Indiana University and its affiliates are dedicated to protecting the rights and welfare of human participants recruited to participate in research conducted under the auspices of these organizations. The Indiana University Human Research Protection Program Standard Operating Procedures and Policies in conjunction with the IU Human Subjects Office website and the supporting guidance documents provide a central resource for researchers to find important information on required federal and state regulations and institutional policies governing these research activities.
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III. Definitions
Section I: Introduction

I. INTRODUCTION

A. MISSION: The overarching mission of the Indiana University Human Research Protection Program (HRPP) is to protect the rights and welfare of human research participants recruited to participate in research conducted under the auspices of Indiana University. Rather than ensuring mere compliance with federal regulations, IU’s HRPP strives to adhere to the highest ethical standards in its protection of human research participants and seeks to further develop the methods and mechanisms for protecting human research participants. In service of this mission, the HRPP endeavors to:

- create an atmosphere of respect for, and awareness of, the rights and welfare of human research participants at IU and its affiliated organizations.
- inform established researchers about changes to and ongoing application of federal regulations and ethical principles to their particular area of research in order to keep researchers current with evolving standards.
- educate students, faculty, and staff who conduct research about the ethical principles and federal regulations guiding research with humans.
- assess the effectiveness of the Institutional Review Boards (IRBs) in their review of research activities, facilitation of compliance of researchers with federal regulations, and protection of research participants.
- develop new approaches that better serve the overarching mission of the HRPP, such as state-of-the-art educational materials, more efficient methods for processing applications, tracking and monitoring research activities, and assessing the overall effectiveness of the HRPP.

B. IRB CHARTER: The Indiana University Institutional Review Boards (IRBs) and their affiliated organizations are responsible for the review and approval of all research involving human subjects conducted under the auspices of these institutions. These boards are charged with protecting the rights and welfare of human subjects recruited to participate in research activities and to ensure compliance with applicable university and organizational policies and federal regulations.

These boards are responsible for reviewing all research projects involving human subjects that are conducted at these institutions’ facilities or property; sponsored by these institutions; conducted by or under the direction of any employees or agents of these institutions in connection with their institutional responsibilities; or that involve the use of these institutions’ non-public information to identify or contact human research subjects or prospective subjects. In addition, the IRBs may be asked by organizational officials to review research protocols on behalf of other institutions with which they have formal affiliation agreements.

The Vice President for Research is the leader of the Human Research Protection Program (HRPP) and has responsibility and authority for implementation of this program. The Vice President for Research relies on IRB staff for knowledge of the regulations and day-to-day operations and is directly involved in allocation of resources to the HRPP. The Vice President for Research employs mechanisms to ensure that:
Section I: Introduction

- Human participants are provided protections.
- The HRPP is provided support.
- The research review unit functions independently and free from coercion and undue influence.
- Legal counsel not conflicted by other organizational responsibilities is made available to the research review unit.
- Access to senior officials of the organization, when the IRB deems it to be warranted, is made available to the research review unit.
- The IRBs’ work and meeting spaces are evaluated and resources adjusted when necessary.
- Educational programs for IRB staff and members are provided and the development of Standard Operating Procedures (SOPs) and Policies is supported.
- The IRBs function independently of other organizational entities.

C. SCOPE. These policies and procedures apply to all research activities of faculty, staff, students, or others who are involved in human subjects research that falls under the jurisdiction of the Indiana University Human Research Protection Program (HRPP). HRPP also applies protections equivalent to HHS regulations for participants in research that is not federally funded. Please note that additional regulatory requirements may apply based on funding source, nature of the research, or subject population; see the applicable section within each SOP/Policy for specific information.
Adult Individuals Lacking Consent Capacity in Research

1.0 Scope
This policy applies to the conduct of all non-exempt human subjects research under the oversight of the IU IRBs involving adults who may lack consent capacity, or may lose capacity during the course of the research.

Research involving adults who may lack consent capacity, or may lose capacity during the course of the research, for which IU or its affiliates are relying on an external IRB for oversight must comply with Section 2.1 of this policy.

2.0 Policy Statement
Since adult individuals lacking consent capacity are likely to be vulnerable to coercion or undue influence, additional protections must be applied to protect the rights and welfare of these subjects. Specifically, in order to approve research involving adults who may lack the capacity to provide consent for themselves, or may lose capacity during the course of the research, the IRB must find that the research plan includes appropriate mechanisms for:

- Assessing potential subjects’ capacity to consent and reassessing that capacity on an ongoing basis, if applicable
- Identifying and obtaining consent from an appropriate representative if the potential subject lacks capacity, unless consent has been waived
- Obtaining assent from the potential subjects, when appropriate

Adult Individuals who lack consent capacity may be enrolled in research where the IRB finds:

- That the proposed research presents at least one of the following:
  - No greater than minimal risk to subjects
  - Greater probability of direct benefit to subjects than harm to subjects
  - Greater than minimal risk and no prospect of direct benefit to individual subjects, but is likely to yield generalizable knowledge about subjects’ disorder
or condition that is of vital importance for the understanding or amelioration of the disorder or condition

- That one of the following are also met:
  - The research cannot be performed solely with persons who possess consent capacity and the focus of the research is the disorder leading to the subjects’ lack of consent capacity, whether or not the lack of consent capacity itself is being evaluated.
  - The research is not directly related to the subjects’ lack of consent capacity but the investigator has presented a compelling argument for including such subjects.

2.1. Obtaining consent

Informed consent must be obtained by an appropriate individual for the potential subject’s participation in the research. Identification of the appropriate individual is based on the subject’s individual circumstances.

- If the potential subject has a court-appointed guardian who has been charged with making medical decisions for the potential subject, the potential subject cannot legally provide informed consent for him/herself, regardless of the subject’s capacity to understand the research.
- If there is not a relevant court-appointed guardian and the study team determines the subject has consent capacity pursuant to the IRB-approved assessment procedures, the subject should consent/authorize for him/herself.
- If the study team determines the subject does not have consent capacity pursuant to the IRB-approved assessment procedures, a legally authorized representative (LAR) must provide consent for the subject’s participation.

Pursuant to Indiana law IC 16-36-1-5, the following individuals may serve as a LAR, in the following order of priority:

1. Health care representative
2. Spouse
3. Adult child
4. Parent
5. Adult sibling
6. Grandparent
7. Adult grandchild
8. The nearest other relative in the next degree of kinship not listed in items 3-7*
9. The individual’s religious superior, if the individual is a member of a religious order*

If none of the above are reasonably available, the IRB may approve, on a case-by-case basis, that a friend may serve as LAR if the friend is an adult, has maintained regular contact with the potential subject, and is familiar with the potential subject’s activities, health, and religious or moral beliefs.

*Individuals listed at priority #8 and #9 may not serve as LAR if the research is subject to VA regulations.

The following individuals may NOT serve as a LAR under this policy:

- A spouse who is legally separated or has a petition for dissolution, legal separation, or annulment of marriage pending in a court from the potential subject
• An individual who is subject to a protective order or other court order that directs that individual to avoid contact with the potential subject
• An individual who is subject to a pending criminal charge in which the potential subject was the alleged victim.

The IRB may waive consent requirements pursuant to the IU HRPP Policy on Informed Consent.

Responsibilities of LARs
LARs are acting on behalf of the potential subjects, therefore:
• LARs 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 LARs must be told they are responsible for determining what is in the subjects’ best interest.

2.2. Obtaining assent
If feasible, the investigator must explain the proposed research to the potential subject even when the subject cannot provide consent for him/herself.

2.3. Research subject to VA regulations
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. However, the IRB must review and approve the plan to ensure that it is appropriate given the population and setting of the research.

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.

2.4. Research subject to Department of Defense (DoD) regulations
If consent is to be obtained from a subject’s LAR, the IRB must determine that the research is intended to be beneficial to the individual subject.

3.0 Procedures

3.1. IRB submission and review
For studies proposing to enroll subjects who lack consent capacity, the investigator completes the IRB application and provides protocol-specific information about the study-specific mechanisms for assessing subjects’ consent capacity, identifying and obtaining consent from an appropriate representative if subjects cannot consent for themselves, and obtaining assent from subjects. The IRB considers the information in the IRB application and documents its determinations as appropriate.

3.2. Identification of the LAR
The study team must conduct due diligence to identify the appropriate LAR based on the priority defined in section 2.1. Specifically, the individual with the highest priority who is reasonably available must serve as the LAR and the study team must do due diligence to ensure and document that an individual with higher priority is not reasonably available.
A study team can find that an individual is not reasonably available after the study team has made and documented repeated attempts to contact the individual over a reasonable time period with no response. The expectation is that study teams will make at least 3 attempts over at least 48 hours, unless the IRB has reviewed and approved a protocol-specific standard for finding that individuals are not reasonably available.

If there are multiple individuals at the same priority level who are reasonably available, those individuals shall make a reasonable effort to reach a consensus as to participation of the potential subject in the research. If the individuals at the same priority level disagree, a majority of the available individuals at the same priority level controls.

If a study team believes that allowing a friend to serve as the LAR for an adult lacking consent capacity would provide reasonable protections for a potential subject, the study team may submit a subject-specific request that the friend serve as LAR for the particular subject and provide appropriate justification.

4.0 **Sanctions**

Individuals found to be in violation of this policy may be subject to sanctions relating to their participation in research with human subjects, up to and including permanent suspension or bar from engaging in research with human subjects at Indiana University.

5.0 **History**


6.0 **Related Information**

**AAHRPP Standards**
- Element II.4.A
- Element II.4.B
- Element III.1.F

**IU HRPP Documents**
- Policies: Informed Consent
- Guidance: [Research with Individuals Lacking Consent Capacity](#)

**KC IRB Questionnaires** *(see [KC Crosswalk](#))*
- Questionnaire G2 – Individuals Lacking Consent Capacity

**Regulatory References**
- [Indiana Code](#) 16-36-1-5
- [NIH Guidance on Research Involving Individuals with Questionable Capacity to Consent: Points to Consider](#)
- [VHA Handbook 1200.05 – Requirements for the Protection of Human Subjects in Research](#), especially section 20
1. INTRODUCTION

One important element of a high-quality human research protection program (HRPP) is the audit function. The primary goal of an audit is to monitor the conduct of the research to assure the rights and welfare of human research participants are protected and to optimize compliance with federal regulations, state laws, and institutional policies.

IU’s Office of Research Compliance (ORC) employs Quality Improvement Office (QIO) staff (hereafter known as the “Auditor(s)”), who conduct on-site scheduled (not-for-cause) reviews and directed (for-cause) investigations of research studies. The intent of these reviews is to ensure human subjects research conducted at or on behalf of IU and its affiliates is of the highest quality and conducted in accordance with all applicable federal regulations, state laws, and institutional policies. Researchers should view the Auditors as a partner in ensuring a high level of regulatory compliance and agency inspection readiness.

2. POLICIES AND PROCEDURES

2.1 Audit Plan

2.1.1 The Auditor(s) develop an audit plan that describes the study/investigator selection process for the IU HRPP. The Plan identifies criteria to select and prioritize studies/investigators for potential scheduled audits. The audit plan is reviewed and approved by the IU IRB Executive Committee, generally on a semiannual basis.

2.2 Audit Process for Scheduled (Not-For-Cause) Audits

2.2.1 A selected auditee is notified to begin on-site audit scheduling with the expectation that the on-site review will occur within a month from notification.

2.2.2 The study team is expected to give full cooperation throughout the entire audit process. At the beginning of the on-site audit, the Auditor(s) meet with members of the research team for a brief introduction to the study and description of the organization of the related records. Generally, at the conclusion of the on-site audit, the Auditor(s) provide a general review of findings at an audit closeout meeting. Also, during the closeout meeting, the Auditor(s) provide education and counseling regarding the findings.

2.2.3 An audit report is then sent to the auditee. If not done already, when the audit report is received, the auditee is expected to take steps to make necessary improvements to align the operation with applicable federal regulations, state
laws, and institutional policies. The auditee is expected to submit a response to
the audit report to the Auditor(s) within ten (10) business days of receiving the
report. The response should include an action plan to correct any problems
identified and an action plan to prevent recurrences, as applicable. Some
findings may require additional information, including an explanation of the
circumstances that identifies the suspected root cause, the individual(s)
responsible for corrective and preventive actions, and a timeline for their
completion.

2.2.4 If the auditee has not provided a response to the audit report or negotiated a
revised response time frame with the Auditor(s) within ten (10) business days of
receipt of the audit report, the auditee is contacted to initiate action. If no action
is taken, the department chair is contacted for assistance. If the department chair
does not provide adequate assistance, the issue will be taken to an IRB Chair or
Chair’s designee for action.

2.2.5 Upon receipt of the auditee’s response, the Auditor(s) assess the response for
completeness and appropriateness. The Auditor(s) work with the auditee if
issues require further clarification until the response is complete. If at any time
during the audit process it becomes apparent to the Auditor(s) an appropriate IRB
or other applicable authority needs to become involved for any reason, the
Auditor(s) will seek that involvement to the extent necessary.

2.2.6 Once the above process has concluded, the audit report and response is submitted
to the IRB.

2.3 Audit Process for Directed (For-Cause) Audits

2.3.1 PIs will ordinarily receive about a week advance notice of directed audits, unless
otherwise directed by the authority requesting the audit. Auditees are expected to
fully cooperate with the Auditor(s) throughout the audit process. The auditee is
expected to take steps to make necessary improvements to align the operation
with applicable federal regulations, state laws, and institutional policies as soon
as possible following the audit, and then make any necessary adjustments at the
time of receipt of the audit report and/or feedback from the applicable authorities.

2.3.2 The Auditor(s) follow the methods listed in section 2.2 above but will make
adjustments as necessary depending on the circumstances surrounding the audit
request and findings.

2.3.3 The required deadline to respond to the audit findings also varies depending on
the circumstances of the audit request and findings. This deadline will be
communicated by the Auditor(s) to the auditee.
2.4 The Audit Cycle (Scheduled – Not-For-Cause)

The Audit Cycle (Scheduled – Not-For-Cause Audits)

Audit plan developed by the Auditor(s)

Review and approval of audit plan by the IRB Executive Committee

Auditee contacted to schedule audit

Audit conducted, including introduction meeting, documentation review and interviews, key findings identified, closeout meeting

Audit report completed and sent to auditee

Auditee provides response to audit report, which include, as applicable, corrective and/or preventive action plan to correct identified problems, a root cause analysis, and timeline for completion of corrective action, to Auditor(s)

Final audit report and auditee response submitted to appropriate IRB for review

As applicable, auditee is notified of IRB’s discussion and any further action required on the auditee’s part. Audit is closed when the IRB is satisfied with the corrective and/or preventive action plans.

Please note that directed (for-cause) audits follow the same cycle described above, but adjustments may be made as necessary, depending on the circumstances surrounding the audit request and findings and including the response time granted to the auditee.

2.5 Audit Findings

2.5.1 Audit reports (including PI responses to findings) are reviewed by an IRB at the conclusion of the audit.

2.5.2 The Auditors track audit findings and prepare periodic summary reports, which will then be presented to the IRB Executive Committee. Reports describe general audit finding trends, any serious or continuing noncompliance, and any
unanticipated problems involving risks to subjects or others determination made in relation to the audit finding. Late responses to audit findings are also reviewed.

2.5.3 Upon recognition of trends in audit findings, the Auditor(s) take appropriate steps to determine any further actions required to address the issues.

2.5.4 The audit reports are meant to be internal to the IU system and will not be shared with outside agencies, unless the audit findings are determined by the IRB to meet criteria that require external reporting pursuant to the SOP on Reporting.

2.5.5 Audit reports for studies in which IU has relied on an external IRB for IRB review and oversight may also be shared with the reviewing IRB in accordance with IU’s reliance agreement.

2.6 External Inspection Compliance Responsibilities

2.6.1 When an investigator receives notification of an upcoming compliance inspection visit by a regulatory agency, funding agency, or study sponsor, he/she shall immediately notify the IU QIO.

2.6.2 During external inspections conducted on behalf of federal agencies, IU QIO staff serve as a liaison designated by the institution to serve as a resource to the PI, study team, and institution to monitor the progress of the inspection and to coordinate key aspects of any written response to the federal agency (e.g., response to FDA Form 483 or Warning Letter).

2.6.3 Investigators shall immediately provide all inspection related correspondence and communications to and from the inspecting federal agency to the IU QIO.

2.7 Other Compliance Responsibilities

2.7.1 The QIO also assists in the improvement of the HRPP’s effectiveness, quality, efficiency, and compliance with federal regulations, state laws, and institutional policies. The QIO systematically evaluates whether the HRPP’s policies and procedures are being followed.

2.7.2 QIO also collaborates with the Human Subjects Office (HSO) to review specific measures of quality, efficiency, and effectiveness. QIO works with the HRPP leadership to identify appropriate actions to be taken for improvement.

2.7.3 Outcomes of the above reviews are periodically provided to the leader of the HRPP in order to direct improvements to the HRPP.

3. ADDITIONAL POLICIES AND PROCEDURES

3.1 Research Subject to FDA Regulations

N/A
3.2 **Research Subject to HIPAA Regulations**

N/A

3.3 **Research Subject to VA Regulations**

3.3.1 The completed audit report will also be promptly shared with the local VA Research Office for audits that include VA subjects.

3.3.2 For-cause audits involving the VA will be conducted in cooperation with the local VA research office.

3.4 **Research Subject to Other Regulations**

N/A

3.5 **Research Subject to Department of Defense (DoD) Regulations**

N/A

3.6 **Research Subject to Department of Education (ED) Regulations**

N/A

3.7 **Research Subject to Department of Justice (DOJ) Regulations**

N/A
1. **INTRODUCTION**

Legal obligations to protect human subjects apply not only to direct contact with a human subject, but also to items that are derived from a human subject, including medical records and biospecimens. For the purposes of this SOP document, biospecimen is defined as a quantity of tissue, blood, urine, or other human-derived material. Examples of biospecimens include: subcellular structures (e.g., DNA), cells, tissue (e.g., bone, muscle, connective tissue, skin), organs (e.g., liver, bladder, heart, kidney), blood, buccal swabs, gametes, embryos, fetal tissue, saliva or other body fluids, and waste (e.g., urine and stool). Portions or aliquots of a biospecimen are referred to as samples.

Such biospecimens may be collected for clinical purposes and stored per regulatory requirements for pathology accreditation, as part of a specific research study and then stored for future use, or as a purposeful collection of biological samples for future distribution to investigators, such as a repository. In addition, the collection, storage, and use of such biospecimens may also be for the purposes of genetics research. In all of these scenarios, identifiable health information may or may not be associated with the biospecimens.

Research studies that propose the collection, storage, and use of biospecimens must be reviewed by the IU IRBs. Research with biospecimens may include any of three common stages: 1) the collection and storage of the biospecimens for current and/or future research purposes; 2) the storage and management of biospecimen repositories; and 3) the use of previously collected/stored biospecimens for research purposes. Each stage requires IRB review and approval.

2. **POLICIES AND PROCEDURES**

2.1 **Existing Collections of Human Biologic Material**

2.1.1 Existing collections of biospecimens may have been developed over a period of time without use of written consent from subjects, or a limited consent from subjects may have been obtained during clinical procedures. Recontact of donors may be difficult or impossible. In such situations, investigators should submit an application to the IRB for continued use (or a new use) of the collection or may adopt a procedure to de-identify their collection. Such procedures to de-identify a collection per HIPAA standards should be approved by the IRB.

2.2. **IRB Review**

2.2.1 IRB review is required for projects meeting the Common Rule definition of human subjects research, specifically any research involving interaction or intervention with living individuals or their identifiable information. In addition, under FDA regulations, some research with biospecimens that does not meet the
Common Rule definition also requires IRB approval. Specifically research using de-identified samples must be reviewed by the IRB when the research may generate or collect data that may be submitted to the FDA for review. Biospecimen research requiring IRB review includes prospective collection of biospecimens for research (including future research), use of clinical samples for research purposes, and secondary use of previously collected biospecimens.

2.2.2 In all cases, a description of the proposed research use of the biospecimens must be submitted to and reviewed by the IRB before the biospecimens may be collected and/or utilized. The level of review and issues of informed consent will be decided by the IRB on a case-by-case basis. The following should be included in the protocol submitted to the IRB for review:

2.2.2.1 The general nature of tests that will be done on the samples, if known.

2.2.2.2 A full description of the mechanisms used to link biospecimens and identifiable information, plans for protecting identifiers related to the biospecimens, and procedures used to maximize the protection against inadvertent release of confidential information.

2.2.2.3 Condition under which biospecimens and data will be accepted into the repository, if applicable.

2.2.2.4 Conditions under which biospecimens and data will be shared with investigators outside of the study team, including how such requests will be evaluated, if applicable. Recipient-investigators should not be provided access to the identities of donor-subjects or to information through which the identities of donor-subjects may readily be ascertained unless such disclosure has been detailed in the informed consent signed by donors.

2.2.2.5 Additional information as requested. See the IU IRB guidance on research with biospecimens for more information.

2.2.3 If additional research is subsequently proposed that is not described in the original IRB-approved protocol, a new IRB application (or an amendment, if appropriate) must be submitted for review and approval.

2.3. Consent and Authorization Issues

2.3.1 The consent and authorization process and documentation (forms), if required, must be approved by an IU IRB. Elements of the consent and authorization process may be waived or modified by the IU IRB.

