the trial as soon as possible and consent to continue and other consent as appropriate should be requested.
8. Records and Reports

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

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

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

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

1. When appropriate, research protocols must be reviewed and approved by the IRB prior to the Department of Defense approval. Consult with the Department of Defense funding component to see whether this is a requirement.
2. Civilian researchers attempting to access military volunteers should seek collaboration with a military researcher familiar with service-specific requirements.
3. Employees of the Department of Defense (including temporary, part-time, and intermittent appointments) may not be able to legally accept payments to participate in research and should check with their supervisor before accepting such payments. Employees of the Department of Defense cannot be paid for conducting research while on active duty.
4. Service members must follow their command policies regarding the requirement to obtain command permission to participate in research involving human subjects while on-duty or off-duty.
5. Components of the Department of Defense might have stricter requirements for research-related injury than the DHHS regulations.
6. There may be specific educational requirements or certification required.
7. When assessing whether to support or collaborate with this institution for research involving human subjects, the Department of Defense may evaluate this institution's education and training policies to ensure the personnel are qualified to perform the research.
8. 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.
9. When research involves large scale genomic data (LSGD) collected on DOD-affiliated personnel, additional protections are required:
  - a. Additional administrative, technical, and physical safeguards to prevent disclosure of DoD-affiliated personnel's genomic data commensurate with risk (including secondary use or sharing of de-identified data or specimens)
  - b. Research will apply an HHS Certificate of Confidentiality
10. DoD Component security review
11. When conducting multi-site research, a formal agreement between institutions is required to specify the roles and responsibilities of each party.
12. Other specific requirements of the Department of Defense research be found in the "Additional Requirements for Department of Defense (DOD) Research" section in the IRB's HRP-318 - WORKSHEET - Additional Federal Agency Criteria.

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

(See [DOE Order 443.1C](#))

1. Research that involves one or more of the following must be submitted to the appropriate IRB for human subjects research review and determination:
  - a. Study of humans in a systematically modified environment. These studies include but are not limited to intentional modification of the human environment:
    - i. Study of human environments that use tracer chemicals, particles or other materials to characterize airflow.
    - ii. Study in occupied homes or offices that:
      1. Manipulate the environment to achieve research aims.
      2. Test new materials.
      3. 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.
  - b. Use of social media data.
  - c. Human Terrain Mapping (HTM).
  - d. All exempt HSR determinations must be made by the appropriate IRB and/or IRB office.
2. Personally identifiable information collected and/or used during HSR projects must be protected in accordance with the requirements of DOE Order 206.1, Department of Energy Privacy Program, current version. The Central DOE IRBs require submission of DOE's HRP- 490-CHECKLIST-Reviewing Protocols that use Personally Identifiable Information (PII) if your research includes PII.
3. You must report the following to the DOE human subjects research Program Manager (and, when an NNSA element is involved, the NNSA HSP Program Manager) prior to initiation of any new human subjects research project, even if it meets the regulatory definition of exempt human subjects research as outlined in 10 CFR Part 745.104, involving:
  - a. An institution without an established Institutional Review Board (IRB);
  - b. A foreign country;
  - c. The potential for significant controversy (e.g., negative press or reaction from stakeholder or oversight groups);
  - d. Research subjects in a protected class (prisoners, children, individuals with impaired decision making capability, or DOE/NNSA federal or DOE/NNSA contractor employees as human subjects, who may be more vulnerable to coercion and undue influence to participate) that is outside of the reviewing IRB's typical range/scope; or
  - e. The generation or use of classified information.
4. The IRB must be notified immediately and the DOE HSP Program Manager (and, when an NNSA element is involved, the NNSA HSP Program Manager) must be notified within 48 hours and consulted regarding planned corrective actions if any of the following occur:

- a. Adverse events. Notify the IRB for all adverse events and the DOE/NNSA HSP Program Manager if the IRB determines them to be significant, as defined in DOE Order 443.1C.
  - b. Unanticipated problems and complaints about the research.
  - c. Any suspension or termination of IRB approval of research.
  - d. Any significant non-compliance with HSP Program procedures or other requirements.
  - e. Any finding of a suspected or confirmed data breach involving PII in printed or electronic form. Report immediately to the IRB, the DOE/NNSA HSP Program Manager(s), and the DOE-Cyber Incident Response Capability, in accordance with the requirements of the CRD associated with DOE O 206.1.
  - f. Serious adverse events and corrective actions taken must be reported immediately to the IRB and the DOE/NNSA HSP Program Manager(s). The time frame for “immediately” is defined as upon discovery.
5. Requirements for human participant protections for classified research apply to all classified research conducted or supported by the DOE and its national laboratories, including contracts, and including Human Terrain Mapping research.
  6. Researchers conducting human subjects research in any other country or on citizens or other individuals residing in that country must be cognizant of country-specific human subjects research requirements and consult the IRB regarding applicability of such requirements.
  7. No human subjects research conducted with DOE funding, at DOE institutions (regardless of funding source), or by DOE or DOE contractor personnel (regardless of funding source or location conducted), whether done domestically or in an international environment, including classified and proprietary research, may be initiated without both a Federalwide Assurance (FWA) or comparable assurance (e.g., Department of Defense assurance) of compliance and approval by the cognizant Institutional Review Board (IRB) in accordance with 10 CFR §745.103. Human subjects research involving multiple DOE sites (e.g., members of the research team from more than one DOE site and/or data or human subjects from more than one DOE site) must be reviewed and approved by one of the Central DOE IRBs prior to initiation, or if authorized by the DOE and/or NNSA HSP Program Manager, other appropriate IRB of record. In all cases, an IRB Authorization Agreement (IAA) or Memorandum of Understanding (MOU) must be in place between the organization(s) conducting the HSR and the organization responsible for IRB review.
  8. Human subjects research that involves DOE Federal and/or contractor employees must first be reviewed and approved by the appropriate DOE IRB (the DOE site IRB or one of the Central DOE IRBs), or if deemed more fitting by the Federally assured DOE site or Headquarters, other appropriate IRB of record, in accordance with an IAA or MOU negotiated between the DOE site or Headquarters and the organization responsible for IRB review.
  9. Classified and unclassified human subjects research that is funded through the Strategic Intelligence Partnership Program (SIPP) must be reviewed and approved by the Central DOE IRB-Classified.
  10. If applicable, federally funded HSR must comply with the requirements of the Paperwork Reduction Act.
  11. Other specific requirements of the DOE research can be found in the “Additional Requirements for Department of Energy (DOE) Research” section in the IRB’s HRP-318 - WORKSHEET - Additional Federal Agency Criteria.



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

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

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

- commit future criminal conduct or harm himself or herself or someone else, or, if the subject is an inmate, indicates intent to leave the facility without authorization.
- e. A statement that participation in the research project will have no effect on the inmate subject's release date or parole eligibility.
13. You must have academic preparation or experience in the area of study of the proposed research.
  14. The IRB application must include a summary statement, which includes:
    - a. Names and current affiliations of the investigators.
    - b. Title of the study.
    - c. Purpose of the study.
    - d. Location of the study.
    - e. Methods to be employed.
    - f. Anticipated results.
    - g. Duration of the study.
    - h. Number of subjects (staff or inmates) required and amount of time required from each.
    - i. Indication of risk or discomfort involved as a result of participation.
  15. The IRB application must include a comprehensive statement, which includes:
    - a. Review of related literature.
    - b. Detailed description of the research method.
    - c. Significance of anticipated results and their contribution to the advancement of knowledge.
    - d. Specific resources required from the Bureau of Prisons.
    - e. Description of all possible risks, discomforts, and benefits to individual subjects or a class of subjects, and a discussion of the likelihood that the risks and discomforts will actually occur.
    - f. Description of steps taken to minimize any risks.
    - g. Description of physical or administrative procedures to be followed to: Ensure the security of any individually identifiable data that are being collected for the study.
    - h. Destroy research records or remove individual identifiers from those records when the research has been completed.
    - 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 Review Board, the regional director, and the warden of each institution that provided data or assistance.
  20. You must include an abstract in the report of findings.
  21. In any publication of results, you must acknowledge the Bureau's participation in the research project.

22. You must expressly disclaim approval or endorsement of the published material as an expression of the policies or views of the Bureau.
23. Prior to submitting for publication, the results of a research project conducted under this subpart, you must provide two copies of the material, for informational purposes only, to the Chief, Office of Research and Evaluation, Central Office, Bureau of Prisons.
24. Other specific requirements of the Department of Justice (DOJ) Research Conducted within the Federal Bureau of Prisons (BOP) can be found in the “Additional Requirements for Department of Justice (DOJ) Research Conducted within the Federal Bureau of Prisons (BOP)” section in the IRB’s HRP-318 - WORKSHEET - Additional Federal Agency Criteria.