2.3.2 When informed consent to the research use of human biospecimens is required, it should be obtained separately from informed consent to clinical procedures (i.e., not combined with a general surgery or pathology consent). The person who obtains informed consent in the clinical setting should make clear to potential
Section II: SOPs/Policies

Standard Operating Procedures
for Research Involving Human Subjects

subjects that their refusal to consent to the research use of biological materials will in no way affect the quality of their clinical care.

2.3.3 The informed consent statement must include the usual required elements of an informed consent (see the SOP on Informed Consent). In addition, the use of biosamples requires special consideration and explanation of issues specific to research with biospecimens. See the IU IRB guidance on research with biospecimens for more information.

3. ADDITIONAL POLICIES AND PROCEDURES

3.1. Research Subject to FDA Regulations

N/A

3.2. Research Subject to HIPAA Regulations

N/A

3.3. Research Subject to VA Regulations. Research involving biological specimens or data obtained from children is considered to be research involving children even if de-identified.

3.4. Research Subject to Other Regulations

3.4.1 Research Subject to Department of Defense (DoD) Regulations

N/A

3.4.2 Research Subject to Department of Education (ED) Regulations

N/A

3.4.3 Research Subject to Department of Justice (DOJ) Regulations

N/A
1. **INTRODUCTION:**

Criteria for approval of research include adequate provisions to protect the privacy interests of subjects and adequate provisions to maintain the confidentiality of identifiable data. The IRB evaluates the privacy and confidentiality provisions to ensure the criteria are satisfied for each research study.

Regardless of the type of research (behavioral or social science, physiologic, therapeutic trials), it is important to remember that privacy and confidentiality are themselves a form of personal protection, so a violation of an individual’s privacy or confidentiality is harmful because it carries the loss of this protective barrier. The risks of loss of privacy or loss of confidentiality include public exposure of personal information, perceived loss of control or security, and erosion of trust on all levels. All individuals have a right to expect that private actions will remain private and that information that others have about them will be kept confidential and only used for their original purpose(s) as stated in the IRB-approved study. Pursuant to 45 CFR 46.116(a)(5), research subjects must be provided a statement describing the extent, if any, to which confidentiality of records identifying them will be maintained.

The IRBs are committed to conducting research in compliance with all applicable laws, regulations and institutional policies and procedures. As part of this commitment, the IRB has adopted a standard operating procedure to clearly define the minimal requirements for the protection of subject confidentiality and privacy, and to detail the circumstances under which Protected Health Information (PHI) may and may not be used or disclosed in connection with research activities under the Health Insurance Portability and Accountability Act (HIPAA).

2. **POLICIES AND PROCEDURES**

2.1. **Privacy** refers to persons and their interest in controlling the access of others to themselves. Individuals have an interest in controlling the time and place where they give information, the nature of the information they give, the nature of the experiences that are given to them, and who receives and can use the information. What is private depends on the individual and can vary according to gender, ethnicity, age, socioeconomic class, education, ability level, social or verbal skill, health status, legal status, nationality, intelligence, personality, and the individual’s relationship with the investigator. For example,

2.1.1 persons might 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; or

2.1.2 protecting the privacy interests of a young child might mean having a parent present at a session with an investigator; or

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**Title:** Confidentiality and Privacy

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2.1.3 protecting the privacy interests of a teenager might mean having a parent absent.

2.2. **Confidentiality** refers to maintenance of the Investigator’s agreement with the subject about how the subject’s identifiable private information will be handled, managed, and disseminated. Methods to protect confidentiality should be described both to the IRB (via the study application) and to subjects (via the informed consent process). Many different strategies can be employed to maintain confidentiality of identifiable information, including controls on storage, handling, and sharing of data. Additionally, for some research, certificates of confidentiality may be used to maintain confidentiality of identifiable data. Confidentiality protections include information obtained preparatory to research, such as information collected from personal records to determine potential sample size or potential subjects as well as the maintenance of the confidentiality of information after the study has ended, when identifiable information is maintained.

2.3. A Certificate of Confidentiality helps researchers protect the privacy of human subjects enrolled in research where an individual is identified, or where there is at least a very small risk that the identity of an individual could be deduced. Certificates protect against compulsory legal demands, such as court orders and subpoenas, for identifying information about human subjects.

2.3.1 Research that qualifies as Human Subjects Research, is funded by the NIH, CDC, FDA, HRSA or SAMHSA is automatically issued a Certificate as a term and condition of being awarded a grant. Researchers funded by federal sources other than those listed, or from non-federal sources, may apply to receive a Certificate via the NIH website.

2.3.2 Investigators who are issued a Certificate are required to be familiar with the rules in 42 USC 241(d) and relevant guidance issued by the NIH. This includes when identifiable information may and may not be disclosed; how to establish effective control to ensure that information is handled in accordance with the regulations, and how to ensure that any recipients of protected information understand that they are also subject to these requirements.

2.3.3 For studies in which informed consent is sought, investigators must inform research participants of the protections and the limits to protections provided by a Certificate.

2.4. For research to be approved by the IRB, the protocol must include, when appropriate, adequate provisions to protect the privacy interests of research subjects and the confidentiality of research data. It is the responsibility of investigators and all research team members to ensure these provisions exist and are followed.

2.5. The confidentiality and security of all records, (e.g., medical, student, criminal history) should be maintained and should not be utilized for research purposes without the approval of the IRB. Research data collected for one study may not be utilized for a subsequent study without the approval of the IRB.
3. ADDITIONAL POLICIES AND PROCEDURES

3.1. Research Subject to Food and Drug Administration (FDA)

N/A

3.2. Research Subject to HIPAA Regulations

3.2.1 As determined by HIPAA, the use of PHI is only allowable for treatment, payment, and health care operations. Any other use (such as for research) is allowable only under certain circumstances. These include:

3.2.1.1 De-identified Health Information. De-identified health information is not considered PHI and may be used or disclosed for research purposes without an authorization from the research subject, or a waiver of authorization from the IRB. Investigators using de-identified information must be able provide documentation, upon request, that the health information was de-identified by one of the following two methods/processes:

3.2.1.1.1 Expert Determination. A person with appropriate knowledge of and experience with generally accepted statistical and scientific principles and methods for rendering information not individually identifiable. (See http://www.hhs.gov/ocr/privacy/hipaa/understanding/coveredentities/De-identification/guidance.html#standard)

3.2.1.1.1.1 Applying such principles and methods, determines that the risk is very small that the information could be used, alone or in combination with other reasonably available information, by an anticipated recipient to identify an individual who is a subject of the information; and

3.2.1.1.2 Documents in writing the methods and results of the analysis that justifies such determination.

3.2.1.2 Safe Harbor Method. Identifiers concerning the individual and the individual’s employer, relatives, and household members must be removed. These include:

3.2.1.2.1 Names

3.2.1.2.2 Geographic subdivisions smaller than a state including:

3.2.1.2.2.1 ZIP codes
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3.2.1.1.2.2 Street address

3.2.1.1.2.3 City

3.2.1.1.2.4 Town

3.2.1.1.2.5 County

3.2.1.1.2.6 Precinct

3.2.1.1.2.3 Elements of dates (except year) directly related to an individual

3.2.1.1.2.4 Telephone numbers

3.2.1.1.2.5 Fax numbers

3.2.1.1.2.6 Electronic mail addresses

3.2.1.1.2.7 Social Security numbers

3.2.1.1.2.8 Medical record numbers

3.2.1.1.2.9 Health plan beneficiary identifiers

3.2.1.1.2.10 Account numbers

3.2.1.1.2.11 Certificate/license numbers

3.2.1.1.2.12 Vehicle identifiers and serial numbers, including license plate numbers

3.2.1.1.2.13 Device identifiers and serial numbers

3.2.1.1.2.14 Web universal resource locators (URL)

3.2.1.1.2.15 Internet protocol (IP) address numbers

3.2.1.1.2.16 Biometric identifiers, including finger and voice prints

3.2.1.1.2.17 Full face photographic images; and

3.2.1.1.2.18 Any other unique identifying number, characteristic or code that could be used to identify the individual.
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3.2.1.3 The following demographic information may be used and still be considered de-identified:

3.2.1.3.1 Age with dates limited to the year (age 90 and over must be aggregated to 90+ to prevent the identification of very old individuals)

3.2.1.3.2 Aggregated ZIP codes in the form of the initial three-digit ZIP codes that contain more than 20,000 people

3.2.1.3.3 Race

3.2.1.3.4 Ethnicity

3.2.1.3.5 Marital status

3.2.1.3.6 Codes

3.2.1.4 If an investigator will be creating his/her own de-identified data set, he/she must provide justification upon request that he/she has legitimate access to the PHI used to create it.

3.2.1.5 If an investigator will be obtaining de-identified data from another individual, he/she must be able to provide documentation upon request that the individual creating the de-identified data set has legitimate access to the PHI. In the review of research involving the use or disclosure of de-identified data sets, the IRB or designee will consider whether the investigator (or appropriate other individual) has legitimate access to the PHI in order to de-identify it.

3.2.1.6 Re-identification Code. The de-identified information may be assigned a code that can be affixed to the research record that will permit the information to be re-identified by the covered entity if necessary, provided that, the key to such a code is not accessible to the investigator requesting to use or disclose the de-identified health information. Codes may not be a derivative of the individual’s name (e.g., initials), Social Security number or other identifiable numerical codes (e.g., birth date, medical record number, fax number). If such a code is utilized, the data will not be considered de-identified.

3.2.1.2 Limited Data Set. An investigator may use or disclose PHI as a limited data set for research purposes without an authorization or waiver of authorization.

3.2.1.2.1 A limited data set is identifiable health information that excludes direct identifiers. This means that the same
identifiers described above must be removed, with the exception of the following direct identifiers:

3.2.1.2.1.1 Town, city, county, precinct, state and ZIP code;

3.2.1.2.1.2 All elements of dates directly related to an individual, including birth date, admission date, discharge date, and date of death.

3.2.1.2.1.3 Unique identifying numbers, characteristics, and codes.

3.2.1.2.2 For any research use of a Limited Data Set, the covered entity disclosing the Limited Data Set must enter into a Data Use Agreement with the recipient of the information.

3.2.1.2.3 Uses or disclosures of PHI as limited data sets for research purposes are subject to the minimum necessary rules.

3.2.1.2.4 Uses and disclosures of PHI as limited data sets are not subject to accounting of disclosures.

3.2.1.3 Authorization from the Research Subject. An authorization must be utilized with any informed consent for research to use or disclose a subject’s PHI. Requests for waivers of authorization to use or disclose PHI require IRB approval.

3.2.1.3.1 An authorization to use and disclose identifiable health information for research purposes must be written in plain language, and must contain all of the following core elements and be approved by the IRB for each approved research study.

3.2.1.3.1.1 A specific and meaningful description of the information to be used or disclosed, written in a language understandable to the subject. Any translation of the authorization must be IRB approved.

3.2.1.3.1.2 The name or identification of the persons or class of persons authorized to make disclosures of identifiable health information (i.e., who is releasing information).

3.2.1.3.1.3 The name or identification of the persons or class of persons authorized to receive the identifiable health information and to use the information for research-related purposes (i.e.,
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the investigators and other individuals who are part of the research team, described as broadly as possible to cover all possible circumstances).

3.2.1.3.1.4 A description of the purpose of each use or disclosure of identifiable health information.

3.2.1.3.1.5 An expiration date for the authorization. This could be a date, an event, or a statement like, “end of research study.”

3.2.1.3.1.6 The individual’s signature (or that of his/her authorized representative, including a description of that representative’s authority to act on behalf of the individual, if applicable) and the date.

3.2.1.3.1.7 A statement that the individual may revoke the authorization if done in writing to a member of the research team, except to the extent that the investigator had already acted in good faith on the signed authorization.

3.2.1.3.1.8 A statement that an individual’s clinical treatment may not be conditioned upon whether or not the individual signs the research authorization. However, participation in research may be conditioned on a signed authorization.

3.2.1.3.1.9 A statement that information disclosed under the authorization could potentially be re-disclosed by the recipient and would no longer be protected under federal privacy regulations.

3.2.1.3.2 To ensure compliance with these elements, a template authorization has been provided and should be utilized and must be approved by the IRB prior to use. Any modifications to this template are discouraged (even if suggested by a Sponsor), will require additional review, may delay processing, and have no guarantee of being approved.

3.2.1.3.3 The principal investigator is responsible for assuring that the authorization form provided to subjects is revised whenever there is a change in any of the core elements of the authorization, including when the persons or classes of persons who will receive disclosures of individually identifiable health information change. Any such change will require prospective IRB approval.
3.2.1.3.4 The research subject or his/her authorized representative must be provided with a copy of the signed authorization.

3.2.1.3.5 When authorization is required, the original signed authorization form should be filed with the subject’s research records. A copy of the signed authorization form should also be kept in the subject’s medical records, when appropriate. HIPAA regulations require the authorization to be kept for a minimum of six (6) years from the date it was obtained. However, Indiana state law requires the retention of medical records for seven (7) years, so it is recommended that signed authorizations be maintained for seven (7) years.

3.2.1.3.6 As a general rule, an individual may revoke his/her authorization, in writing, to a person on the research team, at any time. The revocation will be applicable to the study or studies specified by the individual. However, the investigator may continue to use and disclose, for research integrity and reporting purposes, any identifiable health information that was collected about the individual from the time there was an active authorization until it was revoked. Continued use of data after revocation will be allowed only on a case-by-case basis. Copies of revocations of authorizations should be maintained and reported to the IRB at the time of continuing review.

3.2.1.4 Waiver of Authorization or Alteration of Authorization Requirements from the Privacy Board. The IRB, serving as the Privacy Board, may approve a waiver of authorization or alteration of authorization requirements, provided the following criteria are satisfied and documented:

3.2.1.4.1 The use or disclosure of PHI involves no more than minimal risk to the confidentiality to the subject, based on the presence of the following elements:

   3.2.1.4.1.1 An adequate plan presented to the IRB to protect the identifiers from improper use and disclosure;
   
   3.2.1.4.1.2 An adequate plan to destroy the identifiers at the earliest opportunity consistent with the conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law; and
   
   3.2.1.4.1.3 Adequate written assurance that the PHI will not be reused or disclosed to any other person or entity, except as required by law, for authorized
oversight of the research, or for other research for which the use or disclosure of PHI would be permitted by the Privacy Rule.

3.2.1.4.2 The research could not practicably be conducted without the waiver;

3.2.1.4.3 The research could not practicably be conducted without access to and use of the PHI;

3.2.1.4.4 A request for waiver of authorization or alteration of authorization requirements must be submitted to the IRB for review and approval, and include a brief description of the PHI covered by the waiver or alteration.

3.2.1.4.5 Approved waivers of authorization or alterations of authorization requirements must document the following:

3.2.1.4.5.1 Identification of the IRB of Record;

3.2.1.4.5.2 Date of IRB approval of the waiver;

3.2.1.4.5.3 Statement that the waiver of HIPAA authorization satisfies the criteria outlined above;

3.2.1.4.5.4 A brief description of the PHI for which the IRB has determined use or disclosure to be necessary;

3.2.1.4.5.5 Identification of the IRB review procedure used to approve the waiver; and

3.2.1.4.5.6 Signature of the Chair of the IRB or a qualified voting member designated by the Chair.

3.2.1.4.6 The IRB (Privacy Board) shall maintain the required documentation about the waiver or alteration.

3.2.1.4.7 Uses or disclosures of PHI made pursuant to a waiver of authorization or alteration of authorization requirements are subject to the minimum necessary rules.

3.2.1.4.8 Disclosures of PHI made pursuant to a waiver of authorization or alteration of authorization requirements are subject to accounting of disclosures.
3.2.1.4.9 Investigators will likely be asked to provide a copy of the IRB-approved waiver or alteration when requesting records or other PHI from a covered entity.

3.2.1.5 **Research Involving Decedent PHI.** Investigators may use and disclose decedent-only health information for research purposes without an authorization from the legally authorized representative of the individual or waiver of authorization approved by the IRB (Privacy Board), provided that the investigator provides documentation, upon request, that all the following criteria are satisfied:

3.2.1.5.1 The use will be solely for research on the identifiable health information of decedents;

3.2.1.5.2 The PHI sought is necessary for the purposes of the research; and

3.2.1.5.3 Upon request, the covered entity disclosing the data may require the investigator to provide documentation of the death of the individual about whom information is being sought.

3.2.1.5.4 Investigators may be required to provide the covered entity a written statement regarding the intended use of the decedent information and must keep the information confidential and secure.

3.2.1.5.5 Uses or disclosures of a decedent’s identifiable health information for research purposes are subject to the minimum necessary rules.

3.2.1.5.6 HIPAA applies to deceased individuals for 50 years after date of death. Effective March 26, 2013, records of individuals deceased more than 50 years are no longer protected under the HIPAA Privacy Rule.

3.2.1.6 **Reviews Preparatory to Research.** Investigators may use or disclose identifiable health information without an authorization from a subject or a waiver of authorization approved by the IRB (Privacy Board) for reviews preparatory to research (e.g., feasibility studies). For a covered entity to release this information, the investigator must document to the covered entity (the holder of the PHI) that *all* the following criteria are satisfied:

3.2.1.6.1 The use or disclosure of identifiable health information is solely to prepare a research protocol or for similar purposes that are preparatory to research;

3.2.1.6.2 The investigator shall not record or remove the information from the provider’s facility or office. Investigators may access PHI electronically in order to review the information, but may
not record, store, or otherwise retain the information after the review.

3.2.1.6.3 The information sought is necessary for the purposes of the research (e.g., a feasibility analysis to determine the number of potential subjects with a certain disease for submission in a grant).

3.2.1.6.4 This use and disclosure does not include identifying specific individuals for recruitment purposes, but rather identifying the number of individuals with specific criteria to determine or demonstrate an investigator’s ability to successfully recruit.

3.2.1.6.5 Uses or disclosures of PHI for reviews that are preparatory to research are subject to the minimum necessary rules.

3.2.1.6.6 Uses or disclosures of PHI for reviews that are preparatory to research are subject to accounting of disclosures unless the information is in a de-identified or limited data set format.

3.2.1.6.7 Reviews preparatory to research that fulfill these criteria do not require IRB review and approval.
## Table 1: Summary of Mechanisms to Use PHI for Research Purposes

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Minimum Necessary</th>
<th>Accounting for Disclosure</th>
<th>HIPAA Documentation Requirements</th>
<th>IRB Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>De-identified Data</td>
<td>N/A</td>
<td>N/A</td>
<td>• Document that (18) identifiers are removed under either the Statistical Method or the Safe Harbor Method</td>
<td>IRB approval required if the investigator is creating his/her own de-identified data set</td>
</tr>
<tr>
<td>Limited Data Set</td>
<td>☑</td>
<td>N/A</td>
<td>• Data Use Agreement between investigator and data source provider</td>
<td>IRB approval required if the investigator is creating his/her own limited data set</td>
</tr>
<tr>
<td>Authorization</td>
<td>N/A</td>
<td>N/A, except for Psychotherapy Notes</td>
<td>• HIPAA Authorization</td>
<td>• IRB approval of template authorization required</td>
</tr>
<tr>
<td>Waiver of Authorization</td>
<td>☑</td>
<td>☑</td>
<td>• IRB approval required</td>
<td>• IRB approval required</td>
</tr>
<tr>
<td>Alteration of Authorization</td>
<td>☑</td>
<td>☑</td>
<td>HIPAA Authorization</td>
<td>• Applicable to recruitment purposes as well as study procedures</td>
</tr>
<tr>
<td>Requirements</td>
<td></td>
<td></td>
<td></td>
<td>• IRB approval of altered authorization required</td>
</tr>
<tr>
<td>Research Involving Decedent</td>
<td>☑</td>
<td>☑</td>
<td>• Document in description of study</td>
<td>• Applicable to recruitment purposes as well as study procedures</td>
</tr>
<tr>
<td>Information</td>
<td></td>
<td></td>
<td></td>
<td>N/A</td>
</tr>
</tbody>
</table>

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Review
Preparatory to Research

☑ ☑3

• Document to Covered Entity
  N/A

1 Minimum Necessary means that the amount of information disclosed should be limited to what is necessary to accomplish the purpose.

2 The Privacy Rule grants to a patient a right to request and receive an accounting for some “disclosures” of PHI, including disclosures made in connection with certain research projects. An accounting is a record of each disclosure of each patient’s PHI. A right to an accounting only applies to disclosures of PHI, not to uses of PHI. Patients have a right to an accounting only of those disclosures made by investigators in connection with studies conducted with a waiver of authorization. An accounting of disclosures is not required when a patient authorization is obtained. Please see http://researchadmin.iu.edu/HumanSubjects/hs_hipaa.html for example forms.

3 Simplified if 50 or more records will be utilized.
3.2.2 **Notice of Privacy Practices.** If being recruited or enrolled into a research study is the patient’s first contact with the hospital/clinic/office of the health care provider at IU, a Notice of Privacy Practices must be given to the subject upon contact (e.g., this may also apply for subjects who are recruited through advertisement rather than recruited through clinics). The notice given should be the relevant notice of the facility or covered entity where the research is taking place (i.e., if the research is taking place in Eskenazi Hospital, Eskenazi’s Notice of Privacy Practice should be given to the subject). The patient/subject must sign and acknowledge receipt of the notice for any studies involving direct treatment.

3.2.3 **Recruitment.** Identification, contact, and/or recruitment of potential subjects for research purposes are subject to HIPAA. Studies using informed consent and authorization documents will need to include specific detail in the IRB submission as to how potential research subjects will be identified prior to obtaining consent and/or authorization.

3.2.4 **Use and Disclosure of Psychotherapy Notes Used in Research.** Federal regulations require special restrictions concerning psychotherapy notes. An authorization is required for use and disclosure of psychotherapy notes for research in all instances including for recruitment by the direct treatment provider.

3.2.5 **HIV/Sexually Transmitted Disease Notes Used in Research.** In Indiana, PHI about sexually transmitted diseases or HIV status requires specific authorization prior to use and disclosure. This law is taken into account in the IU authorization template.

3.2.6 **Individual’s Access to Research Information**

3.2.6.1 Individuals who participate in research have a right to access their own identifiable health information that is maintained in a designated record set. However, individuals participating in research studies that include treatment may be denied access to their research records obtained in connection with that research study, provided that:

3.2.6.1.1 The identifiable health information was obtained in the course of the research;

3.2.6.1.2 The individual agreed to the denial of access in the research authorization;

3.2.6.1.3 The research is ongoing; and

3.2.6.1.4 The individual’s rights to access such health information are reinstated once the research study has ended and the research authorization has expired.

3.2.7 **Accounting of Disclosures**
3.2.7.1 A research subject may request that the principal investigator provide a history or list of the disclosures made regarding the subject’s identifiable health information for research purposes. **Note:** If you have an authorization from a research subject, you do not need to account for disclosures if the individuals to whom PHI is disclosed are listed on the authorization. Thus, all parties to whom PHI will be shared should be listed on the authorization.

3.2.7.2 If a subject did not provide authorization for the disclosure of his/her PHI, the principal investigator must keep accounting records of all disclosures of PHI in the following circumstances:

3.2.7.2.1 Disclosures made in research conducted with a waiver of authorization approved by the IRB (Privacy Board) for the study or for recruitment purposes.

3.2.7.2.2 Disclosure of PHI to a person or entity not on the authorization.

3.2.7.2.3 Disclosure of PHI to or from a federal or state mandated registry.

3.2.7.2.4 Disclosure of PHI that is used for reviews preparatory to research unless the information is de-identified or in a limited data set.

3.2.7.2.5 Disclosure of a decedent’s PHI used for research.

3.2.7.3 The principal investigator must provide the covered entity or the holder of the PHI with a written accounting of disclosures of PHI. The following information must be provided to the covered entity or the holder of the PHI:

3.2.7.3.1 For studies where <50 subjects are involved (including screening and recruitment).

3.2.7.3.1.1 Date of disclosure;

3.2.7.3.1.2 Name and address, if known, of the entity or person who received the health information;

3.2.7.3.1.3 Brief description of the health information disclosed; and

3.2.7.3.1.4 Brief statement that reasonably informs the individual of the purpose for disclosure.

3.2.7.3.2 If multiple disclosures are made to the same entity or person for the same reason, the principal investigator may summarize
the disclosure by describing the first disclosure in detail and by noting the frequency or number of disclosures made during the accounting period and the date of the last disclosure in the accounting period (e.g., information provided to the Sponsor three times from X to Y date).

3.2.7.3.3 For studies where PHI from ≥50 individuals were utilized (including screening and recruitment), a simplified accounting procedure can be used. The individual must be provided a list of research studies in which the individual’s information may have been used. The list must provide the following:

- The name of the study or other research activity;
- A description of the purpose of the study and the type of information disclosed; and
- The time frame during which such disclosures occurred.

Upon request, the principal investigator, or his/her designee, will assist the individual in contacting those investigators to whom it is likely that the individual’s health information was actually disclosed.

3.2.8 Use and Disclosure of a Health Care Provider’s Patient Information for Research Purposes

3.2.8.1 A physician or other licensed independent practitioner accessing PHI for research purposes must obtain an authorization from the patient/subject or waiver of authorization from the IRB unless an exception applies.

3.2.8.1.1 A physician or other licensed independent practitioner may contact their own patients to ask if they are interested in a research study or may review their patients’ PHI to determine eligibility for a research study without an authorization or waiver of authorization. In some cases, a physician or other licensed independent practitioner may delegate these responsibilities to a research assistant who is directly under his/her supervision without an authorization or waiver of authorization.

3.2.8.1.2 A physician or other licensed independent practitioner who reviews his/her own patients’ records to determine eligibility and/or to contact to ask about interest in a research study does not need to keep track of disclosures for this recruitment purpose.

3.2.8.2 If a waiver of authorization is granted, any disclosure of the data in an identifiable format (i.e., not de-identified and not a limited data set) to an individual outside the covered entity needs to be tracked. Examples include
3.2.8.3 If physicians or other licensed independent practitioners plan to share any of their patients’ data initially collected for patient care purposes with individuals outside of their covered entity and/or outside of their research team for recruitment or research purposes, it is recommended that a separate study be submitted for approval by the IRB for this purpose, including authorization from the subject for inclusion in this database. If such an authorization is obtained from the patients (research subjects) under this IRB approved database study, then there is no need to track disclosures for recruitment or studies done under waiver of authorization.

3.2.8.4 If the physician or other licensed independent practitioner reports data to public health authorities or government agencies that is not for billing purposes, authorization is not required; however, this disclosure must be tracked by accounting for the disclosure (e.g., tumor registries).

3.2.9 Use of human biological samples labeled with or linked to PHI (e.g., name, medical record number) for research purposes

3.2.9.1 Biospecimens collected for clinical purposes and sent to a research (or clinical) laboratory for analyses to be used solely for clinical/patient care are considered treatment and do not require IRB approval, authorization, or waiver of authorization.

3.2.9.2 Biospecimens collected solely for research purposes under an IRB approved study prior to April 14, 2003, do not require additional IRB approvals or changes in the labels on the specimens.

3.2.9.3 Biospecimens collected solely for research purposes under an IRB approved study after April 14, 2003, require either an authorization from the research subject or a waiver of authorization from the IRB.

3.2.9.4 Biospecimens originally collected for patient care that are to be used for research after April 14, 2003, require IRB approval and must be either:

3.2.9.4.1 De-identified by someone who has clinical authority to be in possession of the specimens (e.g., the physician caring for the patients or the pathologist analyzing the samples for patient care purposes). This entails removal of all identifiable information contained on the labels, containers, or any other method that links the information to the sample, if such information is affixed; or

3.2.9.4.2 Labeled with and/or connected to PHI that is in a limited data set format. In this scenario, the clinician who obtains the specimens must complete a data use agreement with the investigator, in addition to the IRB approval, if the clinician and
Investigator are not within the same covered entity, practice plan, or division.

3.2.9.5 If the samples are not de-identified or linked to a limited data set, the Investigator must obtain: a) an authorization from each individual to use the sample for a specific study; or b) a waiver of authorization from the IRB to use the samples for a specific study, and keep an accounting of disclosures.

3.2.9.6 Core laboratories/Pathology departments or other departments/divisions within the School of Medicine, School of Dentistry, School of Optometry, or any other IU HIPAA affected area or any external covered entity that keeps/stores samples cannot release those samples to anyone else for research purposes without IRB approval and according to appropriate HIPAA guidelines. If samples are de-identified HIPAA does not apply; however, you may need a material transfer agreement (MTA). It is suggested that guidance be sought regarding the responsibilities of the sample holder when samples are not de-identified.

3.2.10 Use of PHI for quality improvement projects or case presentations

3.2.10.1 Use of a patient’s PHI or biospecimen for quality improvement projects is deemed health care operations and does not require IRB approval or authorization or waiver of authorization. Minimum necessary rules apply.

3.2.10.2 Use of a patient’s PHI or biospecimen for a case report for education/teaching purposes is deemed health care operations and does not require IRB approval or authorization or waiver of authorization. Minimum necessary rules apply. Care should be taken to ensure that no patient identifiers are published without express permission from the patient.

3.2.10.3 Use of a patient’s PHI or biospecimen for a single case report for publication does not require IRB approval or authorization or waiver of authorization, providing the patient was treated by the person reporting the case(s) and the information is de-identified.

3.2.11 Data Use Agreements or Business Associate Agreements. There are several instances when an investigator will need to enter into a legal agreement to protect a research subject’s identifiable health information. Faculty must not generate or sign a data use or business associate agreement without first consulting with the appropriate Privacy Office. In some circumstances, master agreements that cover research may already be in place.

3.2.11.1 In general, a data use agreement is utilized when a covered entity shares data in the form of a limited data set with an individual for research purposes. The covered entity and the individual must adhere to the minimum necessary rule, and ensure that the recipient of the information will not disclose the PHI beyond what is described in the data use agreement.
3.2.11.2 If a subject authorizes you to release his/her PHI for this purpose, no data use agreement is necessary. In certain circumstances where an agreement is needed, confidentiality agreements may suffice.

3.2.11.3 A business associate (BA) agreement is utilized when an individual, group, company, or contractor that is outside of the covered entity performs a service involving PHI on behalf of the covered entity. Examples of this include data storage services, survey services, transcription, private auditors, and statistical services. Whenever possible, these outside entities should always be listed on the authorization form as parties that may review or receive PHI and then a business associate agreement would not be necessary. However, there may be rare situations when a business associate agreement is needed, such as when the service is not or cannot be part of the authorization, or the services occur as part of a waiver of authorization. A BA agreement is necessary when the PI de-identifies data or creates a limited data set on behalf of a covered entity.

3.2.12 Training. The principal investigator is responsible for assuring that all members of the research team are knowledgeable about the appropriate uses and disclosures of identifiable health information for the study, the authorization process, and safeguards that must be employed to secure the information. The latter includes but is not limited to the security regulations as it pertains to electronic data and databases. Individuals responsible for training should be listed on the Personnel tab of the KC Protocol.

3.2.13 Electronic data and databases. Special provisions exist regarding the use, disclosure, retention, and transmission of PHI in electronic form. See the SOP for Data Management.

3.2.14 Safeguarding Protected Health Information.

3.2.14.1 The principal investigator is responsible for ensuring investigators involved with the study use appropriate safeguards to maintain the confidentiality, integrity, and availability of PHI that is collected, used, shared, and/or stored for research purposes.

3.2.14.2 Safeguards must be explained in the IRB submission and must consider the data source (i.e., the types of records that are used to gather the data) and the data collection or recording method.

3.2.14.3 A principal investigator must work with the research team to ensure PHI is safely stored and disposed of when it is no longer needed and exchanged. This includes safeguarding the data source, the recording/collection method and data disposal.

3.2.14.4 Research data that includes PHI must be stored on devices that have appropriate safeguards in place. If such data will be accessed from or stored on any mobile device, including but not limited to laptops, USB drives,
smartphones, tablets, etc., the device(s) must be encrypted. (See IU’s Security Policy IT-12.1, https://protect.iu.edu/cybersecurity/policies/IT12/12.1)

3.2.15 **Data Source.** Following are general guidelines for safeguarding the data source when PHI is accessed or gathered for research purposes.

3.2.15.1 When treatment or test results, medical records, and other clinical records are accessed to gather data for a study, proper safeguards must be used.

3.2.15.2 Any treatment or test results, medical records, and other clinical records must be kept in a secure location.

3.2.15.3 Data collected from surveys or questionnaires must be gathered in a secure manner and safeguarded when recorded, stored, and transmitted.

3.2.15.4 Video and audio data must be recorded in a secure manner, considering both the logistics of the subject and the investigator as well as how the data are stored. For instance, the video or audio recording should take place in a private location where possible to ensure that an individual’s PHI is not inadvertently disclosed to anyone except members of the research team.

3.2.16 **Data Recording/Collection Method.** Following are general guidelines for safeguarding PHI once it is recorded or collected:

3.2.16.1 Data collected using a computer (e.g., laptop, hard drive, local shared drive, web-based system, CDs, USB drive) or a tablet must be safeguarded using various methods (see 3.3.14.4).

3.2.16.2 Paper (e.g., notes, case report form)
   - Data recorded in an investigator’s notes, on a case report form or in other documents must be kept in a secure location, such as a locked office, locked cabinet, or other area with limited public access.
   - Printed PHI must be shredded when it is disposed.

3.2.16.3 Video and Audio
   - Once the video or audio recording is completed, ensure that the tapes, CDs, or other media are stored in a secure location (such as a locked cabinet or office).
   - Recordings must be destroyed when they are disposed.

3.2.17 **Data Recording/Collection Method.** In addition to safeguarding the data as it is collected and stored, consider who needs access to PHI and determine the level of access that is appropriate for their particular role, for the following:

3.2.17.1 Principal Investigator
3.2.17.2 Research Coordinator
3.2.17.3 Co-Investigators, i.e., Key and Non-Key Personnel
3.2.17.4 Governmental Agencies
3.2.17.5 Research Sponsor, Monitor, Other Research Organizations
3.2.17.6 Institutional Review Board or its designees
3.2.17.7 Other groups assisting with a study, such as BioStats or other colleagues not listed on the Personnel tab of the KC Protocol.

3.2.18 Secure Disposal. PHI (or other confidential data) must be safeguarded until the data is securely disposed. Following are guidelines for appropriately disposing of PHI (or other confidential data).

3.2.18.1 Determine the length of time you are required to retain the data:
   3.2.18.1.1 Minimum of three (3) years for non-health data.
   3.2.18.1.2 Minimum of seven (7) years for health data per Indiana and HIPAA laws.
   3.2.18.1.3 Indefinitely or per sponsor requirements.
   3.2.18.1.4 Other time frames.

3.2.18.2 Consider how data should be discarded:
   3.2.18.2.1 Shred paper.
   3.2.18.2.2 Permanently delete data from computers, tablets, and smartphones using appropriate standards.
   3.2.18.2.3 Delete files from or destroy all removable media (diskettes, CDs, DVDs, USB drives, etc.).

3.2.19 Sharing Health Data

3.2.19.1 It is not only important to safeguard health data as it is collected, stored and destroyed, but also when sharing the information. For the purpose of this SOP, sharing may include releasing, transmitting, or providing access to research and health data within the research team, outside the university, to research sponsors, etc. You must use reasonable safeguards when sharing any form of research data, health or non-health.
3.2.19.2 When sharing health data, consider the type of data being shared and who has a legitimate need and right to know as well as how the data will be shared.

3.2.19.3 Also, consider the following when data will be shared in any of the following formats:

3.2.19.3.1 Non-health data is not subject to HIPAA protections.

3.2.19.3.2 De-identified data is not subject to HIPAA protections and does not have to be safeguarded; however, re-identification codes must be carefully safeguarded since these codes contain the link that re-identifies the data.

3.2.19.3.3 A limited data set contains certain identifiers and is still considered PHI and protected by HIPAA. A limited data set must be safeguarded.

3.2.19.3.4 Identifiable data (e.g., patient identifiers, names, initials, subject identification numbers) is protected by HIPAA and must be safeguarded appropriately.

3.2.19.3.5 Identifiable health data should not be shared with anyone who is not listed on the Personnel tab of the KC Protocol or the Authorization. If a study requires sharing data with others (e.g., multi-center studies, cooperative studies, individual colleagues within or outside of IU), principal investigators will be expected to explain how the information will be safeguarded. This may involve asking the recipient of the data to explain their safeguards and to provide a written assurance that they will safeguard the data.

3.2.19.3.6 Examples of safeguarding methods for sharing data include secure websites, encrypted emails, Slashtmp, and faxing in secure areas.

3.3. ADDITIONAL POLICIES AND PROCEDURES

3.3.1 Research Subject to Department of Defense (DoD) Regulations

N/A

3.3.2 Research Subject to Department of Education (ED) Regulations

N/A

3.3.3 Research Subject to Department of Justice (DOJ) Regulations

Section II – Confidentiality and Privacy
3.3.3.1 For research funded by the National Institute of Justice (NIJ):

3.3.3.1.1 All projects are required to have a privacy certificate approved by the NIJ Human Subjects Protection Officer.

3.3.3.1.2 All investigators and research staff are required to sign Employee Confidentiality Statements, which are maintained by the responsible investigator.

3.3.3.2 For research conducted with the Bureau of Prisons:

3.3.3.2.1 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.

3.3.3.2.2 Except as noted in the consent statement to the subject, the investigator must not provide research information that identifies a subject to any person without the 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 pertains.

3.3.3.2.3 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.

3.3.3.2.4 If the investigator is conducting a study of special interest to the Office of Research and Evaluation (ORE) but the study is not a joint project involving ORE, the investigator may be asked to provide ORE 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.

3.3.4 Research Subject to Veterans Affairs (VA) Regulations

3.3.4.1 When VA conducts a study that is protected by a Certificate of Confidentiality, the following health record documentation provisions apply:

3.3.4.1.1 For studies that do not involve medical intervention, no
annotation may be made in the health record.

3.3.4.1.2 For studies that involve a medical intervention, a progress note entry should indicate that an individual has been enrolled in a research study, any details that would affect the subject’s clinical care, and the name and contact information for the investigator conducting the study. Subjects’ informed consent forms and HIPAA authorization documents are not to be included in the health record.

3.3.4.2 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.

3.3.4.3 When VA research is subject to HIPAA regulations, HIPAA regulations will be applied. VA-specific considerations are as follows:

3.3.4.3.1 Written Authorization: VA Form 10-0493, Authorization for Use & Release of Individually Identifiable Health Information for VHA Research, must be used to document the authorization. The authorization may not be embedded in the consent form.

3.3.4.3.2 Activities 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.

3.3.4.3.2.1 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:

3.3.4.3.2.1.1 Access to PHI is only to prepare a protocol;

3.3.4.3.2.1.2 No PHI will be removed from the VA; and

3.3.4.3.2.1.3 Access to PHI is necessary for preparation of the research protocol.

3.3.4.3.2.2 Non-VA researchers may not obtain VA
information for preparatory to research activities without appropriate VA approvals.

3.3.4.3.2.2.1 During the preparatory to research activities the VA investigator must only record aggregate data. The aggregate data may be used only 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.

3.3.4.3.2.3 Contacting potential research subjects and conducting pilot or feasibility studies are not considered activities preparatory to research.

3.3.4.3.2.4 Activities preparatory to research encompass only the time to prepare the protocol and end when the protocol is submitted to the IRB.

3.3.4.4 Research records must be retained until disposition instructions are approved by the National Archives and Records Administration and are published in VHA’s Records Control Schedule. VA informed consent and authorization documents should not include a time frame for destruction of identifiers or research records.
1. INTRODUCTION

The regulations protecting human research subjects are based on the ethical principles described in the Belmont Report: respect for persons, beneficence, and justice. These principles should not be compromised by financial relationships of either the institution or the investigator(s). Openness and honesty are indicators of respect for persons, are characteristics that promote ethical research, and can only strengthen the research process.

The institution and investigators at IU and their affiliated research partners and institutions have a major responsibility to discover and transmit new knowledge through scholarly activities. Financial support for such activities comes from both public and private entities usually external to the university. Increasingly, relationships between the institution, faculty, or staff and external entities have become a significant feature of academic research and educational activities. As these relationships become more common and complex, possibilities for conflicts of interest, or at least the appearance of such conflicts, increase.

In order to ensure that protection of human research subjects takes precedence over such collaborations or benefits (financial and others), it is the obligation of the institution and all individuals conducting human subjects research to report financial relationships and, where appropriate, cooperate in the management of such conflicts of interest.

2. POLICIES AND PROCEDURES

2.1. Annual Individual Financial Interests in Research Disclosure Applicable to Researchers Conducting Research at Indiana University

2.1.1 It is the responsibility of all faculty, staff, students, and others responsible for the design, conduct, or reporting of IU research (i.e., key personnel) to disclose all potential or real conflicts of interest according to the Indiana University policy on Financial Conflicts of Interest in Research. These policies are based on the PHS regulations for ensuring Objectivity in Research.

2.1.2 Individuals must report potential conflicts using IU’s disclosure system. All disclosure statements must be submitted annually to the IU Conflict of Interest (COI) Office and updated any time an individual’s outside financial interests change. After submission of the disclosure statement, the COI Office will determine whether the disclosure warrants referral to the COI Committee, or, in the case of non-IU individuals, directly to the HSO for IRB consideration. The COI Committee may determine that the outside financial interest is manageable. In this case, the COI Office will work with the IU individual to develop a management plan to minimize potential conflict of interest issues. The COI Committee may also determine that the outside financial interest must be reduced or eliminated. In those cases, the COI Office will meet with the individual to
discuss how reduction or elimination may be accomplished. In all cases, the COI Committee recommendations will be transmitted back to the investigator for implementation.

2.1.3 In accordance with the Indiana University policy on Financial Conflict of Interest in Research key personnel are required to disclose annually any significant financial interests of themselves or their family members that reasonably would appear to affect, or be affected by, IU research activities or sponsored programs in which they are engaged, and any financial interest of themselves or their family members in external companies or other organizations whose financial interests would reasonably appear to affect, or be affected by, their IU research and sponsored program activities. This must also be updated whenever a new significant financial interest is acquired or an interest is eliminated. Please refer to the policy for additional information.