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

1. The project must have a privacy certificate approved by the National Institute of Justice Human Subjects Protection Officer.
2. All investigators and research staff are required to sign employee confidentiality statements, which are maintained by the responsible investigator.
3. The confidentiality statement on the consent document must state that confidentiality can only be broken if the subject reports immediate harm to subjects or others.
4. Under a privacy certificate, investigators and research staff do not have to report child abuse unless the subject signs another consent document to allow child abuse reporting.
5. A copy of all data must be de-identified and sent to the National Archive of Criminal Justice Data, including copies of the informed consent document, data collection instruments, surveys, or other relevant research materials.
  - a. At least once a year, the researcher shall provide the Chief, Office of Research and Evaluation, with a report of the progress of the research.
  - b. At least 12 working days before any report of findings is to be released, the researcher shall distribute one copy of the report to each of the following: the chairperson of the Bureau Research Review Board, the regional director, and the warden of each institution that provided data or assistance. The researcher shall include an abstract in the report of findings.
  - c. In any publication of results, the researcher shall acknowledge the Bureau's participation in the research project.
  - d. The research shall expressly disclaim approval or endorsement of the published material as an expression of the policies or views of the Bureau.
  - e. Prior to submitting for publication, the results of a research project conducted under this subpart, the researcher shall provide two copies of the material, for informational purposes only, to the Chief, Office of Research and Evaluation, Central Office, Bureau of Prisons
6. Other specific requirements of the Department of Justice (DOJ) Research Funded by the National Institute of Justice can be found in the “Additional Requirements for Department of Justice (DOJ) Research” section in the IRB’s HRP-318 - WORKSHEET - Additional Federal Agency Criteria.

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

1. Each school at which the research is conducted must provide an assurance that they comply with the Family Educational Rights and Privacy Act (FERPA) and the Protection of Pupil Rights Amendment (PPRA).
2. Provide a copy of all surveys and instructional material used in the research. Upon request parents of children<sup>16</sup> involved in the research<sup>17</sup> must be able to inspect these materials.
3. The school in which the research is being conducted must have policies regarding the administration of physical examinations or screenings that the school may administer to students.
4. Other specific requirements of the Department of Education (ED) Research can be found in the “Additional Requirements for Department of Education (ED) Research” section in the IRB’s HRP-318 - WORKSHEET - Additional Federal Agency Criteria.

---

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

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

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

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

## ***Additional Requirements for Veterans Administration (VA) Research***

- The investigator must follow this institution’s procedures to ensure reporting in writing to the IRB within 5 business days of becoming aware of unanticipated problems involving risks to subjects or others (local SAEs or serious problems that are unanticipated and related to the research), apparent serious or continuing non-compliance, suspension of IRB approval, termination of IRB approval. Any unanticipated problem involving risks to subjects or others that is a local research death must be reported orally to the IRB immediately upon becoming aware of the information.
- The investigator must give first priority to the protection of research subjects, uphold professional and ethical standards and practices, and adhere to all applicable VA and other federal requirements, including the local VA facility’s policies and procedures, regarding the conduct of research and the protection of human subjects. The investigator must hold a current VA appointment to conduct VA research.
- Any study conducted by researchers while on VA time, including Without Compensation and Intergovernmental Personnel Act appointments, is subject to review and approval by the Madison Veterans Administration (VA) Research and Development Committee. The VA determines whether a particular study falls under VA purview.
- The responsibilities of the investigator may be defined in the protocol or IRB application. Specifically, the principal investigator’s and local site investigator’s responsibilities include, but are not limited to
  - Qualifications to Conduct Human Subjects Research. VA investigators must have the appropriate training, education, expertise, and credentials to conduct the research according to the research protocol.
    - Students or trainees cannot serve as PI on VA human subjects research, but may participate as a study team member if enrolled at an institution with an educational affiliation agreement with the Madison VA or be directly appointed to a VA training program that has no external institutional sponsorship.
    - PIs must ensure that all research staff are qualified (e.g., including but not limited to appropriate training, education, expertise, and credentials) to perform procedures assigned to them during the course of the study.
    - Investigators and their staff conducting human subjects research must be credentialed and privileged as required by current local and VA requirements (see VHA Handbook 1100.19 and VHA Directive 2012-030, Credentialing of Health Care Professionals, or successor policy). Investigators and their research staff may only perform those activities in a research study for which they have the relevant credentials and privileges.
    - Investigators and co-investigators must be identified on the IRB application and must provide credentials, conflict of interest statements or other documentation required by VA and local facility policies.
    - All individuals involved in conducting VA human subjects research are required to complete training in ethical principles on which human subjects research is to be conducted. Specific requirements regarding the type and frequency of training are found on ORD’s Web site at: [https://www.research.va.gov/programs/orppe/education/ord\\_training/default.cfm](https://www.research.va.gov/programs/orppe/education/ord_training/default.cfm). All other applicable VA and VHA training requirements at the local and national level must be met (e.g., privacy and information security training).