2.2. Transactional COI Disclosure to the IRB

2.2.1 The conduct of human subjects research is subject to higher standards than other types of research regarding potential conflicts of interest, including those based on FDA regulations. In addition to filing the annual disclosure (per IU Policy on Financial COI in Research), all PIs and key personnel applying to conduct human subjects research must also disclose on each IRB application:

2.2.1.1 any proprietary interest related to the research, including but not limited to a patent, trademark, copyright, or licensing agreement;

2.2.1.2 any arrangement, ownership interest, or compensation that could be affected by the outcome of the research; and

2.2.1.3 whether any of the interests disclosed by the investigator in the IU annual financial conflict of interest process (or home institution COI process if not a staff, student, or faculty member at IU) could affect or be affected by the research.

2.3. IRB Process for Reviews of Conflict of Interest

2.3.1 The HSO staff will review each protocol to ensure all key personnel have appropriately submitted annual disclosures as described in Section 2.1 above. Any management plans established to manage a disclosed interest related to the project will be made available to the IRB. In addition, HSO staff will determine if any investigator listed in the IRB submission has a financial interest in the specific research by reviewing the information contained in the COI Questionnaire of the IRB submission.

2.3.1.1 If an investigator indicates that he or she has a financial interest which relates to the research study, or an HSO staff member reviewing the transactional disclosure determines that an outside interest may relate
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to the research, the HSO staff member will obtain the management plan or best practices memo made available by the IU COI Office.

2.3.1.1 If the reported interests have not previously been disclosed to the IU COI Office, the investigator will be instructed to contact the IU COI Office for further instruction and disclosure. The COI Office will review issues referred to it by the HSO staff and notify the IRB of its review. The IRB will not approve any research until the conflict has been reviewed by the IU COI Office or Committee.

2.3.1.2 The IRB will evaluate the COI Committee’s determination for any considerations relating to the protection of human subjects. If there is a significant financial interest that the IRB believes relates to the study, the IRB will require the investigator to disclose the interest(s) to potential subjects by including appropriate language in the informed consent statement. In addition, the IRB may take any of the following actions:

a) Limit the enrollment of subjects to a maximum percentage (not more than 20%) of the national projected enrollment for multi-centered clinical trials;

b) Require an independent investigator to obtain consent;

c) Require an independent investigator to conduct the study;

d) Require independent safety monitoring;

e) Require frequent renewal; and/or

f) Any other restrictive action deemed appropriate based on the nature of the conflict.

2.3.2 The IRB has final authority to decide whether the interest and management, if any, allow the research to be approved.

2.4 Institutional Financial Interests

2.4.1 Intellectual Property and Investment of Indiana University Technology Research Corporation (IURTC)

2.4.1.1 All Indiana University Intellectual Property and Investment is held and managed by Indiana University Technology Research Corporation (IURTC).

2.4.1.2 IURTC is committed in principle and practice to respecting and maintaining the autonomy of IU’s research integrity and operations in
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general and to its human research protection program and processes in particular.

2.4.1.3 IURTC has passed a resolution committing itself to non-interference with IU’s program and processes for protecting human subjects in research.

2.4.2 Major Gifts and Investments of the Indiana University Foundation (IUF)

2.4.2.1 All major gifts to IU and investments of the Indiana University Foundation (IUF) are held and managed by the IUF.

2.4.2.2 IUF is committed in principle and practice to respecting and maintaining the autonomy of IU’s research integrity and operations in general and to its human research protection program and processes in particular.

2.4.2.3 IUF has passed a resolution committing itself to non-interference with IU’s program and processes for protecting human subjects in research.

2.4.3 Senior administrative officials must comply with the IU Policy on Financial Conflict of Interest in Research and state law on Conflict of Interest (IC 35-44-1-3).

2.4.4 When to Disclose

2.4.4.1 Submission of an IRB protocol requires Investigators to identify whether or not, to the best of their knowledge, the proposed research involves IU intellectual property or IU gifts.

2.4.4.2 IURTC and IUF are committed to providing relevant information as requested by the IRB and IU Conflict of Interest Committee in support of their reviews and deliberations.

2.4.5 IRB Review of Conflict of Interest

2.4.5.1 The HSO staff and IRB will review the protocol for institutional significant financial interests related to the conduct of human subjects research, when and if they occur, in the same manner that individual significant financial interests are processed (see 2.3.1).

3. ADDITIONAL POLICIES AND PROCEDURES

3.1 Research Subject to FDA Regulations. The FDA requires that sponsors submit financial disclosure forms for each of the Investigators involved in any study mentioned in their New Drug Application (NDA) report. These forms are sent to the Investigators from the Sponsor.

3.2 Research Subject to HIPAA Regulations

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3.3. **Research Subject to VA Regulations**

   N/A

3.4. **Research Subject to Other Regulations**

   3.4.1 **Research Subject to Department of Defense (DoD) Regulations**

   N/A

   3.4.2 **Research Subject to Department of Education (ED) Regulations**

   N/A

   3.4.3 **Research Subject to Department of Justice (DOJ) Regulations**

   N/A
1. INTRODUCTION

Standardized methods of data collection and recording are essential to enable others to reconstruct the events of a study, to confirm protocol compliance, and to verify the data are complete, accurate, and appropriate. Document retention, storage, and disposal requirements allow data to be reviewed by sponsors and auditors to enable studies to be recreated, to demonstrate that the IRB approved protocol was followed, and to ensure confidentiality of research documents are secured until such time it is appropriate to destroy such documents. Guidelines for document retention, storage, and disposition will assist the Principal Investigator and the research team in determining the appropriate steps for keeping and destroying documents after the research has been completed. Ultimately, it is the PI’s responsibility to ensure that all study-related activities are completely and accurately documented and that documents are retained in accordance with IU policies, federal and state regulations, and sponsor requirements.

In order to protect the integrity of the data as well as the confidentiality of the information being collected, stored, and transmitted, it is essential to have standards for data management. Researchers, including their colleagues and support staff, are ethically bound to minimize all risks to human subjects, including the loss of confidentiality. In addition, they are legally bound to manage this information/data according to existing regulations and policies.

2. POLICIES AND PROCEDURES

2.1. Ownership of Data

2.1.1 Research data generated with external funding (such as NIH, foundations, or grants) that does not involve a contract or agreement that explicitly details ownership is the property of Indiana University. Sponsored research agreements are entered into with IU, and not with the individual investigator. Thus, IU is legally responsible for meeting all obligations of such agreements with respect to the creation, distribution, and preservation of the data.

2.1.2 In the case of externally sponsored or funded research involving a contract (e.g., a pharmaceutical or device company), the contract will define data ownership. In such cases, the data ownership typically lies with the sponsoring company; however, the details of the contract should define all policies, procedures, and issues related to ownership and will be the determining document for resolution of disputes.

2.1.3 Non-externally funded research data is the property of Indiana University.

2.1.4 If research is done by individuals who are employees of, or conduct work at, the Veterans Affairs Department or other government agency and Indiana
2.1.5 Regardless of ownership, the PI has custodial responsibility for the management, custody, retention, and destruction of the research data as detailed in this SOP.

2.1.6 If an investigator leaves the institution he/she may take only copies of the original data. The original data must remain with the owner as above unless a specific request is granted by the IU department or school.

2.2. Data Management Responsibility

2.2.1 The PI has primary responsibility for the collection, management, custody, and retention of research data.

2.2.2 The PI should adopt an orderly system of data recording, organization, and safeguards and should ensure all members of the research team (including appropriate administrative personnel) understand and follow the system.

2.2.3 The PI should ensure that appropriate safeguards and security are employed by all members of the research team. See the IU SOPs on Confidentiality and Privacy and Security of Research Data for additional guidance.

2.3. Data Collection

2.3.1 Study records and data collection methodology must enable the reconstruction of the entire study process and verification of the accuracy of all data with sufficient clarity, completeness, and organization that an external reviewer could readily determine that the IRB approved protocol was followed, the data are true and accurate, and that all regulatory responsibilities have been met.

2.3.2 The ICH Guidelines (Section 8) contain a complete listing of “essential” documents. These documents are generally collected in three phases: before the data collection phase commences, during the conduct of the study, and after termination of the study.

2.3.3 During each of these phases, different types of information will be collected:

2.3.3.1 Regulatory. Regulatory documents record the official conduct of the study as prescribed by the sponsor, IRB-approved protocol, and regulatory agencies. This information is generally not subject-specific, but rather relates to the project and/or all study subjects. Examples of regulatory information include but are not limited to regulatory binder, IRB forms, FDA Form 1572, IND/IDE submissions, lab normals and certifications, MedWatch forms, enrollment and drug accountability logs, etc.

2.3.3.2 Source. Source documents are the original documents (or certified copies of originals) onto which information, findings, or
observations are first recorded. In most cases this is not the same as the data collection or case report forms, but rather the first place that the information is recorded, such as handwritten hospital or clinic notes, subject’s diary, photographic negative, lab notebooks, or X-rays. When original observations or data are entered directly into computerized systems, including laptops and Personal Digital Assistants (PDA), the electronic record is the source document. With PDAs, not only the PDA but also the associated synchronized files become the source documents.

2.3.3.3 Case Report Form (CRF) or Data Collection Forms. Case report/data collection forms typically represent the summary or collation of data from the original source documents. They may be in electronic, optical, or paper formats, such as forms or spreadsheets. While not the original source documents, they may be used as such only when they are the first place in which the original observation is recorded and have been signed and dated by the original observer/recorder. While CRFs are typically designed as a method to report subject-specific information to the study sponsor, they are also necessary in investigator-initiated studies. CRFs allow quick review and analysis of subject-specific information and data trends, such as number and types of specific serious adverse events.

2.4. Transcription of Data

2.4.1 The transcription of source documents to case report or data collection forms, including remote data entry, requires care and accuracy. Therefore, the following procedures should be followed:

2.4.1.1 For paper documents, record all observations/data in black or blue ballpoint pen.

2.4.1.2 Correct errors by striking through the error, dating and initialing it, and making the correction. Ensure the original entry is not obliterated. If necessary, note an explanation in the right margin. Note that in FDA-regulated studies involving electronic data, a similar electronic audit trail must be created to track data corrections. (See 21 CFR 11: Electronic Records; Electronic Signatures.)

2.4.1.3 Complete all fields on the forms according to sponsor or other predetermined specifications.

2.4.1.4 If the sponsor/protocol requires remote data entry, ensure that staff are appropriately trained and that data are entered by computer according to sponsor/protocol specifications promptly from the source documentation.

2.5. Retention of Documents
The retention and maintenance of study-related documents are governed by several regulatory bodies. Their specific requirements are discussed below. Ultimately, it is the Principal Investigator’s responsibility to ensure that documents are retained in accordance with IU policies, federal regulations, and sponsor requirements.

2.5.1 IU Policy

2.5.1.1 These minimum standards apply to all research with human subjects unless there are more stringent retention requirements from a sponsor, funding agency, employer, or other regulatory body.

2.5.1.2 All records produced or collected in connection with a research project, including primary (e.g., laboratory, medical, interview), financial, statistical, supporting, administrative, and regulatory documentation, shall be retained for a period of three (3) years from the date of the submission of the final expenditure report to the funding agency or for three (3) years from the date of study closure with the IRB, whichever is longer. For studies involving individually identifiable health information (e.g., medical records), HIPAA requires that supporting documentation be kept for at least six (6) years, whereas Indiana state law requires that supporting documentation be kept for at least seven (7) years.

Important Note: In the state of Indiana, standard medical records may be destroyed after seven (7) years. Therefore, if retention of source documents is required for longer than 7 years (as it is for most sponsored trials), the PI should make copies of relevant source data. The investigator may need to make arrangements to obtain original documents before they are destroyed to prevent destruction of source documents or make certified copies of relevant medical records to be kept with study documents.

2.5.1.3 Data must be kept for as long as may be necessary to protect any intellectual property claims resulting from the work.

2.5.1.4 If any charges regarding the research arise, such as allegations of misconduct in research or financial conflict of interest, data must be retained until such charges are fully resolved.

2.5.1.5 If a student investigator is involved in a research project, data must be retained at least until the degree is awarded, or it is clear that the student has abandoned the work, or for three (3) years from the date of study closure from the IRB, whichever is longer.

2.5.1.6 The retention requirements of sponsors may exceed the minimal standards of IU; therefore, contractual obligations with sponsors will determine requirements in those instances.

2.6. Transfer of Responsibility
2.6.1 If an investigator is leaving the university and a study is to remain open with the IRB, notification of a transfer of responsibility must be made to the IU IRB in the form of a study amendment that identifies the researcher who has agreed to become the new PI. Upon approval by the IRB, the new PI will become responsible for all future data management issues pertaining to the study. This includes but is not limited to submissions to the IRB and other regulatory agencies; storage, retention, and final disposition; and arranging access for authorized monitors and/or auditors.

2.6.2 If an investigator is leaving IU and a study is closed with the IRB, the investigator may withdraw from the responsibility of maintaining the research documents for the period required above and transfer the responsibility and custody of the documents to any other appropriate person who will accept responsibility for them as described above. The PI who is leaving is responsible for notifying his/her department and division regarding who has agreed to accept this responsibility. The department/division then becomes responsible for keeping record of the person who has agreed to accept this responsibility in case of future inquiries, such as requests for inspection by authorized IU and/or federal auditors. In the absence of someone willing to accept responsibility for the documents, the department chairman will become responsible for assuring that documents are stored per regulatory and IU requirements.

2.6.3 For studies conducted under the jurisdiction of the FDA, where an investigator is leaving IU, the investigator may withdraw from the responsibility of maintaining the research documents for the period required above and transfer the responsibility and custody of the documents to an appropriate person who will accept responsibility for them as described above. Notice of such a transfer of responsibility shall be given to the sponsor and FDA within 10 working days after the transfer occurs (21 CFR 812.140).

2.7 Data Integrity

2.7.1 Data integrity must be maintained through appropriate security measures. All data must be retrievable and identifiable, and must relate to an actual subject.

2.7.2 Records and source documents must be retained to enable reconstruction of the study.

2.7.3 Audit trails must identify who made the changes, when, and why they were made.

2.7.4 Studies conducted under the regulation of the FDA (IND, IDE studies) must maintain full audit trails. All original entries made in source documents, case report forms, spreadsheets, or databases and all subsequent modifications must be maintained. New entries and/or corrections must not obscure or obliterate the previously entered data. The original data must remain visible within the system. For paper records, this includes drawing one line through the original entry, entering the correction in a way that does not obliterate the original entry, and initialing and dating the change.
2.7.5 Studies conducted under FDA regulations must also comply with 21 CFR 11: Electronic Records; Electronic Signatures. This regulation applies to all records in electronic form that are created, modified, maintained, archived, retrieved, or transmitted under any records requirements set forth by the FDA. It also applies to electronic records submitted to the agency under the federal Food, Drug, and Cosmetic Act and Public Health Service Act, even if such records are not specifically identified in agency regulations. However, this regulation does not apply to paper records that are, or have been, transmitted by electronic means. The regulation deals with electronic systems and electronic signatures, including security, validation, audit trails, data integrity, legacy systems, equipment, documentation, copies of records, and record retention. Similar to the requirements for paper records, this regulation requires that original data remain in the system, and that all changes must indicate the date of the change, the person who changed the data, and the reason for the change. It is important to note that standard database software such as Excel, Access, and FileMaker are not capable of an electronic audit trail. Thus, investigators are encouraged to utilize paper records for FDA-regulated studies unless they have specific software programs to adhere to these requirements. For specific details, consult FDA 21 CFR 11, Electronic Records; Electronic Signatures.

2.8. Data Security

2.8.1 For data containing PHI, additional measures may be required under the Health Information Privacy and Accountability Act (HIPAA). See the IU SOP on Confidentiality and Privacy for additional guidance.

2.8.2 For all research data, there are three levels of data safeguards that must be undertaken to ensure security of data. They are:

2.8.3 Administrative Safeguards, which include documented practices to manage the selection and execution of measures used to protect data and the conduct of personnel. Examples include: trust agreements, backup plans, recovery plans, access authorization plans, security management plans, security incident plans, training, accounting for disclosures, and disposal plans.

2.8.4 Physical Safeguards, which include protection of the actual locations of computer systems, related buildings, and equipment from natural or environmental hazards, such as fire, as well as from intrusion. Examples include locks, keys, controlled access, and access tracking.

2.8.5 Technical Safeguards, which include processes to monitor, protect, and control information access. This includes the prevention of unauthorized access to data transmitted via communications networks. Examples include access plans, audits, authorization, authentication, encryption, and firewalls.

2.9. Sharing Data

2.9.1 When sharing data within the research team or collaborators at IU, appropriate security measures should be undertaken as described above.
2.9.2 If data containing PHI is shared, additional requirements may apply. See the IU SOP on Confidentiality and Privacy for detailed information.

2.9.3 Pursuant to Indiana Code 4-1-10, the disclosure of social security numbers (SSNs) outside IU is prohibited, except in limited circumstances outlined in the Code.

2.9.4 Effective October 1, 2003, NIH requires a written plan to share data with the public and general research community for certain grants. See the NIH Data Sharing Policy, the NIH Data Sharing Policy and Implementation Guidance, and the IU SOP on Genomic Data Sharing for more information.

2.9.5 Both federal and state laws may impact public access to university records relating to research. Public access requests seeking documents containing information concerning research should be carefully evaluated and forwarded to the IU Office of University Counsel for further review and analysis, including a determination as to whether the records requested are or are not publicly available.

2.10. **Storing of Research Documents**

2.10.1 All documentation from a research study should be stored in such a manner that a request from the sponsor, regulatory agency, or internal audit can be met promptly and efficiently. Data that are archived or placed in long-term storage should be securely stored. Storage of documents containing PHI in a commercial facility may require the establishment of a Business Associate agreement between the covered entity to which the Principal Investigator belongs and the storage company. The PI should maintain an inventory of the records/files placed in internal or external long-term storage. The following points are provided as suggested steps for appropriate storage. Each department and/or investigator should have a specified method for accomplishing each of the following tasks:

2.10.1.1 Generate a master inventory list

2.10.1.2 Collect all study documentation

2.10.1.3 Define location of all study documentation

2.10.1.4 Determine retention policy (i.e., whether institutional, federal, and/or sponsor requirements apply)

2.10.1.5 Prepare documents ensuring they are secured and protected against breaches of confidentiality

2.10.1.6 Finalize inventory and accounting

2.10.1.7 Obtain and ensure appropriate storage container
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2.10.1.8 Notify sponsor, if applicable

2.10.2 See the IU SOP on Security of Research Data for additional information.

2.11. Disposition of Research Documentation

2.11.1 After the specified period of time has elapsed, the investigator may dispose of the documentation relating to a research study. Source documentation should be retained in its original form until this time.

2.11.2 The following are suggested ways to securely dispose of documents containing PHI:

2.11.2.1 Shred paper documents.

2.11.2.2 Destroy diskettes, CDs, USB drives, and/or hard drives.

2.11.2.3 Permanently delete files and data from computers and PDAs using special programs. (Note: Hitting the “delete” key on a computer does not permanently remove a file from the hard drive.)

2.11.2.4 Destroy video or audio recordings, files, or other media.

2.11.2.5 Depending on the funding agency, an investigator should not discard documentation until notification has been given to the sponsor and the sponsor has confirmed in writing that the documentation will no longer be required. The sponsor may specify the method for disposal or request documents be transferred to them. If not, arrangements for destruction should be made in a manner that adequately protects the confidentiality of the information (e.g., shredding).

2.11.3 Pursuant to Indiana Code 24-4-14, certain measures to protect against access by a third party are required to be taken when disposing of “personal information.” Acceptable methods of disposal include encrypting, shredding, incinerating, mutilating, erasing, and otherwise rendering the information illegible or unusable.

2.11.4 For additional information see the IU SOP on Security of Research Data.

2.12. Laws for Artifacts

For research involving historical artifacts, additional special handling procedures may apply. Indiana state laws regarding curation can be found at 312 IAC 21 Archaeological Review and Recovery. This includes curation standards that are governed at the federal level by 36 CFR 79. The responsibility of the National Park Service to maintain federal archaeological policy, is summarized at: Curation of Federally Owned and Administered Archeological Collections.

2.13. IRB Records – Retention and Access
2.13.1 IRB membership rosters, agendas, minutes, or other general correspondence with investigators, faculty, students, or staff will be retained indefinitely or until the Assistant Vice President, Research Compliance, gives the authority to dispose of such records.

2.13.2 After a research protocol is closed, terminated, or has expired, the physical IRB study file will be kept for a period of three (3) years following closure, termination, or expiration of IRB approval. The study file, which may be retained electronically for research not subject to 21 CFR Part 11 requirements, includes:

2.13.2.1 Protocol or research plan;
2.13.2.2 Investigator brochure, if any.
2.13.2.3 Scientific evaluations, when these are provided by an entity other than the IRB;
2.13.2.4 Recruitment materials.
2.13.2.5 Consent documents.
2.13.2.6 IRB determinations required by IU policies, state or federal regulations, and sponsor requirements.
2.13.2.7 Progress reports submitted by researchers.
2.13.2.8 Reports of injuries to subjects.
2.13.2.9 Records of continuing review activities.
2.13.2.10 Data and safety monitoring reports, if any.
2.13.2.11 Modifications to previously approved research.
2.13.2.12 Unanticipated problems involving risks to subjects or others.
2.13.2.13 Documentation of noncompliance.
2.13.2.14 Significant new findings.
2.13.2.15 All correspondence between the IRB and researchers.
2.13.2.16 Documentation of the justification for exemption determination, as applicable.
2.13.2.17 Documentation of the justification for using the expedited procedure, as applicable.
2.13.2.18 Description of the action taken by the reviewer.