- Investigators must prospectively document their research with their supervisor in writing.
- Investigators must submit exempt protocols that require limited IRB review to the IRB for limited IRB review/approval.
- Research Protocol. The investigator must develop and submit a research protocol that is scientifically valid, describes the research objectives, background and methodology, provides for fair and equitable recruitment and selection of subjects, minimizes risks to subjects and others, and describes a data and safety monitoring plan consistent with the nature of the study. The research must be relevant to the health or welfare of the Veteran population. When relevant, the protocol must include the following safety measures:
  - The type of safety information to be collected including AEs;
  - Frequency of safety data collection;
  - Frequency or periodicity of review of cumulative safety data;
  - Statistical tests for analyzing the safety data to determine if harm is occurring; and
  - Conditions that trigger an immediate suspension of the research, if applicable.
- Approvals. The investigator must submit the protocol for initial review and obtain written approvals from the IRB, other applicable committees, and from the R&D Committee. In addition, the investigator must receive written notice from the ACOS/R&D that the research may commence before initiating the research.
  - An investigator may not self-certify that a study is exempt.
  - Once approved by the IRB, the protocol must be implemented as approved. All modifications to the approved research protocol or consent form must be approved by the IRB prior to initiating the changes except when necessary to eliminate apparent immediate hazards to the subject.
  - The investigator must also obtain continuing review and approval at a frequency established by the IRB, but not less than once every year and is expected to submit all materials required for continuing review in sufficient time to assure approval prior to the expiration date. No research activities may be conducted at any time without a currently valid IRB approval.
- Conflict of Interest. The investigator must disclose to the IRB any potential, actual, apparent, or perceived conflict of interest of a financial, professional, or personal nature that may affect any aspect of the research, and comply with all applicable VA and other federal requirements regarding conflict of interest.
- Initial Contact. During the recruitment process, members of the research team must make initial contact with potential subjects in person or by letter prior to initiating any telephone contact, unless there is written documentation that the subject is willing to be contacted by telephone about the study in question or a specific kind of research as outlined in the study. (NOTE: This does not apply to situations where a Veteran calls in response to an advertisement. If existing information from sources such as a medical record or database, research or non-research, are used to identify human subjects, there must be an IRB approved HIPAA waiver for this activity in the new protocol.)
  - Any initial contact by letter or telephone must provide a telephone number or other means that the potential subject can use to verify that the study constitutes VA research.
  - If a contractor makes the initial contact by letter, the VA investigator must sign the letter.

- Informed Consent for Research. The investigator must obtain and document legally effective informed consent of the subject or the subject's LAR prospectively (i.e., no screening or other interaction or intervention involving a human subject can occur until after the IRB-approved informed consent requirements have been met) that is in alignment with ethical principles that govern informed consent for research. The only exceptions are if the IRB determines the research is exempt, or approves a waiver of the informed consent process, or approves a waiver of the signed informed consent document.
  - If the investigator does not personally obtain informed consent, the investigator must delegate this responsibility in writing (e.g., by use of a delegation letter) to research staff sufficiently knowledgeable about the protocol and related concerns to answer questions from prospective subjects, and about the ethical basis of the informed consent process and protocol.
    - If the investigator contracts with a firm, e.g., a survey research firm, to obtain consent from subjects, collect private individually identifiable information from human subjects, or are involved in activities that would institutionally engage the firm in human subjects research, the firm must have its own IRB oversight of the activity. In addition, the PO must determine that there is appropriate authority to allow the disclosure of individual names and other information to the contracted firm.
    - The investigator must ensure that all original signed and dated informed consent documents are maintained in the investigator's research files, readily retrievable, and secure.
  - HIPAA Authorization. The investigator or designee must obtain HIPAA authorization for the use and disclosure of the subject's PHI, or obtain an IRB-approved waiver of HIPAA authorization unless there is a limited data set and appropriate DUA. The written HIPAA authorization may either be a standalone document or combined with the research informed consent approved by the IRB. If a standalone document is used as the written HIPAA authorization, VA Form 10-0493: Authorization for Use and Release of Individually Identifiable Health Information Collected for VHA Research, must be used to document the authorization.
- Reporting. The investigator is responsible for reporting unanticipated problems involving risks to subjects or others, serious unanticipated problems involving risks to subjects or others, apparent serious or continuing noncompliance, any termination or suspension of research; and privacy or information security incidents related to VA research, including: any inappropriate access, loss, or theft of PHI; noncompliant storage, transmission, removal, or destruction of PHI; or theft, loss, or noncompliant destruction of equipment containing PHI, in accordance with local facility or IRB SOPs and VHA Handbook 1058.01.
- Research Records. All written information given to subjects must be in the investigator's research file along with the consent form(s). All records regardless of format (paper, electronic, electronic systems) must be managed per NARA approved records schedules found in VHA RCS 10-1 and therefore must be retained until disposition instructions, as approved by NARA, are published in VHA RCS 10-1. NOTE: Once the disposition schedule is determined, records should be disposed in accordance with VHA RCS 10-1. If the investigator leaves VA, all research records must be retained by the VA facility where the research was conducted.
- VHA Health Record. A VHA health record must be created or updated, and a progress note created, for all research subjects (Veterans or Non-Veterans) who are admitted to VA



- medical facilities as in-patients, treated as outpatients at VA medical facilities, or when research procedures or interventions are used in or may impact the medical care of the research subject at a VA medical facility or at facilities contracted by VA to provide services to Veterans (e.g., Community-Based Outpatient Clinics or nursing homes) (see VHA Handbook 1907.01). Informed consent and HIPAA authorization documents are not required to be in the health record.
- Investigational Drugs and Devices. The investigator must conduct VA human subjects research involving investigational drugs and devices in accordance with all applicable VA policies and other federal requirements including, but not limited to: VHA Directive 1200.05, VHA Handbook 1108.04, and applicable FDA regulations. The storage and security procedures for test articles used in research must be reviewed and approved by the IRB and follow all applicable federal rules.
    - The PI or Local Site Investigator (LSI) must provide the Pharmacy Service with the following:
      - Written approval letter signed by the ACOS for R&D that all relevant approvals have been obtained and that the study may be initiated at the site (VHA Directive 1200.01);
      - An IRB approval letter;
      - A copy of the approved study protocol;
      - A copy of VA Form 10-9012, when appropriate;
      - An IB, when appropriate;
      - Any sponsor-provided documents relating to the storage, preparation, dispensing, and accountability of the investigation products;
      - Protocol revisions, modifications, and updates after IRB approval and after the IRB approved the modification;
      - Updates and changes to authorized prescribers after IRB approval;
      - Documentation of IRB continuing review approval;
      - Notice to the Chief, Pharmacy Service, the research pharmacy when applicable and the IRB in writing and the Research and Development Committee when a study involving investigational drugs has been suspended, terminated, or closed.
    - The PI or LSI must provide Pharmacy Service and/or the Research Service Investigational Pharmacy, investigational drug information on each patient receiving an investigational drug through the electronic medical record or other locally-approved means. This documentation is to include allergies, toxicities, or adverse drug events related to the investigational drug, or the potential for interaction with other drugs, foods, or dietary supplements (herbals, nutraceuticals).
    - The PI or LSI must place the completed VA Form 10-9012, or electronic equivalent, in the subject's medical record.
  - Initiation of Research Projects. IRB approval is for a specified time period based on the degree of risk of the study, not to exceed 1 year except for research subject to the 2018 Requirements where continuing review is not required. The IRB determines the expiration date based upon its date of review and communicates that date to the investigator in the written approval letter. The investigator must not initiate the IRB approved research protocol until all applicable requirements in VHA Directive 1200.01 have also been met including obtaining R&D Committee approval.
  - Expiration of IRB Approval. There is no provision for any grace period to extend the conduct of research beyond the expiration date of IRB approval. Therefore, continuing review and

re-approval of research must occur on or before the date when IRB approval expires. If approval expires, the investigator must:

- Stop all research activities including, but not limited to, enrollment of new subjects, analyses of individually identifiable data, and research interventions or interactions with currently participating subjects, except where stopping such interventions or interactions could be harmful to those subjects; and
- Immediately submit to the IRB Chair a list of research subjects who could be harmed by stopping specified study interventions or interactions. The IRB Chair must determine within 2 business days whether or not such interventions or interactions may continue.
- Documentation of Informed Consent
  - When documentation of informed consent is not waived by IRB, the investigator or designee must ensure that the informed consent document is signed and dated by the subject or the subject's legally authorized representative,
  - If consent is obtained electronically, the following must be met:
    - Authentication controls on electronic consent provide reasonable assurance that such consent is rendered by the proper individual; and
    - The subject dates the consent as is typical or that the software provides the current date when signed.
- Other specific requirements of Veterans Administration (VA) research be found in the "Additional Requirements for Veterans Administration (VA) Research" section in the IRB's HRP-318 - WORKSHEET - Additional Federal Agency Criteria.
- Vulnerable Subjects
  - The following populations are considered categorically vulnerable and have specific VA requirements for their inclusion in research:
    - Neonates. Interventional research enrolling neonates cannot be conducted by VA investigators while on official duty, or at VA facilities, or at VA approved off-site facilities. Noninvasive monitoring and prospective observational and retrospective record review studies that involve neonates or neonatal outcomes are permitted.
    - Pregnant Women. The VA medical facility Director must certify that the medical facility has sufficient expertise in women's health to conduct the proposed research if the research includes interventional studies or invasive monitoring of pregnant women as subjects.
    - Prisoners
    - Children
    - Subjects who Lack Decision-making Capacity.
- Research Involving Prisoners
  - Research involving prisoners cannot be conducted by VA investigators while on official VA duty, at VA facilities, or at VA-approved off-site facilities unless a waiver has been granted by the CRADO.
  - Waiver requests must be submitted electronically to the CRADO by the VA medical facility Director with the following documents:
    1. A letter from the VA medical facility Director supporting the conduct of the VA study involving prisoners;
    2. Rationale for conducting the research involving prisoners to include additional ethical protections taken by the proposed research for prisoners to make voluntary and uncoerced decisions whether or not to participate as subjects in research;