2.13.2.19 Any finding required by laws, regulations, codes, and guidance to be documented.

2.13.3 Until disposal of IRB records has occurred, they will be made accessible for inspection and copying by authorized representatives of federal agencies or departments at reasonable times and in a reasonable manner.

2.13.4 For federally regulated studies involving electronic documentation, particularly electronic source documents, it may be necessary to retain not only the electronic media but also the device on which it is recorded so that the data is retrievable in years to come. For example, data recorded on compact discs may require the storage of a CD player.

2.13.5 The IRB will not accept or retain data in its records which is classified as Critical Data per the IU Policy on Management of Institutional Data.

3. ADDITIONAL POLICIES AND PROCEDURES

3.1 Research Subject to FDA Regulations

3.1.1 Investigational New Drug (IND) Clinical Trials. Pursuant to 21 CFR 312.62(c), the investigator shall retain required clinical trial-related material for a period of two (2) years following the date a marketing application is approved for the drug for the indication for which it is being investigated. If no application is to be filed or if the application is not approved for such indication, the records should be retained for a period of two (2) years after the investigation is discontinued and the FDA is notified. Note: For sponsors conducting global clinical trials, international retention policies may apply. In many cases this may be 15 years or longer. In those instances, the contractual obligations to the sponsor will supersede institutional minimum standards.

3.1.2 Investigational Device Exemption (IDE) Clinical Trials. Pursuant to 21 CFR 812.140(c), the investigator shall maintain the documents required during the investigation and for a period of two (2) years after the latter of the following two dates: the date on which the investigation is terminated or completed or the date that the records are no longer required for purposes of supporting a pre-market approval application or a notice of completion of a product development protocol. Note: For sponsors conducting global clinical trials, international retention policies may apply. In many cases this may be 15 years or longer. In those instances, the contractual obligations to the sponsor will supersede institutional minimum standards.

3.1.3 Financial Disclosure and Conflict of Interest Documents. Investigators who are involved in the submission of a marketing application for an IND or IDE are required to retain documentation relating to “financial disclosure” for two (2) years after the date of approval of the application. Similarly, any documents related to conflict of interest should be kept for the same time period as is applicable for the research project as detailed above.
3.2. Research Subject to HIPAA Regulations

N/A

3.3. Research Subject to VA Regulations

3.3.1 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.

3.3.2 Research Investigator Files - Research records maintained by the investigator that span the entire lifecycle of the project and the records required by regulations such as the investigator’s regulatory file. Refer to VHA RCS 10-1 for list of records.

NOTE: If the investigator leaves VA, all research records are retained by the VA facility where the research was conducted. If the grant is ongoing and the investigator leaves one VA facility to go to another VA facility, the investigator must obtain approval for a copy of relevant materials to be provided to the new VA facility’s research office. The investigator is not the grantee, nor does the investigator own the data.

3.3.2.1 Retention: Temporary; cutoff at the end of the fiscal year after completion of the research project. Destroy 6 years after cutoff, may retain longer if required by other Federal regulations.

3.3.3 Research Review Committee and Subcommittee Protocol Files – Committee and subcommittee files related to the review and oversight of research protocols submitted by VA investigators for research conducted at the field facility.

3.3.3.1 Protocols approved by the Committee or Subcommittee:

3.3.3.1.1 Retention: temporary; cutoff at the end of the fiscal year after the research project has been completed or terminated. Destroy 6 years after cutoff.

3.3.3.2 Protocols disapproved by the Committee or Subcommittee or withdrawn by the Investigator:

3.3.3.2.1 Retention: temporary; cutoff at the end of the fiscal year after the research project has been disapproved or withdrawn. Destroy 3 years after cutoff.

3.3.4 Research Review Committee or Subcommittee Operating Files – Files related to the ongoing operations of the review committees or subcommittees.
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3.3.4.1 Implementation Records – Records include but are not limited to agreements by VA facilities to use a review committee or subcommittee from the affiliated university or other entity; standard operating procedures, policies and educational materials, etc. (refer to RCS 10-1)

3.3.4.1.1 Retention: temporary; cutoff at the end of the fiscal year after final action, expiration, or when superseded. Destroy 3 years after cutoff.

3.3.4.2 Review Committee or Subcommittee Records - copies of all research protocols reviewed, scientific evaluations, if any, that accompany the proposals, approved consent documents, progress reports submitted by investigators, and reports of injuries to subjects, including, but not limited to:

3.3.4.2.1 Minutes of IRB meetings;

3.3.4.2.2 Records of continuing review activities;

3.3.4.2.3 Copies of all correspondence between the IRB and the investigators;

3.3.4.2.4 A roster of IRB members, including a resume or CV for each voting IRB member that is updated at the time of reappointment, appointment letters, and training records;

3.3.4.2.5 Written procedures for the IRB;

3.3.4.2.6 Statement of significant new findings provided to subjects;

3.3.4.2.7 Retention: Temporary; cutoff at the end of the fiscal year after final action; expiration, or when superseded. Destroy 6 years after cutoff.

3.3.5 IRB records, including ownership and storage, are addressed in the Memorandum of Understanding.

3.4. Research Subject to Other Regulations

3.4.1 Research Subject to Department of Defense (DoD) Regulations

3.4.1.1 Records maintained that document compliance or noncompliance with DoD regulations must be made accessible for inspection and copying by representatives of the DoD at reasonable times and in a reasonable manner as determined by the supporting DoD component.

3.4.2 Research Subject to Department of Education (ED) Regulations
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Section II – Data Management

N/A

3.4.3 Research Subject to Department of Justice (DOJ) Regulations

N/A
1. INTRODUCTION

Circumstances may arise that require the emergency use of an investigational test article. The FDA regulations allow for such use with unapproved investigational drugs (§312.36) and unapproved medical devices (§812.35(2)) in life-threatening situations. There are, however, certain criteria that must be satisfied before proceeding with the use of an unapproved investigational drug or medical device in an emergency situation. HHS regulations for the protection of human subjects, 45 CFR 46, do not permit research activities to be started, even in an emergency, without prior IRB review and approval. However, pursuant to §46.116(f), HHS regulations are not intended to limit the authority of a physician to provide emergency medical care, to the extent the physician is permitted to do so under applicable federal, state, or local law.

This SOP discusses the various options available to investigators/physicians when the emergency use of an investigational test article becomes necessary. It does not apply to:
- Compassionate use, which is a term used for a method of providing experimental therapeutics prior to final FDA approval for use in humans. This procedure is used with very sick individuals who have no other treatment options. Often, case-by-case approval must be obtained from the FDA for compassionate use of a drug or therapy. Participation in compassionate use programs requires the submission of a protocol and IRB approval.
- Treatment or open-label studies, meaning IRB approval may still be required for these types of studies.
- Off-label use of approved drugs in emergent situations, which may be done without IRB approval if used in the course of clinical care.

2. POLICIES AND PROCEDURES

2.1. Procedures for the Emergency Use of an Investigational Drug or Biologic

2.1.1 When a physician/investigator determines that a patient is in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval (§56.102(d)), the following steps should be taken:

2.1.1.1 If the patient qualifies, he/she should be enrolled into an active IRB-approved research study using the needed investigational drug or biologic.

2.1.1.2 If the patient does not qualify for an active IRB-approved research study or if such a study does not exist, the usual procedure is to contact the manufacturer and determine if the drug or biologic can be made available for the emergency use under the company’s Investigational New Drug (IND) application. The need for an investigational drug or biologic may arise in an emergency situation that does not allow time for submission of an IND. In such a case, FDA may authorize shipment of the test article in advance of the IND submission.
Requests for such authorization may be made by telephone or other rapid communication means.

2.1.1.3 During regular business hours, contact the IU Human Subjects Office, which will assist the physician/investigator to determine if the test article has been previously used at the institution and if the conditions described in 21 CFR 56.102(d) are met, in consultation with an IRB Chair.

2.1.1.3.1 If the conditions described in 21 CFR 56.102(d) are met, the investigator will be notified. However, such notification should not be construed as an IRB approval but rather as a tracking mechanism for the IRB to ensure that the investigator files a report within the five-day time frame required by 21 CFR 56.104(c). If assistance is required in dispensing the test article, Investigational Drug Services (IDS) should be contacted at 317-944-1900.

2.1.1.3.2 If, however, the conditions described in 21 CFR 56.102(d) are not met, the investigator cannot be granted an emergency waiver.

2.1.1.3.3 If the test article has already been used at the institution, subsequent use of the test article must be prospectively reviewed and approved by the IRB. The FDA and IRB acknowledge, however, that it would be inappropriate to deny emergency treatment to an individual if the only obstacle is that the IRB has not had sufficient time to convene a meeting to review the issue.

2.1.1.4 After regular business hours, contact Investigational Drug Services (IDS) at 317-944-1900 for assistance in determining if the test article has been previously used at the institution and for assistance in dispensing the test article, if required.

2.1.1.5 If the IU Human Subjects office or the IDS cannot be reached or the emergency use does not involve an investigational drug, the investigator may proceed with the emergency use provided the conditions described in 21 CFR 56.102(d) are met. The IU Human Subjects office must be notified of the use the following business day.

2.2. Reporting Requirements for an Emergency Use of a Test Article

2.2.1 Pursuant to 21 CFR 56.104(c), emergency use of a test article is exempt from prospective IRB review provided that such emergency use is reported to the IRB within five (5) business days. Thus, the investigator must notify the IRB of an emergency use within 5 business days and shall include the following information in the report:
2.2.1.1 A full description of the situation, including justification for the emergency use;

2.2.1.2 A full description of the test article, including the trade name, generic name, chemical name, and/or device name, the IND or IDE number, and name of sponsor/manufacturer;

2.2.1.3 A full description of the procedure(s) employed; and

2.2.1.4 A description of the consent process used, including an unsigned copy of the informed consent and authorization documents.

2.2.2 Pursuant to HHS regulations, whenever emergency care is initiated without prior IRB review and approval, the patient may not be considered a research subject. Such emergency care may not be claimed as research, nor may the outcome of such care be included in any report of a research activity. However, if the emergency care involves drugs, biologics, or devices that are considered to be investigational by the FDA, then the emergency use of a test article in a life threatening situation initiated without prior IRB review and approval is considered research and the person given the test article(s) on an emergency basis is a research subject. In order to maintain this distinction, data from persons given test articles on an emergency basis may not be included in any prospectively conceived research study. The IRB may consider granting an exemption determination to a retrospective review of existing data from one or more emergency uses, provided the emergency use provisions were not used as a mechanism to circumvent IRB review for a prospectively conceived research study.

2.2.3 The investigator should evaluate the likelihood of a similar need for emergency use of the test article. If the need is likely, prospective FDA (if not already in existence) and IRB approval should be initiated. FDA regulations and IU policy require that any subsequent use of the test article at the institution have prospective IRB review and approval.

2.2.4 Likewise, in its review of the emergency use, the IRB shall request the investigator submit a new study, including a protocol and associated new study material for prospective IRB review and approval when it anticipates that the test article may likely be used again.

2.2.5 When the IRB receives notification of an emergency use that has taken place, HSO staff will review the report to determine if the use complied with FDA and institutional requirements. If requirements were met, an acknowledgement letter will be sent to the investigator. If it is determined that requirements were not met, the matter will be handled according to the noncompliance procedures delineated in the IU SOP on Reportable Events.

2.3. Procedures for a New Study Submission When a One-Time Emergency Use Does Not Qualify
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2.3.1 If the use of the test article does not qualify for a one-time emergency use, prospective IRB approval is required. Once it is determined that an emergency IRB review is required, the following process will be followed:

2.3.1.1 If there is sufficient time, a new study application should be completed and submitted for review at the next regularly scheduled IRB meeting.

2.3.1.2 If there is not sufficient time to wait for a regularly scheduled IRB meeting, the IU Human Subjects Office may convene a special meeting. Because of the IRB’s concern that protocols receive thorough IRB review, the IRB may approve a protocol for use in one patient only with a request that the investigator submit the protocol (with requested revisions) for full IRB review for future patients.

2.3.1.3 If there is not sufficient time to convene a meeting, the IU Human Subjects Office will consult with an IRB Chair (or his/her designee) to determine the appropriateness of the test article’s use. In this case, the investigator is required to report the use in the manner explained above.

2.4. Informed Consent and Authorization Requirements

2.4.1 Unless any of the exceptions listed below apply, the investigator is required to obtain prospective informed consent from the subject or the subject’s legally authorized representative. The consent should clearly document the rationale for using the test article in emergency use situations and describe potential risks.

2.4.2 In addition, if an informed consent is required, the investigator is also required to obtain an authorization to use the subject’s health information for research purposes.

2.5. Exception from Informed Consent Requirements for Clinical Investigations.

Pursuant to 21 CFR 50.23(a), the obtaining of informed consent shall be deemed feasible unless, before use of the test article, both the investigator and a physician who is not otherwise participating in the clinical investigation certify in writing all of the following:

2.5.1 The subject is confronted by a life-threatening situation necessitating the use of the test article.

2.5.2 Informed consent or authorization cannot be obtained because of an inability to communicate with or obtain legally effective consent or authorization from the subject.

2.5.3 Time is not sufficient to obtain consent or authorization from the subject's legally authorized representative.
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2.5.4 No alternative method of approved or generally recognized therapy is available that provides equal or greater likelihood of saving the life of the subject.

2.6. If, in the investigator's opinion, immediate use of the test article is required to preserve the life of the subject and time is not sufficient to obtain the independent determination required in advance of using the test article:

2.6.1 The determination shall be made by the investigator and, within five (5) business days after the use of the article, be reviewed and evaluated in writing by a physician who is not participating in the clinical investigation.

2.6.2 The investigator shall notify the IRB within five (5) business days after the use of the test article according to the reporting requirements outlined above. In its review of a one-time emergency use which employed an exception to the informed consent requirement, the IRB will ensure that all regulations were appropriately followed.

3. ADDITIONAL POLICIES AND PROCEDURES

3.1 Research Subject to FDA Regulations

Preceding text is specific to FDA Regulations

3.2 Research Subject to HIPAA Regulations

N/A

3.3 Research Subject to VA Regulations. VA patients receiving a test article in an emergency use situation as defined by the FDA may not be considered to be research subjects, nor can the data obtained be classified as human subjects research, nor may the outcome of such care be included in any report of a research activity subject to VA regulations pertaining to research involving human subjects.

3.4 Research Subject to Other Regulations

3.4.1 Research Subject to Department of Defense (DoD) Regulations

N/A

3.4.2 Research Subject to Department of Education (ED) Regulations

N/A

3.4.3 Research Subject to Department of Justice (DOJ) Regulations

N/A
Exempt Research

About This Policy

Effective Date:
02/2005

Last Updated:
03/29/2018

Policy Contact:
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1.0 Scope
This policy applies to all human subjects research conducted by Indiana University (IU) faculty, staff, and students, or others which falls under the jurisdiction of the Indiana University Human Research Protection Program (HRPP).

2.0 Policy Statement
Human subjects research activities must be reviewed to determine whether the research meets one or more of the exemption categories described below and, if so, whether the research complies with applicable ethical standards. Research determined to be exempt is subject to the provisions of 45 CFR 46 only where specified below.

Investigators do not have the authority to make an independent determination that research involving human subjects is exempt and must obtain determination of exemption prior to beginning the research.

Research qualifies as exempt only if it falls into one or more of the exempt categories described below and meets these additional requirements:

- The research must present no more than minimal risk to subjects.
- The research is consistent with the ethical principles established by the Belmont Report to ensure the ethical conduct of research: autonomy/respect for persons, beneficence, and justice.
- As appropriate, there are adequate provisions to maintain the privacy interests of participants and the confidentiality of data.
- The research does not involve a test article regulated by the FDA, unless the research meets the criteria for exemption described in 45 CFR 46.101(b)(6) and 21 CFR 56.104(d) (Category 6 below).
• The research does not involve prisoners.
• For research conducted at or funded by the VA, the research does not involve pregnant women.
• The research does not utilize identifiable information and/or protected health information from VA patient records for screening and recruitment of potential subjects.

2.1. Exempt Human Subjects Research Categories under Federal Regulations

Pursuant to 45 CFR 46.101(b), research activities in which the only involvement of human subjects will be in one or more of the following categories are exempt from 45 CFR 46.

Category 1
Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as 1) research on regular and special education instructional strategies; or 2) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

Category 2
Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless both of the following are true:
- Information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and
- Any disclosure of the human subjects responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects’ financial standing, employability, insurability, or reputation.

This exemption does not apply to research involving children that uses survey procedures, interview procedures, or observation of public behavior when the investigator participates in the activities being observed. Research may qualify for exemption if it involves children as subjects and their participation is limited to educational tests (cognitive, diagnostic, aptitude, achievement) and observation of public behavior when the investigator does not participate in the activities being observed.

Category 3
Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under Category 2, if:
- The human subjects are elected or appointed public officials or candidates for public office; or
- Any applicable federal statute requires without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

Category 4
Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available
or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

To qualify for this exemption, data, documents, records, or specimens must exist at the time the research is proposed and not be prospectively collected.

Under this exemption, an investigator (with proper institutional authorization) may inspect private, identifiable records, but may record information only in a non-identifiable manner. The data must be permanently and completely de-linked at the time of extraction. A code may be used to organize data as it is collected; however, the code may not be a means of re-linking the data set to the original source and/or other sources.

Because Exempt Category 4 does not permit information to be recorded in a manner that allows subjects to be identified directly or through identifiers linked to subjects, no VA research may be approved under this exemption and must be submitted, at a minimum, for expedited review.

**Category 5**
Research and demonstration projects conducted by or subject to the approval of department or agency heads, and which are designed to study, evaluate, or otherwise examine:

- Public benefit or service programs; or
- Procedures for obtaining benefits or services under those programs; or
- Possible changes in or alternatives to those programs or procedures; or
- Possible changes in methods or levels of payment for benefits or services under those programs.

The program under study must deliver a public benefit (for example, financial or medical benefits as provided under the Social Security Act) or service (for example, social, supportive, or nutrition services as provided under the Older Americans Act).

The research or demonstration project must be conducted pursuant to specific federal statutory authority, must have no statutory requirement that an institutional review board (IRB) review the project, and must not involve significant physical invasions or intrusions upon the privacy of the subjects.

This exemption is for projects conducted by, or subject to approval of, federal agencies and requires authorization or concurrence by the funding agency.

**Category 6**
Taste and food quality evaluation and consumer acceptance studies:

- If wholesome foods without additives are consumed; or
- If food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural, chemical, or environmental contaminant at or below the level found to be safe, by the FDA or the U.S. Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture. (See also 21 CFR 56.104[d])
2.2. **Exempt Human Subjects Research under Flexibility Options**

Research that is not federally-funded and/or regulated and involves research activities in which the only involvement of human subjects will be in one or more of the following categories are also considered exempt (Exempt Flex). For purposes of the Exempt Flex options described below, not federally regulated means not subject to FDA or VA regulations.

**Category 2 Flex:**
Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior where all of the following are true:

- The information obtained is recorded by the investigator in such a manner that the identity of human subjects can readily be ascertained, directly or through identifiers linked to the subjects; and
- Disclosure of the human subjects’ responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects’ financial standing, employability, educational advancement, or reputation; and
- The IRB conducts a limited IRB review to make the determination that there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

Research involving children as subjects may qualify for exemption under this category only when their participation is limited to observation of public behavior and the investigator does not participate in the activities being observed.

**Category 3 Flex:**
Research involving benign behavioral interventions in conjunction with the collection of information from an adult subject through verbal or written responses (including data entry) or audiovisual recording if the subject prospectively agrees to the intervention and information collection and at least one of the following criteria is met:

- The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects; or
- Any disclosure of the human subjects’ responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects’ financial standing, employability, educational advancement, or reputation; or
- The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subject, and an IRB conducts a limited IRB review to make the determination that there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

Benign behavioral interventions are brief in duration, harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact on the subjects, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing.

If the research involves deceiving the subjects regarding the nature or purposes of the research, the subject must authorize the deception through a prospective agreement.
to participate in the research in circumstances in which the subject is informed that he or she will be unaware of or misled regarding the nature or purposes of the research.

Category 4 Flex:
Secondary research uses of identifiable private information and identifiable biospecimens, if:
- The study qualifies for exemption under Category 4 above, except that at least some of the data, documents, records, or specimens do not exist at the time the research is proposed, and the researcher agrees not to re-identify or contact subjects; or
- The research involves only information collection and analysis involving the investigator’s use of identifiable health information when that use is regulated under the HIPAA Privacy Rule (45 CFR parts 160 and 164, subparts A and E) for the purposes of “health care operations” or “research” as those terms are defined at 45 CFR 164.501 or for “public health activities and purposes” as described under 45 CFR 164.512(b).

3.0 Reason for the Policy
To foster the practice of research that meets the highest ethical standards and adheres to all applicable laws, principles, best practices, and policies related to research with human subjects.