3. Documentation of the VA investigator's qualifications to conduct the research involving prisoners, such as a biosketch and a list of all research team members;
  4. Location of institutions where the research is proposed to be conducted;
  5. A copy of the IRB approval letter specifically documenting its review determinations according to 45 CFR 46.305(a);
  6. A copy of the IRB minutes approving the research with documentation that at least one member of the IRB included a prisoner or a prisoner representative for the review of the research;
  7. A copy of the IRB-approved research study;
  8. A copy of the IRB-approved informed consent document; and
  9. A copy of the written HIPAA authorization.
- If such a waiver is granted, the research must comply with the requirements of 45 CFR 46.301 - 46.306.
- Research Involving Children
    - Research involving children must not present greater than minimal risk.
    - The VA medical facility Director must approve participation in the proposed research that includes children.
    - Research involving biological specimens or data obtained from children is considered to be research involving children even if de-identified. If the biological specimens or data were previously collected, they must have been collected under applicable policies and ethical guidelines.
    - The IRB must have the appropriate expertise to evaluate VA research involving children and must comply with the requirements of 45 CFR 46.401 - 46.404 and 46.408.
  - Research Involving Persons Who Lack Decision-Making Capacity
    - The protocol must include a plan, that it is appropriate given the population and setting of the research, for how investigators will determine when a legally authorized representative will be required to provide informed consent. In general, the research staff must perform or obtain and document a clinical assessment of decision-making capacity for any subject suspected of lacking decision-making capacity.
    - When the potential subject is determined to lack decision-making capacity, investigators must obtain consent from the LAR of the subject (i.e., surrogate consent). NOTE: Investigators and IRBs have a responsibility to consult with the Office of General Counsel (OGC) regarding state or local requirements for surrogate consent for research that may supersede VA requirements.
    - The following persons are authorized to consent on behalf of persons who lack decision-making capacity in the following order of priority:
      - (1) Health care agent (i.e., an individual named by the subject in a Durable Power of Attorney for Health Care);
      - (2) Legal guardian or special guardian;
      - (3) Next of kin: a close relative of the patient 18 years of age or older, in the following priority: spouse, child, parent, sibling, grandparent, or grandchild; or
      - (4) Close friend.
    - If feasible, the investigator must explain the proposed research to the prospective research subject even when the legally authorized representative gives consent. Although unable to provide informed consent, some persons may resist participating in a research protocol approved by their representatives. Under no circumstances may a subject be forced or coerced to participate in a research study even if the LAR has provided consent.

- Legally authorized representatives must be told that their obligation is to try to determine what the subjects would do if able to make an informed decision. If the potential subjects' wishes cannot be determined, the legally authorized representatives must be told they are responsible for determining what is in the subjects' best interest.
- Research Involving Certificates of Confidentiality
  - If information about the subject's participation will be included as part of the VHA medical record that information must be given to the prospective subject as part of the informed consent process that information regarding study participation will be included in the medical record.
  - In instances where a written informed consent form is used, inclusion of a statement that the study has been issued a CoC is required.
  - Investigators should work with the research office in their facility to assure that when Veterans are enrolled in a study protected by a Certificate of Confidentiality, they are not simultaneously enrolled in other interventional studies unless it is absolutely clear that this enrollment does not raise safety issues.
- Collaborative Research
  - This addresses collaborations between VA and non-VA investigators. Collaboration is encouraged when VA investigators have a substantive role in the design, conduct, and/or analysis of the research. VA may also serve as a Coordinating Center for collaborative studies. NOTE: Collaborative studies do not include studies conducted under a CRADA with pharmaceutical companies or other for-profit entities.
  - IRB of Record Approval. Each institution is responsible for safeguarding the rights and welfare of human subjects and providing oversight of the research activities conducted at that institution.
    - Each collaborating institution engaged in human subjects research must obtain approval from its IRB of Record and hold a FWA or another assurance acceptable to VA, e.g., DoD assurance.
    - VA investigators must submit a protocol or other documentation to their VA IRB of Record that delineates which research activities will be conducted by VA.
    - Each institution engaged in the collaborative research must use the informed consent document and HIPAA authorization required by their respective institutional policies for subjects recruited from that institution, or procedures requiring participation of the subject at that institution. The informed consent document may contain information on the project as a whole as long as the document clearly describes which procedures will be performed at VA and which will be performed at other institutions.
      - The VA informed consent document must clearly state when procedures mentioned at other institutions are part of the VA's portion of the study.
      - The informed consent document and HIPAA authorization must be consistent and include information describing the following:
        - PHI to be collected and/or used by the VA research team;
        - PHI to be disclosed to the other institutions; and
        - Purpose for which the PHI may be used.
    - Waivers. PHI obtained in research for which the IRB of Record has waived the requirements to obtain a HIPAA authorization and a signed informed consent document may not be disclosed outside VA unless the VA facility Privacy Officer ensures and documents VA's authority to disclose the PHI to another institution. A waiver of HIPAA authorization is not

sufficient to fulfill the requirements of other applicable privacy regulations such as the Privacy Act of 1974 (5 U.S.C. 552a).

- Research Data. The protocol, addendum, and/or IRB of Record application must describe the data to be disclosed to collaborators, the entity(ies) to which the data are to be disclosed, and how the data are to be transmitted. This includes data from individual subjects as well as other data developed during the research such as the analytic data and the aggregate data.
  - Each VA facility must retain a complete record of all data obtained during the VA portion of the research in accordance with privacy requirements, the Federal Records Act, and VHA Records Control Schedule (RCS) 10-1.
  - All disclosures and data transmission must meet privacy and security requirements per VA Directive 6500, VHA Handbook 6500, and VHA Handbook 1605.1.
  - Written agreements. Collaborative research involving non-VA institutions may not be undertaken without a signed written agreement (e.g., a CRADA or a Data Use Agreement (DUA)) that addresses such issues as the responsibilities of each party, the ownership of the data and the reuse of the data for other research. NOTE: Any reuse must be consistent with the protocol, the informed consent document, and the HIPAA authorization.
- Photography, Video and/or Audio Recording for Research Purposes
  - The informed consent for research must include information describing any photographs, video, and/or audio recordings to be taken or obtained for research purposes, how the photographs, video, and/or audio will be used for the research, and whether the photographs, video, and/or audio will be disclosed outside the VA.
    - An informed consent to take a photograph, video, and/or audio recording cannot be waived by the IRB.
    - The consent for research does not give legal authority to disclose the photographs, video, and/or audio recordings outside the VA. A HIPAA authorization is needed to make such disclosures.
- International Research:
  - VA international research is defined as any VA-approved research conducted at international sites (i.e., not within the United States (U.S.), its territories, or Commonwealths), any VA-approved research using either identifiable or de-identified human biological specimens or identifiable or de-identified human data originating from international sites, or any VA-approved research that entails sending such specimens or data out of the U.S. This definition applies regardless of the funding source (funded or unfunded) and to research conducted through any mechanism of support including MOUs, CRADAs, grants, contracts, or other agreements. NOTE: Research conducted at U.S. military bases, ships, or embassies is not considered international research.
    - Sending specimens or data to individuals with VA appointments at international sites (e.g., a WOC appointment, a VA investigator on sabbatical at an international site) is considered international research. Remote use of data that is maintained on VA computers within the U.S. or Puerto Rico and accessed via a secure connection is not considered international research.
    - International research includes multi-site trials involving non-U.S. sites where VA is the study sponsor, a VA investigator is the overall study-wide PI, VA holds the Investigational New Drug (IND), or the VA manages the data collection and the data analyses.

- International research does not include studies in which VA is only one of multiple participating sites where the overall study-wide PI is not a VA investigator (i.e., the PI for the study as a whole is not a VA investigator).
- Before approving international research involving human subjects research, the IRB must ensure that human subjects outside of the U.S. who participate in research projects in which VA is a collaborator receive equivalent protections as research participants inside the U.S. (see OHRP guidance at <http://www.hhs.gov/ohrp/international/index.html>). NOTE: The VA medical facility Director must approve participation in the proposed international research.
- All international research must also be approved explicitly in a document signed by the VA medical facility Director, except for Cooperative Studies Program activities which must be approved by the CRADO.
- Use Preparatory to Research:
  - VA investigators may use individually-identifiable health information to prepare a research protocol prior to submission of the protocol to the IRB for approval without obtaining a HIPAA authorization or waiver of authorization.
    - VA investigators must not arbitrarily review PHI based on their employee access to PHI until the investigator documents the following required information as “Preparatory to Research” in a designated file that is readily accessible for those required to audit such information (e.g., Health Information Manager or PO):
      - Access to PHI is only to prepare a protocol;
      - No PHI will be removed from the covered entity (i.e., VHA); and
      - Access to PHI is necessary for preparation of the research protocol.
    - Non-VA researchers may not obtain VA information for preparatory to research activities without appropriate VA approvals (see VHA Directive 1605.01).
    - During the preparatory to research activities the VA investigator:
      - Must only record aggregate data. The aggregate data may only be used for background information to justify the research or to show that there are adequate numbers of potential subjects to allow the investigator to meet enrollment requirements for the research study;
      - Must not record any individually identifiable health information; and
      - Must not use any individually identifiable information to recruit research subjects.
      - Preparatory activities can include reviewing database output (computer file or printout) containing identifiable health information generated by the database owner, if the investigator returns the database output to the database owner when finished aggregating the information.
    - Contacting potential research subjects and conducting pilot or feasibility studies are not considered activities preparatory to research.
    - Activities preparatory to research only encompass the time to prepare the protocol and ends when the protocol is submitted to the IRB.
  - Posting of Clinical Trial Consent Forms
    - For studies subject to the 2018 Requirements, if a VA research study is a clinical trial, one IRB-approved informed consent form used to enroll subjects, unless the IRB waived documentation of informed consent, must be posted by either the investigator or the Federal department or agency conducting or supporting the study. The informed consent form must be posted after the clinical trial is closed to recruitment and no later than 60 days after the last study visit by any subject as described in the IRB-approved protocol. For multi-site studies, it applies when the entire study has closed to subject