4.0 Procedures
4.1. Exempt Submissions
Proposed exempt research is submitted through the KC IRB system. Investigators complete a Questionnaire, and, depending on the nature of the research, make the following additional materials available, as applicable:
- Data collection instruments, including surveys, questionnaires, interview questions, etc.
- Recruitment materials, including flyers, advertisements, letters, email scripts, etc.
- Other documents as applicable, e.g., letters of cooperation from research sites
- Grant proposal, if the research is funded by an agency within HHS, such as NIH, and the IU investigator is the direct recipient of the funds

4.2. Granting Exemptions
Exemption may be granted by an IRB member or by a qualified Human Subjects Office (HSO) staff member. Qualified HSO staff are those who have been involved in the review of human subjects research for more than one (1) year, have participated in the HRPP workshop for reviewing exempt research, have signed the HSO Confidentiality Agreement, and have completed applicable CITI training.

When the exemption requires the IRB conduct a limited IRB review, an IRB member must review and grant the exemption and determine whether there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data in accordance with 45 CFR 46.111(a)(7).

If the research is subject to HIPAA and the investigator requests a waiver of authorization, an IRB member, acting as a member of the Privacy Board, will determine whether it is appropriate to waive the requirement to obtain authorization or
documentation of authorization for the study.

Exemption is documented via the KC IRB Notice of Exemption which describes the specific category(ies) under which exemption is granted and any applicable IRB determinations.

For research funded or regulated by the VA, the IRB Chair or an experienced IRB member designated by the Chair reviews all requests for exemptions. Exemptions for VA research cannot be granted by a member of the HSO Staff who is not also an IRB member. The determination is recorded and signed by the IRB Chair or designee who reviewed the research and made the determination to grant or deny exempt status. If the request is granted, the documentation includes the specific categories under which exemption was granted. If the request for exempt status is denied, the reason for the denial is included.

4.3. **Ongoing Review**

Exempt research is not required to undergo renewal.

Minor modifications to exempt studies do not require review and approval unless the modification may change the study’s eligibility for exemption.

Substantive modifications that have the potential to change the nature of the research and, therefore, the study’s eligibility for exemption, require review and approval prior to implementation of the modification.

Investigators request review of substantive changes by submitting an amendment through the KC IRB system. The changes are reviewed to ensure that they do not affect the exempt status of the research. If the changes do not affect the exempt status, the investigator will be notified. If the changes result in the research no longer qualifying for exemption, the investigator will be notified accordingly and instructed to submit an appropriate expedited or full board IRB submission.

Investigators should notify the HSO that exempt research is complete by taking the “Close” action in the Protocol Actions tab in KC IRB.

5.0 **Sanctions**

University faculty, staff, and students that are found to be in violation of this policy may be subject to sanctions relating to their participation in research with human subjects, up to and including permanent suspension or bar from engaging in research with human subjects at Indiana University.

6.0 **History**

Replaces the previous IU SOP for Research Involving Human Subjects – Exemptions (v07/2015)

7.0 **Related Information**

AAHRPP Standards
- Standard II-1, Element I.1.D
- Standard II-2, Elements II.2.A, II.2.B
- Tip Sheet 9: Exemptions: Determinations and Review
IU HRPP Documents
  • Guidance: Exempt Research

KC IRB Questionnaires
  • Exempt Research

Regulatory References
  • 45 CFR 46, especially 45 CFR 46.101(b)
  • OHRP Guidance:
    o Exempt Research and Research that May Undergo Expedited Review
    o Exemptions for Public Benefit and Service Programs
  • VHA Handbook 1200.05, Requirements for the Protection of Human Subjects in Research, especially Appendix A
Section II – Genetic Information Nondiscrimination Action (GINA)

1. INTRODUCTION

The Genetic Information Nondiscrimination Act (GINA) is a federal law that, together with already existing nondiscrimination provisions of the Health Insurance Portability and Accountability Act (HIPAA), prohibits discrimination in health coverage and employment based on genetic information.

2. POLICIES AND PROCEDURES

2.1 GINA Protections

2.1.1 In general, GINA prohibits health insurers or health plan administrators from requesting or requiring genetic information of an individual or an individual’s family members, or using such information for decisions regarding coverage, rates, or preexisting conditions.

2.1.2 GINA also prohibits employers from using genetic information for hiring, firing, or promotion decisions, and for any decisions regarding terms of employment.

2.2. IRB Responsibilities Under GINA

2.2.1 When reviewing proposed or ongoing genetic research, the IRBs will consider the protections provided by GINA when determining whether the research satisfies all of the following criteria required for IRB approval of research:

2.2.1.1 Risks to subjects are minimized (a) by using procedures that are consistent with sound research design and that do not unnecessarily expose subjects to risk; and (b) whenever appropriate, by using procedures that are already being performed on the subjects for diagnostic or treatment purposes (45 CFR 46.111(a)(1)).

2.2.1.1 GINA’s protections do not apply to life insurance, disability insurance, or long-term care insurance. GINA does not mitigate potential risks to subjects in terms of their ability to obtain such insurance or purchase such financial products. The IRBs will consider whether protections against disclosures of genetic data are adequate.

2.2.1.2 Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result (45 CFR 46.111(a)(2)).
2.2.1.3 When appropriate, there are adequate provisions to protect the privacy of subjects and maintain the confidentiality of data (45 CFR 46.111(a)(7)).

2.2.1.4 A description of any reasonably foreseeable risks or discomforts to the subjects (45 CFR 46.116(a)(2)).

2.2.1.5 The informed consent document includes a statement describing the extent, if any, to which confidentiality of records identifying the subjects will be maintained (45 CFR 46.116(a)(5)).

2.3. Informed Consent

2.3.1 The protections provided by GINA should be disclosed to subjects during the informed consent process. Such protections include:

2.3.1.1 Health insurance companies and group health plans may not request an individual’s genetic information obtained from research.

2.3.1.2 Health insurance companies and group health plans may not use an individual’s genetic information when making decisions regarding the individual’s eligibility or premiums.

2.3.1.3 Employers with fifteen (15) or more employees may not use an individual’s genetic information obtained from research when making a decision to hire, promote, or fire the individual, or when setting the terms of his/her employment.

2.3.2 The protections provided by GINA should not be overstated during the informed consent process. Specifically, subjects should be informed that:

2.3.2.1 The discrimination protections provided by GINA address health coverage and employment only.

2.3.2.2 GINA provisions prohibiting discrimination in health coverage based on genetic information do not extend to life insurance, disability insurance, or long-term care insurance.

2.3.2.3 GINA generally does not apply to employers with fewer than 15 employees. Therefore, subjects who are or will be employed by such employers receive none of the GINA protections that prohibit discrimination in employment on the basis of genetic information.
3. ADDITIONAL POLICIES AND PROCEDURES

3.1. Research Subject to FDA Regulations
N/A

3.2. Research Subject to HIPAA Regulations
N/A

3.3. Research Subject to VA Regulations
N/A

3.4. Research Subject to Other Regulations

3.4.1 Research Subject to Department of Defense (DoD) Regulations
N/A

3.4.2 Research Subject to Department of Education (ED) Regulations
N/A

3.4.3 Research Subject to Department of Justice (DOJ) Regulations
N/A
1. **INTRODUCTION**

The National Institutes of Health (NIH) is interested in advancing genomic research to identify common genetic factors that influence health and disease. Sharing genomic data provides opportunities to accelerate that research through the power of combining large and information-rich datasets. Whole genome information, when combined with clinical and other phenotype data, offers the potential for increased understanding of basic biological processes affecting human health, improvement in the prediction of disease and patient care, and ultimately the realization of the promise of personalized medicine. To promote robust sharing of human and non-human data from a wide range of genomic research and to provide appropriate protections for research involving human data, the NIH issued the Genomic Data Sharing Policy. This policy pertains to all NIH-funded research generating large-scale human or non-human genomic data and the use of these data for subsequent research. Examples of large-scale genomic data include but are not limited to Genome-Wide Association Studies (GWAS); single nucleotide polymorphism (SNP) arrays; and genome sequence, transcriptomic, epigenomic, and gene expression data.

The potential for public benefit to be achieved through sharing genomic data is significant. However, genotype and phenotype information generated about individuals, such as data related to the presence or risk of developing particular diseases or conditions and information regarding paternity or ancestry, may be sensitive. Therefore, protecting the privacy of the research subjects and the confidentiality of their data is critically important. Risks to individuals, groups, or communities should be balanced carefully with potential benefits of the knowledge to be gained through this genomic data. The sensitive nature of genomic information about subjects and the broad data distribution goals of these data repositories highlight the importance of the informed consent process to this research.

2. **POLICIES AND PROCEDURES**

2.1. **Investigator Responsibilities**

2.1.1 As part of a study’s initial submission (or with an amendment, for studies that are already in progress), an Institutional Certification memo must be submitted to the IRB to be signed upon approval. This memo should be provided by the institute or center to which the data is being sent.

2.1.2 Because the IRB is responsible for determining the following, information (template available on HSO website) clearly denoting how each of the following elements is met must be submitted to the IRB along with the Institutional Certification memo:

2.1.2.1 Submission of the data and subsequent sharing for research purposes are consistent with the informed consent of study subjects from whom the data were obtained.
Section II: SOPs/Policies

Section II: Genomic Data Sharing (GDS)

2.1.2.2 The investigator’s plan for de-identifying datasets is consistent with the standards outlined in the policy.

2.1.2.3 Consideration was given to risks to individual subjects and their families associated with data submitted to NIH-designated data repositories and subsequent sharing.

2.1.2.4 To the extent relevant and possible, consideration was given to risks to groups or populations associated with submitting data to NIH-designated data repositories and subsequent sharing.

2.1.2.5 The genotype and phenotype data to be submitted were collected in a manner consistent with 45 CFR 46 (Protection of Human Subjects, also known as “the Common Rule”).

2.1.3 Considerations for Informed Consent

2.1.3.1 NIH expects investigators to obtain subjects’ consent for their genomic and phenotypic data to be used for future research purposes and to be shared broadly. The informed consent should state whether the data will be shared via unrestricted (data accessible to anyone via a public website) or controlled-access (data are available if certain stipulations are met) repositories.

2.1.3.2 For studies proposing to use genomic data from cell lines or clinical specimens that were created or collected after August 27, 2014, NIH expects that informed consent for future research use and broad data sharing will have been obtained even if the cell lines or clinical specimens are de-identified. Although this research would normally be considered non-human subjects research under the common rule, the NIH feels that it is no longer ethically tenable simply to de-identify clinical specimens or derived cell lines to generate data for research use without an individual’s consent, given growing concerns about future re-identification based on genetic and genomic information.

2.1.3.3 If there are compelling scientific reasons that necessitate the use of genomic data from cell lines or clinical specimens that were created or collected after August 27, 2014, and that lack consent for research use and data sharing, investigators should provide a justification in the funding request for their use. The funding organization will review the justification and decide whether to make an exception to the consent expectation.

2.1.3.4 For studies proposing to use genomic data from cell lines or clinical specimens that were created or collected before August 27, 2014, there may be considerable variation in the extent to which future genomic research and broad sharing were addressed in the informed consent materials for the primary research. In these cases, an
assessment by an IRB, privacy board, or equivalent body is needed to ensure that data submission is not inconsistent with the informed consent provided by the research participant. NIH will accept data derived from de-identified cell lines or clinical specimens lacking specific consent for research use that were created or collected before August 27, 2014.

2.1.3.5  Scope of Written Consent

2.1.3.5.1  Is the informed consent consistent with anticipated research activities?

\[ \begin{align*}
2.1.3.5.1.1 & \quad \text{Does the consent form either allow or preclude certain activities, such as:} \\
& \quad 2.1.3.5.1.1.1 \quad \text{Genetic research or analysis;} \\
& \quad 2.1.3.5.1.1.2 \quad \text{Future use and broad sharing of the subject’s coded phenotype and genotype data for research; and/or} \\
& \quad 2.1.3.5.1.1.3 \quad \text{Submission of the subject’s coded phenotype and genotype data to a government health research database for broad sharing to qualified investigators.}
\end{align*} \]

\[ \begin{align*}
2.1.3.5.1.2 & \quad \text{Does the consent form include restrictions, such as:} \\
& \quad 2.1.3.5.1.2.1 \quad \text{Types of subsequent research using the subject’s phenotype and genotype data;} \\
& \quad 2.1.3.5.1.2.2 \quad \text{Location of research;} \\
& \quad 2.1.3.5.1.2.3 \quad \text{Types of medical conditions or diseases studied;} \\
& \quad 2.1.3.5.1.2.4 \quad \text{Duration of storage and use of phenotype and genotype data; and/or} \\
& \quad 2.1.3.5.1.2.5 \quad \text{Limitations on who can use the subject’s phenotype and genotype data.}
\end{align*} \]

2.1.3.5.2  Potential Benefits

\[ \begin{align*}
2.1.3.5.2.1 & \quad \text{Does the consent form discuss that potential benefits may accrue broadly to the public through the advancement of science and understanding of health and}
\end{align*} \]
disease, rather than resulting in direct benefits to individuals?

2.1.3.5.3 Risks

2.1.3.5.3.1 Does the consent form discuss risks associated with genetic or genomic research?

2.1.3.5.3.2 Are these risks consistent with the risks involved in GDS activities?

2.1.3.5.4 Return of Research Results

2.1.3.5.4.1 Does the consent form include a discussion of whether or not research results will be returned to subjects, and under what conditions?

2.1.3.5.5 Privacy and Confidentiality Protections

2.1.3.5.5.1 Does the consent form address how individual privacy and data confidentially will be protected?

2.1.3.5.5.2 Is the manner in which privacy and confidentiality measures are described consistent with the NIH GDS policies?

2.1.3.5.5.3 The NIH encourages investigators submitting large-scale human genomic datasets to NIH-designated data repositories to seek a Certificate of Confidentiality as an additional precaution because genomic data can be re-identified.

2.1.3.5.6 Withdrawal of Consent

2.1.3.5.6.1 Does the consent form address whether a subject can withdraw his/her phenotype and genotype data from research use?

2.1.3.5.6.2 Submitting investigators and their institutions may request removal of data on individual subjects from NIH-designated data repositories, in the event that a research participant withdraws or changes his or her consent. However,
some data that have been distributed for approved research use cannot be retrieved, and this information should be conveyed in the consent form.

### 2.1.3.5.7 Commercial Use

**2.1.3.5.7.1** Does the consent form allow for or preclude commercial use of the subject’s phenotypic and genotypic data?

### 2.1.3.6 Other Issues

**2.1.3.6.1** Is there any other information in the consent form that is inconsistent with the information provided about the NIH-designated data repository and its policies and procedures?

### 2.1.4 Data Repositories

**2.1.4.1** Investigators shall register all studies with human genomic data in dbGaP (the NIH database of Genotypes and Phenotypes) by the time that data cleaning and quality control measures begin, regardless of which NIH-designated data repository will receive the data. After registration, the data may be submitted to the relevant NIH-designated data repository.

**2.1.4.2** Investigators may also elect to submit data to non-NIH-designated data repositories in addition to an NIH-designated repository. If this occurs, investigators must ensure that appropriate data security measures are in place, and that the non-NIH-designated data repository has confidentiality, privacy, and data use measures consistent with the GDS policy.

### 2.2 Institutional Responsibilities

#### 2.2.1 Role of the Institutional Official

**2.2.1.1** An Institutional Signing Official is generally a senior official at an institution who is credentialed through NIH eRA Commons system and is authorized to enter the institution into a legally binding contract and sign on behalf of an investigator who has submitted data or a data access request to NIH.

**2.2.1.2** By signing the Institutional Certification, the Institutional Official asserts the following:

**2.2.1.2.1** The data submission is consistent with all applicable laws and regulations as well as institutional policies;
2.2.1.2.2 The appropriate research uses of the data and the uses that are specifically excluded by the informed consent documents are delineated;

2.2.1.2.3 The identities of research subjects will not be disclosed to the NIH-designated data repository; and

2.2.1.2.4 An IRB and/or Privacy Board, as applicable, reviewed, and verified the items below.

2.2.2 Role of the Institutional Review Board (IRB)

2.2.2.1 By signing the Institutional Certification, the IRB reviewer asserts the following:

2.2.2.1.1 Data is consistent with all applicable laws and regulations as well as institutional policies.

2.2.2.1.2 The appropriate research uses of the data and the uses that are specifically excluded by the informed consent documents are delineated.

2.2.2.1.3 The identities of research subjects will not be disclosed to the NIH-designated data repositories. Data submitted to these repositories will be de-identified and coded using a random, unique code. Data should be de-identified according to the following criteria:

2.2.2.1.3.1 The identities of data subjects cannot be readily ascertained or otherwise associated with the data by the repository staff or secondary data users;

2.2.2.1.3.2 The 18 identifiers enumerated at section 45 CFR 164.514(b)(2) (the HIPAA Privacy Rule) are removed; and

2.2.2.1.3.3 The submitting institution has no actual knowledge that the remaining information could be used alone or in combination with other information to identify the subject of the data.

2.2.2.1.4 IRB has reviewed and verified that:

2.2.2.1.4.1 Submission of the data and subsequent sharing for research purposes are consistent with the informed consent of study subjects from whom the data were obtained.
2.2.2.1.4.2 The investigator’s plan for de-identifying datasets is consistent with the standards outlined in the policy.

2.2.2.1.4.3 Consideration was given to risks to individual subjects and their families associated with data submitted to NIH-designated data repositories and subsequent sharing.

2.2.2.1.4.4 To the extent relevant and possible, consideration was given to risks to groups or populations associated with submitting data to NIH-designated data repositories and subsequent sharing.

2.2.2.1.4.5 The genotype and phenotype data to be submitted were collected in a manner consistent with 45 CFR 46 (Protection of Human Subjects, also known as “the Common Rule”).

3. ADDITIONAL POLICIES AND PROCEDURES

3.1. Research Subject to FDA Regulations

N/A

3.2. Research Subject to HIPAA Regulations

Please see the IU SOP on Confidentiality and Privacy for details.

3.3. Research Subject to VA Regulations

N/A

3.4. Research Subject to Other Regulations

3.4.1 Research Subject to Department of Defense (DoD) Regulations

N/A

3.4.2 Research Subject to Department of Education (ED) Regulations

N/A

3.4.3 Research Subject to Department of Justice (DOJ) Regulations

N/A
1. INTRODUCTION

Because several sets of regulations exist that govern the use of medical devices, there is much confusion related to how these devices can be used. Of particular confusion is the use of Humanitarian Use Devices (HUDs). These devices fall somewhere between research and ordinary clinical practice. They do not undergo the same stringent requirements that investigational devices do in order to be commercially marketed, yet they may be recognized as the “approved” standard and, in some cases, the preferred medical device.

A HUD, because of its small expected market (fewer than 4,000 cases per year), is not expected to ever be able to get the type of efficacy data required by ordinary premarket approval (PMA), so the FDA grants a special humanitarian device exemption (HDE) from some of the requirements for marketing approval. Although an HDE does not require results of scientifically valid clinical investigations demonstrating that the device is effective for its intended purpose, it must contain sufficient information for the FDA to determine that the device does not pose an unreasonable or significant risk of illness or injury, and that the probable benefit to health outweighs the risk of injury or illness from its use, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment. An HDE must, however, demonstrate that no comparable device is available to treat or diagnose the disease or condition, and that the device could not otherwise be brought to market unless it is granted HUD status.

An approved HDE authorizes marketing of the HUD for clinical use; however, clinical use of the device is limited to the indication specified in the product labeling. Also, a HUD may only be used in facilities that have established a local institutional review board (IRB) to oversee the clinical introduction and use of the device within that institution. Once a device has received an HUD designation from the FDA, whether for treatment, diagnosis, or research, the use of an HUD must be reviewed and approved by the IRB.

2. POLICY AND ASSOCIATED PROCEDURES

2.1. The IRB’s Role in the Use of a Humanitarian Use Device (HUD)

Pursuant to 21 CFR 814.124(a), the FDA requires IRB review and approval before an HUD is used, as well as continuing review of the use of the HUD. The IRB must ensure that the proposed use is within the FDA-approved indication and that the use of the device does not exceed the scope of the FDA’s approval.

2.2. Determining whether the HUD Use Is Part of a Clinical Investigation

2.2.1. The level of IRB review and the specific responsibilities of the IRB regarding an HUD use will differ depending on whether the use is part of a clinical investigation.
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2.2.2. An HUD use is not part of a clinical investigation if the HUD will be used for its HDE-approved indication(s) and safety and effectiveness data will not be collected for the purpose of supporting a PMA application for the HDE-approved indication.

2.2.3. An HUD use will be considered to be part of a clinical investigation if one of the following are true:

2.2.3.1. Safety and effectiveness data will be collected for the purpose of supporting a PMA application for the HDE-approved indication; or

2.2.3.2. The HUD will not be used for its HDE-approved indication(s).

2.2.4. If an HUD use is considered part of a clinical investigation, the project is considered research and the investigator must follow all policies and procedures applicable to human subjects research.

2.3. IRB Review of an HUD Use that Is Not Part of a Clinical Investigation

2.3.1. The use of an HUD must be initially reviewed at a convened IRB meeting and approved before the device can be used. To facilitate initial review, the physician (investigator) must create and submit an HUD study via KC IRB and attach the following documentation:

2.3.1.1. The HUD manufacturer’s product labeling, clinical brochure, and/or other pertinent manufacturer informational materials; and

2.3.1.2. The FDA HDE approval letter.

2.3.2. Informed consent and authorization are not required.

2.3.3. The IRB must conduct continuing review of the use of the HUD; however, review of HUD uses that are not part of a clinical investigation will be conducted via the expedited procedure.

2.3.3.1. Continuing review of the use of an HUD must occur within the appropriate time frame as specified by the IRB or the use of the HUD must cease until such time that it can be reviewed.