recruitment. Any proprietary or personal information (such as names and phone numbers) must be redacted prior to posting the informed consent form.

- For any ORD-funded clinical trial, the applicable ORD funding service will be responsible for posting the informed consent form.
- For a clinical trial funded or supported by a Federal agency or department other than VA, the awardee is responsible for posting the informed consent form.
- For a clinical trial funded or supported by a non-Federal agency or department (e.g., university, industry, nonprofit organization) or not funded, the VA Investigator conducting the clinical trial is responsible for ensuring that the informed consent form is posted. If the clinical trial includes multiple sites engaged in the clinical trial, an agreement must exist specifying who is responsible for posting the informed consent form.

## Appendix A-10 *Single IRB Studies*

1. That National Institutes of Health expects that all sites participating in multi-site studies involving non-exempt human subjects research funded by the NIH will use a single Institutional Review Board (sIRB) to conduct the ethical review required by the Department of Health and Human Services regulations for the Protection of Human Subjects at 45 CFR Part 46.
  - a. This policy applies to the domestic sites of NIH-funded multi-site studies where each site will conduct the same protocol involving non-exempt human subjects research, whether supported through grants, cooperative agreements, contracts, or the NIH Intramural Research Program. It does not apply to career development, research training or fellowship awards.
  - b. This policy applies to domestic awardees and participating domestic sites. Foreign sites participating in NIH-funded, multi-site studies will not be expected to follow this policy.
  - c. Exceptions to the NIH policy will be made where review by the proposed sIRB would be prohibited by a federal, tribal, or state law, regulation, or policy. Requests for exceptions that are not based on a legal, regulatory, or policy requirement will be considered if there is a compelling justification for the exception. The NIH will determine whether to grant an exception following an assessment of the need.
2. The Office for Human Research Protections expects that all sites located in the United States participating in cooperative research must rely upon approval by a single IRB for that portion of the research that is conducted in the United States. The reviewing IRB will be identified by the Federal department or agency supporting or conducting the research or proposed by the lead institution subject to the acceptance of the Federal department or agency supporting the research.

The following research is not subject to this provision:

- a. Cooperative research for which more than single IRB review is required by law (including tribal law passed by the official governing body of an American Indian or Alaska Native tribe); or
- b. Research for which any Federal department or agency supporting or conducting the research determines and documents that the use of a single IRB is not appropriate for the particular context.
- c. For research not subject to paragraph (b) of this section, an institution participating in a cooperative project may enter into a joint review arrangement, rely on the review of another IRB, or make similar arrangements for avoiding duplication of effort.



Appendix A-11      ***Additional Requirements for Research Subject to EU General Data Protection Regulations (GDPR)***

1. Human Research involving personal data about individuals located in (but not necessarily citizens of) European Union member states, Norway, Iceland, Liechtenstein, and Switzerland is subject to EU General Data Protection Regulations.
2. For all prospective Human Research subject to EU GDPR, contact institutional legal counsel or your institution's Data Protection Officer to ensure that the following elements of the research are consistent with institutional policies and interpretations of EU GDPR:
  - a. Any applicable study design elements related to data security measures.
  - b. Any applicable procedures related to the rights to access, rectification, and erasure of data.
  - c. Procedures related to broad/unspecified future use consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens.
3. Where FDA or DHHS regulations apply in addition to EU GDPR regulations, ensure that procedures related to withdrawal from the research, as well as procedures for managing data and biospecimens associated with the research remain consistent with Appendices A-1 and A-2 above.