2.3.3.2. The physician-investigator should track and/or be prepared to report the following at the time of renewal:

2.3.3.2.1. The number of patients who received the HUD for all physicians/investigators listed on the protocol since the last review.

2.3.3.2.2. All unanticipated problems, including serious adverse events and deviations since the last review. **Note:** HUD
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physicians/investigators must comply with the IU SOP for Reportable Events.

2.3.3.2.3. Summary of actual benefits experienced by enrolled HDE patients.

2.3.3.2.4. Any recent published/presented literature having a significant impact on the HUD’s use and well-being of patients.

2.3.3.2.5. Any audits conducted since the last review from a federal agency that identified significant deviations or problems.

2.3.3.2.6. Any new conflicts of interest that have arisen since the last review.

2.4. IRB Review of an HUD Use that Is Part of a Clinical Investigation (Investigational Use)

2.4.1. The investigational use of an HUD must be initially reviewed at a convened IRB meeting and approved before the device can be used. To facilitate initial review, the physician (investigator) must create and submit a full Board study via KC IRB and attach the following documentation:

2.4.1.1. The HUD manufacturer’s product labeling, clinical brochure, and/or other pertinent manufacturer informational materials;

2.4.1.2. The FDA HDE approval letter; and

2.4.1.3. Additional applicable documents normally required for review of a full Board study, including the research informed consent and HIPAA authorization form.

2.4.2. If the HUD use is part of a clinical investigation, a separate research consent form must be submitted for IRB review (refer to the FDA’s “IRB Review of HUDs” figure below). Since the HUD is approved for clinical use by the FDA, words such as “research” or “study” should be avoided. The consent form should be generally modeled after other clinical consent forms for invasive procedures and should include the following:

2.4.2.1. A description of the HDE/HUD approval process (e.g., for use in fewer than 4,000 individuals per year; no comparable device is available).

2.4.2.2. A description of the HUD and how this device will be used in the clinical setting. Based on this description, it should be clear to the patient why she/he is a candidate for the use of this device.

2.4.2.3. A discussion of possible risks, side effects, and/or adverse events associated with the HUD and its proposed clinical use.
2.4.2.4. A discussion of the possible benefits associated with the clinical use of the HUD.

2.4.2.5. A discussion of any alternative treatments or procedures (if any) that the patient may wish to consider in lieu of clinical use of the HUD.

2.4.2.6. Voluntary Consent statement(s) with patient signature and date lines.

2.4.2.7. Physician Certification statement with physician signature and date lines.

2.4.3. The IRB must conduct continuing review of the use of the HUD. When the use of the HUD is part of a clinical investigation, the review will be conducted at a convened IRB meeting.

2.4.3.1. Continuing review of the use of an HUD must occur within the appropriate time frame as specified by the IRB or the use of the HUD must cease until such time that it can be reviewed.

2.4.3.2. The physician-investigator should track and/or be prepared to report the following at the time of continuing review:

2.4.3.2.1. The number of patients who received the HUD for all physicians/investigators listed on the project since the last review.

2.4.3.2.2. All unanticipated problems, including serious adverse events and deviations since the last review. Note: HUD physicians/investigators must comply with the IU SOP for Reportable Events.

2.4.3.2.3. Summary of actual benefits experienced by enrolled HDE patients.

2.4.3.2.4. Any recent published/presented literature having a significant impact on the HUD’s use and well-being of patients.

2.4.3.2.5. Any audits conducted since the last review from a federal agency that identified significant deviations or problems.

2.4.3.2.6. Any new conflicts of interest that have arisen since the last review.

2.5. Modifications to the HUD or Device Labeling
2.5.1. After the FDA has granted approval for use of the HUD for additional clinical indications, IRB approval is required before the HUD can be used for the additional indications.

2.5.2. The physician-investigator should:

2.5.2.1. Submit an amendment to the existing study via the KC IRB system describing the modifications to the device, the proposed clinical use of the device, and the rationale for such modification(s) and attach:

2.5.2.1.1. A copy of the FDA’s approval of the modification.

2.5.2.1.2. A copy of the HUD manufacturer’s amendments to the HUD product labeling, clinical brochure, and/or other pertinent manufacturer information materials corresponding to the requested modification(s).

2.5.2.1.3. A copy of the revised clinical use statement and clinical consent form with the modifications highlighted.

2.6. Off-Label Use of an HUD in Emergency or Compassionate Situations

2.6.1. It is recognized that there may be circumstances in which off-label use of an HUD may be necessary to save the life or protect the well-being of a patient. When this situation arises, the physician-investigator should:

2.6.1.1. Determine if the situation meets the requirements for a one-time emergency use. To make this determination and for additional information on how to proceed, the procedures outlined in the IU SOP on Emergency Use of Investigational Agents should be followed.

2.6.1.2. If the situation use does not qualify for the one-time emergency procedure, a new study application must be completed and submitted according to the process outlined in the IU SOP on Emergency Use of Investigational Agents. In emergency situations, the Human Subjects Office may convene an emergency IRB meeting to consider the emergency use.

2.6.2. Prior to requesting emergency or compassionate use from the IRB, the following should occur:

2.6.2.1. The physician-investigator must obtain authorization for the proposed off-label use of the HUD from the device manufacturer (i.e., HDE holder).

2.6.2.2. The device manufacturer (i.e., HDE holder) must obtain approval from the FDA for the off-label use of the HUD.

2.7. Overview of IRB Review of HUDs
3. ADDITIONAL POLICIES AND PROCEDURES

3.1. Research Subject to FDA Regulations

N/A

3.2. Research Subject to HIPAA Regulations

N/A

3.3. Research Subject to VA Regulations

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3.4. Research Subject to Other Regulations

3.4.1 Research Subject to Department of Defense (DoD) Regulations
N/A

3.4.2 Research Subject to Department of Education (ED) Regulations
N/A

3.4.3 Research Subject to Department of Justice (DOJ) Regulations
N/A
1. INTRODUCTION

The ethical conduct of research on human subjects is based upon the voluntary consent of the subjects who have been appropriately informed of the study’s risks and benefits. Informed consent is an ongoing process that provides (a) the prospective subject or the subject’s legally authorized representative (LAR) with adequate information pertaining to the research study; (b) sufficient opportunity to consider aspects of the research, including the risks and benefits, and whether to participate; and (c) the opportunity for the subject to ask questions and receive answers to those questions, thus minimizing the possibility of coercion or undue influence. Unless waived by the Institutional Review Board (IRB), the informed consent process must be appropriately performed and documented. In clinical research, documentation must be recorded in the source documents for each subject. It is the responsibility of the Principal Investigator (PI) to obtain IRB approval or waiver for the informed consent process to be used and to ensure that all federal and state regulations and IU policies have been satisfied in the language of the informed consent documents and by the process, and that any informed consent documents have been approved by IRB prior to being presented to potential subjects.

2. POLICIES AND PROCEDURES

2.1. Pursuant to 45 CFR 46.116 and 21 CFR 50.20, unless waived or altered, no investigator may involve a human being as a subject in research unless the investigator has obtained the legally effective informed consent of the subject or the subject’s LAR. If the informed consent process will involve an LAR, the IRB must approve an informed consent process for obtaining surrogate consent. An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether to participate and that minimizes the possibility of coercion or undue influence. The information that is given to the subject or the representative (whether orally or in writing) shall be in language understandable to the subject or the representative. No informed consent, whether oral or written, may include or have the appearance of including any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject’s legal rights, or that releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence.

2.2. The Informed Consent Process. Informed consent is more than just a signature on a form; it is a process of information exchange that may include, in addition to reading and signing the informed consent document, subject recruitment materials, verbal instructions, question/answer sessions, and measures of subject understanding. The responsibility for ensuring that the informed consent process is adequate is shared by research sponsors, investigators, and the IRB. The following should be considered when seeking consent from a subject to a research study:
2.2.1 The consent process begins when a potential research subject is initially contacted. This means that the use of direct advertising is the start of the informed consent and subject selection process.

2.2.2 Giving the subject adequate information concerning the research in language that is as nontechnical as possible (eighth grade language or lower, as appropriate for the subject population);

2.2.3 Providing ample time and opportunity for the subject or the subject’s LAR to inquire about the details of the research and to decide whether to participate in the research, as well as to consider other available options, if any;

2.2.4 Responding to subject’s or the subject’s LAR’s questions to his/her/their satisfaction;

2.2.5 Ensuring, to the degree possible, that the subject has comprehended the information provided about the research;

2.2.6 Obtaining the subject’s or the subject’s LAR’s voluntary consent;

2.2.7 Documenting that the process has occurred;

2.2.8 Continuing the informed consent process throughout the subject’s participation in the study.

2.3. **The Informed Consent Document.** Pursuant to 45 CFR 46.116 and 21 CFR 50.25, certain basic elements must be included in any informed consent document that is presented to potential research subjects. Additional elements should be included, when appropriate. See the specific IU IRB Guidance document for more details. Basic elements required in the informed consent include:

2.3.1 A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject’s participation, and a description of the procedures to be followed, including identification of any procedures that are experimental;

2.3.2 A description of any reasonably foreseeable risks or discomforts to the subjects. If relevant animal data are available, the significance should be explained to potential subjects;

2.3.3 A description of any benefits to the subject or to others which may reasonably be expected from the research;

2.3.4 A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;

2.3.5 A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained, including a statement that notes the
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possibility that specific regulatory authorities (e.g., HHS, FDA, ED, DoD, DOJ, as applicable) may inspect the records;

2.3.6 For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;

2.3.7 An explanation of whom to contact for answers to pertinent questions about the research and research subjects’ rights, whom to contact to discuss problems, concerns, and questions about a research study, obtain information, and offer input, and whom to contact in the event of a research-related injury to the subject; and

2.3.8 A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled. Language limiting the subject’s right to withdraw from the study is not permitted.

Note: If a subject wishes to discontinue participation in the research and the investigator would like to continue to follow the subject’s health and collect clinical data from his/her medical records, a separate IRB-approved informed consent containing all required elements must be developed and presented to the subject at the time of his/her withdrawal from the study requesting this follow-up to be done. The subject must give permission (i.e., sign this separate informed consent document) in order for clinical data to be collected.

2.4. When appropriate and pursuant to 45 CFR 46.116(b) and 21 CFR 50.25(b), one or more of the following additional elements are required in the informed consent:

2.4.1 A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) that are currently unforeseeable. If measures to prevent pregnancy should be taken while in the study, that should also be explained;

2.4.2 Anticipated circumstances under which the subject’s participation may be terminated by the investigator without regard to the subject’s consent. An unexplained statement that the investigator or sponsor may withdraw subjects at any time does not adequately inform the subjects of anticipated circumstances for such withdrawal. A statement that the investigator may withdraw subjects if they do not “follow study procedures” is not appropriate. Subjects are not in a position to know all the study procedures. Subjects may be informed, however, that they may be withdrawn if they do not follow the instructions given to them by the investigator;

2.4.3 Any additional costs to the subject that may result from participation in the research;
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2.4.4 For studies involving payment for subject participation, a payment statement explaining details and any conditions of payment;

2.4.5 The consequences of a subject’s decision to withdraw from the research and procedures for orderly termination of participation by the subject. An unexplained statement that the subject will be asked to submit to tests prior to withdrawal does not adequately inform the subject why the tests are necessary for the subject’s welfare.

2.4.6 A statement that significant new findings developed during the course of the research that may relate to the subject’s willingness to continue participation will be provided to the subject; and

2.4.7 The estimated enrollment (approximate number) of subjects that investigators need for the research.

2.5. The IRB follows applicable federal, state, or local laws, which may require additional information to be disclosed in order for informed consent to be legally effective.

2.6. Additionally, the IRB may require that information in addition to that specifically required by applicable regulation be given to subjects when, in the IRB’s judgment, the information would meaningfully add to the protection of the rights and welfare of subjects.

2.6.1 If the IU Conflict of Interest Office or Committee determines that an investigator has a significant financial interest related to a research study, the IRB will require the investigator to disclose the interest(s) to potential subjects by including appropriate language in the informed consent statement.

2.7. For studies conducted or supported by the U.S. Public Health Service (PHS) involving HIV testing, PHS requires that subjects whose test results are associated with personal identifiers must be informed of their own test results and provided the opportunity to receive appropriate counseling unless the situation calls for an exception under special circumstances.

2.8. For studies involving genetic information, the informed consent should include information regarding the protections provided by the Genetic Information Nondiscrimination Act (GINA). See the IU SOP for Genetic Information Nondiscrimination Act (GINA) for more information.

2.9. Documentation of Informed Consent.

2.9.1 Pursuant to 45 CFR 46.117(a), and except as provided at 45 CFR 46.117(c), informed consent shall be documented by the use of a written consent document approved by the IRB and signed and dated by the subject or the subject’s LAR at the time of consent. The form may be read to the subject or the subject’s LAR, but in any event, the investigator shall give either the subject or the representative adequate opportunity to read it before it is signed. A copy shall be given to the person signing the form.
2.9.2 Pursuant to 45 CFR 46.117(c) and 21 CFR 56.109(c)(1), the IRB may waive the requirement for the investigator to obtain a signed consent document for some or all subjects if it finds and documents:

2.9.2.1 That the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject’s wishes will govern; or

2.9.2.2 That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

2.9.3 In cases in which the documentation requirement for informed consent is waived, the IRB may require the investigator to provide subjects with a written document that includes all elements of an informed consent document (unless otherwise waived by the IRB), which the IRB must prospectively review and approve.

2.9.4 The investigator may request these alterations or waivers during the IRB submission process. The information provided will be used by the IRB when considering this request.

2.10. **Required Informed Consent Document Signatures**

2.10.1 The subject (or subject’s LAR) must sign a copy of the stamped, IRB-approved informed consent document via physical or verified signature before any study-related procedures are initiated.

2.10.1.1 If the subject is unable to provide a signature, they should make a mark on the informed consent document and the study team should document the circumstances.

2.10.1.2 If the subject is unable to make a mark, an impartial witness should witness the documentation process and sign the consent document.

2.10.2 In addition to signing the consent document, the subject (or LAR) must enter the date of signature on the consent document to permit verification that consent was actually obtained before the subject began participation in the study. The subject’s medical records/case report form should document that the consent process occurred prior to participation in the research.

2.10.3 The person conducting the consent interview must also sign and date the informed consent document as the “person obtaining consent.” The signature of the PI is not required on the consent document, unless he/she is the person conducting the consent interview.

2.10.4 There may be situations when the subject wishes to take the consent document home in order to review it and/or further consider participation in the research study before signing. In fact, all subjects should be encouraged to do so. In
these situations, the person conducting the consent interview (i.e., explaining the details of the study) may sign the consent document at that time, signifying that the consent interview took place. Once the subject has decided to participate, he/she (or LAR) should sign the consent document at that time. Thus, it is possible for the signature date of the person obtaining consent to precede that of the subject.

2.11. **Revisions to the Informed Consent Document**

2.11.1 Although the PI is ultimately responsible for assuring that the written consent document and any other written information to be provided to subjects is revised whenever important new information becomes available that may be relevant to the subject’s willingness to participate, he/she may delegate this responsibility to appropriate members of the research team. Any such revisions must receive IRB approval prior to use.

2.11.2 When revised informed consent documents have been approved by the IRB, newly enrolled subjects must sign this new approved version of the consent document.

2.11.3 While some changes to the informed consent document do not require currently enrolled subjects to re-consent, such as minor changes that do not affect the risk/benefit ratio, there are some situations that do require currently enrolled subjects to re-consent, such as after the discovery of a previously unknown serious side effect. When an already enrolled subject re-consents using a new informed consent document, a note should be made in the subject’s record. Additionally, the original signed new consent document must be retained in the study records and a copy provided to the subject (or LAR). Any previously signed consent documents should be retained and not discarded.

2.11.4 In cases where subjects have completed active study or follow-up procedures and new safety information is discovered that may affect a subject’s participation or long-term risks from the treatment, the subject must be informed of this new information. This may be accomplished through re-consenting subjects with a revised consent document that explains this new information or by other methods of notification approved by the IRB. The timeliness of informing subjects and/or re-consenting them will depend on the seriousness of the new information.

2.12. **Informed Consent Procedures for Non-English-Speaking Subjects**

2.12.1 Pursuant to 45 CFR 46.116 and 21 CFR 50.20, information that is given to a subject or a subject’s representative shall be in language understandable to the subject or the representative. Thus, when speaking to a potential subject who speaks English, the consent interview shall be conducted in English and the consent document shall be written in English. Likewise, when speaking to a potential subject who does not speak English, the consent interview shall be conducted in a language understandable to the individual and the consent document shall be written in a language understandable to the individual.
2.12.2 If the investigator anticipates that non-English-speaking individuals will likely be enrolled in the study, plans for language-appropriate consent procedures should be considered and described in the IRB submission.

2.12.2.1 In some circumstances, a non-English consent document may be required. The IRB must approve all consents, including non-English versions. In these circumstances, the IRB will require certification that the translated documents are correct or documentation that the non-English versions have been reviewed by an expert in the required language.

2.12.3 If a non-English-speaking subject is unexpectedly encountered, investigators should carefully consider the ethical and legal implications of enrolling a subject when a language barrier exists. If, after careful consideration, the investigator believes it would be in the best interest of the potential subject to enroll in the study, the subject may still be enrolled as long as the consent interview is conducted in a language understandable to the subject with the use of a translator or other appropriate individual, and a consent document in a language understandable to the subject is available to provide to the subject.

2.12.3.1 The informed consent process must be documented using the IRB-approved short form written consent document and following the procedures below:

2.12.3.1.1 Appropriate short form documents in various languages are available on the IU Human Subjects Office website. Each document states that the elements of informed consent required by §46.116 have been presented orally to the subject or the subject’s LAR.

2.12.3.1.2 A written summary embodying the basic and required additional elements of disclosure must be available for use during the oral presentation.

2.12.3.1.3 There shall be a witness to the oral presentation. The witness must be conversant in both English and the language of the subject. The translator may serve as the witness.

2.12.3.1.4 The subject or the subject’s LAR will sign the short form consent document.

2.12.3.1.5 The witness will sign both the short form consent document and a copy of the summary.

2.12.3.1.6 The person actually obtaining consent will sign a copy of the summary.
2.12.3.1.7 A copy of the signed short form consent document and summary will be given to the subject or the subject’s LAR.

2.12.3.2 The informed consent process shall be documented in the subject’s records. The translator or other appropriate individual should be part of the ongoing communication throughout the research study and should be conversant in both English and the language of the subject.

2.12.3.3 If such a situation occurs, it shall be reported to the IRB at time of renewal. The IRB will consider the circumstances of the subject’s enrollment and determine the appropriateness of requiring the investigator to develop a language-appropriate consent document for future enrollment purposes.

2.13. **Informed Consent Procedures For Subjects Who Are Unable to Read the Consent Document**

2.13.1 Subjects who can understand and comprehend spoken English but are unable to read the informed consent document for any reason (e.g. illiteracy, blindness or diminished vision, dyslexia, unable to obtain a copy of the consent document for review, etc.) may be enrolled in a study; however, special care must be taken to ensure the individual is able to understand the concepts of the study and evaluate the risks and benefits of being in the study when it is explained orally.

2.13.2 The study team must present the information orally and document the circumstances.

2.13.3 An impartial witness must observe the entire consent process and sign the consent document. Although not required, a video recording of the consent interview is recommended.

2.14. **Informed Consent Procedures Via Telephone**

2.14.1 There are situations when the informed consent process may be conducted over the telephone. In these situations, the person obtaining consent must document that the informed consent process took place by making appropriate notation regarding the process in the proper files.

2.14.2 If a waiver of documentation of informed consent has not been approved by the IRB, the person discussing the research study with the potential subject must sign and date the consent document prior to sending it to the potential subject. Once the subject receives, signs, and returns the informed consent document to the study site, the document should again be signed and dated by the appropriate member of the research team who receives the document. Research-related intervention may not begin until the signed informed consent document is received by the study team.

2.15. **Informed Consent Procedures Via Fax or Email**
2.15.1 There are situations when obtaining informed consent from subjects via fax or email may be appropriate. This is acceptable in situations where the informed consent process has already been appropriately conducted in person. For example, it is acceptable for the informed consent process to take place in person, for the potential subject to then take the consent document home in order to consider participation, and then for the subject to sign and fax or email the informed consent document back to the research site. In this case, the person obtaining the consent should sign the informed consent document and make appropriate notes in the subject’s records upon completion of the informed consent discussion. The subject may then fax or email a signed copy of the informed consent document to the research site (preferably to the interviewer and/or investigator). Upon receipt, the PI or appropriate designee should again sign and date the document as acknowledgement of receipt and make appropriate notations in the subject’s record. The subject may then fax or email a signed copy of the informed consent document to the research site (preferably to the interviewer and/or investigator). Upon receipt, the PI or appropriate designee should again sign and date the document as acknowledgement of receipt and make appropriate notations in the subject’s record. The subject should still return the signed original informed consent document (either at the next visit or via postal mail) to the research site at his/her earliest opportunity. The appropriate recipient of the signed original informed consent document should sign and date the document, file it with the faxed or emailed copy, and make appropriate notes in the subject’s record. The notes in the file coinciding with the dates and signatures on the informed consent documents provide the source documentation that confirms and explains how the process occurred.

2.16. **Informed Consent Procedures with Special Populations.** Because of the special vulnerability of certain populations of subjects (including children, prisoners, pregnant women, and individuals lacking consent capacity), federal regulations, state and local laws, and institutional policies require additional protections regarding their consent to participate in a research study. Please see the IU SOP on Vulnerable Populations for guidance on the additional consent requirements when involving these vulnerable populations in research.

2.17. **Alteration or Waiver of Informed Consent**

2.17.1 Pursuant to 45 CFR 46.116(c), the IRB may approve a consent procedure that does not include, or that alters, some or all of the elements of informed consent set forth under Section 2.3 The Informed Consent Document above, or may waive the requirement to obtain informed consent provided the IRB finds and documents that:

2.17.1.1 The research or demonstration project is to be conducted by or subject to the approval of state or local government officials, and is designed to study, evaluate, or otherwise examine (a) public benefit of service programs; (b) procedures for obtaining benefits or services under those programs; (c) possible changes in or alternatives to those programs or procedures; or (d) possible changes in methods or levels of payment for benefits or services under those programs; and

2.17.1.2 The research could not practicably be carried out without the waiver or alteration.
2.17.2 Pursuant to 45 CFR 46.116(d), the IRB may approve a consent procedure that does not include, or that alters, some or all of the elements of informed consent set forth in 2.3 above, or may waive the requirement to obtain informed consent provided the IRB finds and documents that:

2.17.2.1 The research procedure involves no more than minimal risk to the subjects;

2.17.2.2 The waiver or alteration will not adversely affect the rights and welfare of the subjects;

2.17.2.3 The research could not practicably be carried out without the waiver or alteration (Note: The IRB typically considers face-to-face interaction between the PI or other member of the research team and the subject to practicably enable the informed consent process to take place, and thus would likely not grant a waiver of the informed consent process); and

2.17.2.4 Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

2.17.3 The informed consent requirements in this policy are not intended to preempt any applicable federal, state, or local laws that require additional information to be disclosed in order for informed consent to be legally effective.

2.17.4 Nothing in this policy is intended to limit the authority of a physician to provide emergency medical care, to the extent the physician is permitted to do so under applicable federal, state, or local law.

3. ADDITIONAL POLICIES AND PROCEDURES

3.1. Research Subject to FDA Regulations

3.1.1 Exception from Informed Consent Requirements for in vitro diagnostic device studies using leftover human specimens that are not individually identifiable. Pursuant to FDA guidance titled Informed Consent for In Vitro Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable (issued April 25, 2006), studies which use leftover samples for FDA-regulated in vitro diagnostic (IVD) device investigations may be conducted without informed consent if certain criteria are satisfied. For clinical investigations involving leftover human specimens, informed consent does not provide additional protection to human subjects and/or subjects can be adequately safeguarded through less burdensome measures. As such, the FDA has indicated that it will not enforce the informed consent requirements of 21 CFR 56, if the criteria below (3.1.1.2 – 3.117) are met. Investigators may request and the IRB may give permission for investigators to conduct such studies without obtaining informed consent.

3.1.1.1 The investigation meets the Investigational Device Exemption criteria at 21 CFR 812.2(e)(3).
3.1.1.2 The study uses leftover specimens, that is, remnants of specimens collected for routine clinical care that would have been discarded. The study may also use specimens obtained from specimen repositories or leftover specimens that were previously collected for other research purposes.

3.1.1.3 The specimens are not individually identifiable, i.e., the identity of the subject is not known to and may not readily be ascertained by the investigator or any other individuals associated with the investigation, including the sponsor. If the specimen is coded, it will be considered to be not individually identifiable if neither the investigator(s) nor any other individuals associated with the investigation or the sponsor can link the specimen to the subject from whom the specimen was collected, either directly or indirectly through coding systems.

3.1.1.4 The specimens may be accompanied by clinical information as long as this information does not make the specimen source identifiable to the investigator or any other individual associated with the investigation, including the sponsor.

3.1.1.5 The individuals caring for the subjects are different from and do not share information about the subject with those conducting the investigation.

3.1.1.6 The specimens are provided to the investigator(s) without identifiers and the supplier of the specimens has established policies and procedures to prevent the release of personal information.

3.1.1.7 The study has been reviewed by an IRB in accordance with 21 CFR Part 56, except as described in section 7 of this guidance document.

3.1.2 **Exception from Informed Consent Requirements for Planned Emergency Research.** Pursuant to 21 CFR 50.24, the IRB may approve a proposed clinical investigation without requiring that informed consent of all research subjects be obtained for a limited class of research activities involving human subjects who are in need of emergency medical intervention, but who cannot give informed consent because of their life-threatening medical condition, and who do not have a legally authorized person to represent them. See the IU SOP on Emergency Use of Investigational Test Articles for additional information.

3.1.3 **Exception from Informed Consent Requirements for Emergency Use.** Pursuant to 21 CFR 50.23(a), an exception to the informed consent requirements for a single subject may be appropriate if the subject is in a life-threatening situation for which no standard acceptable treatment is available and in which there is not sufficient time to obtain appropriate IRB approval. See the IU SOP on Emergency Use of Investigational Test Articles for additional information.
3.1.4 **Waiver of Documentation of Informed Consent for Minimal Risk Research.** Pursuant to 21 CFR 56.109(c), the IRB may, for some or all subjects, waive the requirement that the subject or the subject’s LAR sign a written consent form if it finds that the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside the research context.

3.1.5 **When a Subject Withdraws from a Clinical Trial.** Data collected on a subject to the point of the subject’s withdrawal from a study remains part of the study database and may not be removed. The consent document cannot give the subject the option of having data removed. If a participant withdraws from the interventional portion of a study and does not consent to continued follow-up of associated clinical outcome information, the researcher must not access for purposes related to the study the participant’s medical record or other confidential records, but may view the 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.

3.1.6 **Notice added for research required to be listed on ClinicalTrials.gov.** Studies approved after March 7, 2012 that are required by FDA regulation to be listed on ClinicalTrials.gov are required to have the following statement in the consent: “A description of this clinical trial will be available on http://www.clinicaltrials.gov, as required by U.S. law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.”

3.2. **Research Subject to HIPAA Regulations**

N/A

3.3. **Research Subject to VA Regulations**

3.3.1 The VA consent document must include the following:

3.3.1.1 A statement that in the event of a research-related injury the VA will provide necessary medical treatment.

3.3.1.2 When appropriate, a statement that neither VA research subjects nor their insurance will be charged for any costs related to the research. Certain veterans have to pay co-payments for medical care and services provided by VA; these requirements continue to apply to medical care and services that are not part of the research procedures or interventions.

3.3.1.3 If someone other than the investigator conducts the interview and obtains consent, policies and procedures require the investigator to formally delegate this responsibility and require the person so
delegated to have received appropriate training to perform this activity.

3.3.1.4 Information describing any photographs, video, and/or audio recordings to be taken or obtained for research purposes, how the photographs, video, and/or audio recordings will be used for the research, and whether the photographs, video, and/or audio recordings will be disclosed outside VA.

3.3.1.4.1 An informed consent to take a photograph, video, and/or audio recording cannot be waived by the IRB.

3.3.1.4.2 The consent for research does not give legal authority to disclose the photographs, video, and/or audio recordings outside VA. This requires a HIPAA authorization.

3.3.2 The IRB approval must be documented on the consent form indicating the date of approval.

3.3.3 Consent may be obtained electronically so long as the informed consent process meets all applicable requirements; and

3.3.3.1 Authentication controls on electronic consent provide reasonable assurance that such consent is rendered by the proper individual; and

3.3.3.2 The subject dates the consent as is typical or the software provides the current date when signed.

3.4. Research Subject to Other Regulations

3.4.1 Research Subject to Department of Defense (DoD) Regulations

3.4.1.1 The IRB must determine that the disclosure includes that provisions for research-related injury follow the requirement of the DoD component.

3.4.1.2 If the research subject meets the definition of “experimental subject,” a waiver of the consent process is prohibited unless a waiver is obtained from the Assistant Secretary of Defense for Research and Engineering. If the research subject does not meet the definition of experimental subject, the IRB may waive the consent process unless the research is classified.

3.4.2 Research Subject to Department of Education (ED) Regulations

3.4.2.1 Research sponsored by the Department of Education must comply with the Family Educational Rights and Privacy Act (FERPA) in regards to granting parental/student consent to release student confidentiality information.

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records for research. An educational agency or institution may disclose personally identifiable information from an education record of a student without consent if the disclosure is to organizations conducting studies for or on behalf of educational agencies or institutions to:

3.4.2.1.1 Develop, validate, or administer predictive tests;

3.4.2.1.2 Administer student aid programs;

3.4.2.1.3 Improve instruction.

3.4.2.2 A school district or postsecondary institution that uses this exception is required to enter into a written agreement with Indiana University (IU) or the investigator conducting the research that specifies:

3.4.2.2.1 The determination of the exception;

3.4.2.2.2 The purpose, scope, and duration of the study;

3.4.2.2.3 The information to be disclosed;

3.4.2.2.4 That information from education records may be used only to meet the purposes of the study stated in the written agreement and must contain the current requirements in 34 CFR 99.31(a)(6) on re-disclosure and destruction of information.

3.4.2.2.5 That the study will be conducted in a manner that does not permit personal identification of parents and students by anyone other than representatives of IU with legitimate interests.

3.4.2.2.6 That IU is required to destroy or return all personally identifiable information when no longer needed for the purposes of the study.

3.4.2.2.7 The time period during which IU must either destroy or return the information.

3.4.2.3 Education records may be released without consent under FERPA if all personally identifiable information has been removed, including:

3.4.2.3.1 The student’s name and other direct personal identifiers, such as the student’s Social Security number or student number;

3.4.2.3.2 Indirect identifiers, such as the name of the student’s parent or other family members, the student’s or
family’s address, personal characteristics or other information that would make the student’s identity easily traceable, and date and place of the birth mother’s maiden name;

3.4.2.3.3 Biometric records, including one or more measurable biological or behavioral characteristics that can be used for automated recognition of an individual, including fingerprints, retina and iris patterns, voiceprints, DNA sequence, facial characteristics, and handwriting;

3.4.2.3.4 Other information that alone or in combination is linked or linkable to a specific student in any way that would allow a reasonable person in the school community who does not have personal knowledge of the relevant circumstances to identify the student with reasonable certainty.

3.4.2.4 Investigators at IU who are conducting research directly related to improving instruction, learning, or other operations of the university but who plan to publish their research results in aggregate and de-identified form may access student education records without consent as “school officials with a legitimate educational interest,” provided that the university’s Annual Notification of FERPA Rights for students appropriately identifies such researchers within its definition of “school officials with a legitimate educational interest.”

3.4.2.5 For other exceptions to consent to release student records for research, refer to the IU Release of Student Information Policy available at [http://www.policies.iu.edu/policies/categories/academic-faculty-students/university-student-services-systems/USSS-05-release-student-information.shtml](http://www.policies.iu.edu/policies/categories/academic-faculty-students/university-student-services-systems/USSS-05-release-student-information.shtml), or contact the appropriate campus registrar’s office.

3.4.2.6 For research funded by or sponsored by the U.S. Department of Education, no student shall be required as part of any research project to submit without prior consent to surveys, psychiatric examination, testing or treatment, or psychological examination, testing, or treatment, in which the primary purpose is to reveal information concerning one or more of the following:

3.4.2.6.1 Political affiliations;

3.4.2.6.2 Mental and psychological problems potentially embarrassing to the student or his or her family;

3.4.2.6.3 Sex behavior and attitudes;
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3.4.2.6.4 Illegal, anti-social, self-incriminating, and demeaning behavior;

3.4.2.6.5 Critical appraisals of other individuals with whom the student has close family relationships;

3.4.2.6.6 Legally recognized privileged and analogous relationships, such as those of lawyers, physicians, and ministers;

3.4.2.6.7 Religious practices, affiliations, or beliefs of the student or student’s parent;

3.4.2.6.8 Income, other than that required by law to determine eligibility for participation in a program or for receiving financial assistance under a program.

3.4.2.7 Prior consent means either prior consent of the student, if the student is an adult or emancipated minor or prior written consent of the parent or guardian, if the student is an unemancipated minor. Schools and contractors obtain prior written parental consent before minor students are required to participate in any ED-funded survey, analysis, or evaluation.

3.4.2.8 For research not funded by the U.S. Department of Education, the IRB must verify compliance with ED regulations that schools are required to develop and adopt policies in conjunction with parents regarding the following:

3.4.2.8.1 The right of parents to inspect, upon request, a survey created by a third party before the survey is administered or distributed by a school to students.

3.4.2.8.2 Arrangements to protect student privacy in the event of the administration of a survey to students, including the right of parents to inspect, upon request, the survey, if the survey contains one or more of the same eight items of information listed above.

3.4.2.8.3 The right of parents to inspect, upon request, any instructional material used as part of the educational curriculum for students.

3.4.2.8.4 The administration of physical examinations or screenings that the school may administer to students.

3.4.3 Research Subject to Department of Justice (DOJ) Regulations

3.4.3.1 For research funded by the National Institute of Justice:
3.4.3.1.1 Consent forms must include the name(s) of the funding agency(ies).

3.4.3.1.2 Subjects should be informed that private, identifiable information will be kept confidential and will be used only for research and statistical purposes. If, due to sample size or some unique feature, the identity of the individual cannot be maintained, the subjects need to be explicitly notified. If the researcher intends to disclose any information, subjects must be explicitly informed what information would be disclosed, under what circumstances, and to whom. Subjects also must be informed of any risks that may result from this disclosure and must explicitly provide written consent prior to participating in the research.

3.4.3.1.3 The confidentiality statement on the consent document must state that confidentiality can be broken only if the subject reports immediate harm to subjects or others.

3.4.3.1.4 Under a privacy certificate, investigators and research staff do not have to report child abuse unless the subject signs another consent form to allow child abuse reporting.

3.4.3.2 For research conducted within the Bureau of Prisons, the following additional elements of disclosure are required:

3.4.3.2.1 Identification of the investigators.

3.4.3.2.2 Anticipated uses of the results of the research.

3.4.3.2.3 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).

3.4.3.2.4 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.

3.4.3.2.5 A statement that participation in the research project will have no effect on the inmate subject’s release date or
parole eligibility.
1. INTRODUCTION

Investigators share with the Institutional Review Board (IRB) and Funding Organizations the responsibility for ensuring that research with human subjects is properly conducted such that participants are adequately protected. The environment in which investigators conduct research and the type of research they conduct influence their roles and responsibilities. Competent, informed, conscientious, compassionate, and responsible investigators provide the best possible protection for research subjects. Additionally, there are many regulatory agencies to guide investigators in the proper conduct of research involving human subjects. Investigators must be properly qualified and trained and have adequate experience to undertake this type of research.

The Principal Investigator (PI) is ultimately responsible for the proper conduct of the research; however, research-related responsibilities may be delegated to co-investigators (key personnel) and/or research personnel (non-key), provided these individuals are appropriately qualified and trained. As such, the responsibilities delineated in the SOP apply to all investigators, unless otherwise specified.

2. POLICIES AND PROCEDURES

2.1. General Responsibilities. Investigators shall:

2.1.1 Make an initial determination of whether an activity meets the definition of human subjects research, and if it does, obtain appropriate IRB approval of the research, including informed consent (or waiver), authorization for the release of health information (or waiver), and other study-related documents, as required. Additional guidance in determining when an activity requires IRB review can be found on the IU Human Subjects Office website or by speaking to an HSO staff member.

2.1.2 Ensure research is conducted according to the investigational plan, any conditions of approval imposed by the IRB, and applicable regulations for protecting the rights, safety, and welfare of human subjects involved in research. This involves ensuring that:

2.1.2.1 The study design protects the safety and welfare of research subjects;

2.1.2.2 The personal dignity and autonomy of the research subjects are respected;

2.1.2.3 Subjects are protected from harm by maximizing anticipated benefits and minimizing possible risks; and

2.1.2.4 The benefits and risks of the research are distributed fairly.
2.1.3 Be familiar and comply with the ethical principles of human subjects research (The Belmont Report, the requirements of applicable federal regulations, the Common Rule (45 CFR 46), applicable state laws, relevant professional standards, institutional policies, and any other applicable regulations, such as the HIPAA Privacy Rule and Security Rule). Compliance with the federal regulations will in no way render inapplicable pertinent state or local laws or regulations that may otherwise be applicable and that provide additional protections for human subjects.

2.1.4 Review and understand the definition of a human subject and when activities are subject to IRB review and/or when to seek guidance.

2.1.5 Review and comply with the relevant IU Standard Operating Procedures (SOPs).

2.1.6 Complete the appropriate IU CITI modules. Refresher modules are required every three (3) years. This requirement is verified for all investigators listed on a new protocol and at the time of the study’s continuing review. Research studies cannot receive final IRB (re)approval until this requirement has been met by all investigators listed in the application.

2.1.7 Complete the applicable IU CITI Good Clinical Practice (GCP) course when performing any interventional clinical research. Refresher training is required every three (3) years. This requirement is verified for all investigators and co-investigators listed on a new interventional protocol and at the time of the study’s continuing review. Research studies cannot receive final IRB (re)approval until this requirement has been met by all investigators and co-investigators listed in the application.

2.1.7.1 For any NIH-funded trials, there is an additional GCP training completion requirement for all clinical trial site staff responsible for the conduct, management, and/or oversight of trials (“Key Personnel” as defined by the IU IRB). This requirement can be met via completion of an applicable GCP class/course, academic training program, or certification from a recognized clinical research professional organization.

2.1.8 Be appropriately qualified and trained according to applicable Human Resources policies, role-related responsibilities, and institutional requirements.

2.1.9 Ensure all investigators are listed appropriately in the KC Protocol and have completed all associated investigator requirements.

2.1.10 Ensure that all research staff are qualified to perform procedures assigned to them, including but not limited to appropriate training, education, expertise, credentials and, when relevant, privileges.

2.1.11 Ensure continuous and timely communication with all members/entities of the research team, including those not under the control of the investigator, such as pathology, nursing, pharmacy, radiology, and counseling, to ensure the proper
Section II: Investigator Responsibilities

conduct of research and subjects protection. Steps should be taken to ensure entities not under the control of the investigator are qualified to perform the delegated task(s).

2.1.12 The PI is responsible for assessing the safety and risk of the research and ensuring an appropriate research oversight plan is in place for monitoring the research. Additional guidance related to safety/risk assessment can be found in the IU SOP for Safety Monitoring Plans.

2.1.13 Ensure appropriate retention and maintenance of research records, including signed informed consent documents, signed release of health information authorization forms and other HIPAA-specific documentation, in accordance with all agency regulations and in a manner which will facilitate reconstruction of study events by the IRB, should the necessity for an audit and/or an in-depth review arise. Additional guidance on record retention and maintenance can be found in the IU SOP for Data Management.

2.1.14 Cooperate fully with and be adequately prepared for all internal and external auditing and monitoring activities, such as those initiated by the research sponsor or a federal agency. See the IU SOP for Auditing Human Subjects Research for additional guidance.

2.1.15 Ensure the quality and authenticity of the research data.

2.1.16 Maintain the privacy of research subjects and the confidentiality of their data. Persons can be wronged even if they are not physically harmed, such as if sensitive or embarrassing personal information is made public, either intentionally or unintentionally. Thus, a breach of subject confidentiality is considered a significant risk. The study design should adhere to these principles. Additional guidance related to privacy and confidentiality can be found in the IU SOP for Confidentiality and Privacy.

2.1.17 Ensure that all study subjects meet the inclusion and exclusion criteria set forth by the study protocol.

2.1.18 Notify subjects of any significant new findings during the study that may affect their willingness to participate.

2.1.19 Respond appropriately to questions, concerns, complaints, or requests for information that come from potential subjects, subjects in the recruitment process, current research subjects, and/or past research subjects.

2.1.19.1 If a question, concern, complaint, or request is made from a subject, and the investigator cannot readily supply an answer or resolution, the subject should be given a short time frame in which to receive a reply. During this time, the investigator may obtain necessary information from other research staff, department heads, institutional administrators, HSO office, or others as needed to address the issue.
2.1.19.2 In situations where a subject is asking about his/her rights as a research participant, the investigator should provide the subject with the appropriate HSO office telephone number to call.

2.1.19.3 Subject complaints received in this manner should be reported to the IRB at the time of renewal, unless they require prompt reporting to the IRB as per the IU SOP for Reportable Events.

2.1.20 Ensure that appropriate resources are available to protect subjects, including adequate time to conduct and complete the research, adequate number of qualified staff, adequate facilities, access to a population that will allow recruitment of the necessary number of subjects, and availability of medical or psychosocial resources that subjects may need as a consequence of the research. A research study should not commence without ensuring adequate resources are available and should stop if resources become unavailable. If a research study is stopped for this reason, appropriate individuals should be contacted, such as pharmacy, IRB, and department head, depending on the resource issue that caused the study to be stopped.

2.1.21 Employ the following practices when students will be recruited as subjects:

2.1.21.1 Informed consent for participation must be sought only under circumstances that minimize the possibility of coercion or undue influence.

2.1.21.2 The faculty-investigator should include genuinely equivalent alternatives for those students who wish not to participate.

2.1.22 Obtain all appropriate approvals before commencing the research. This includes but may not be limited to IRB, VA Research & Development, Scientific Review Committee (SRC), and departmental approvals.

2.2. Human Subjects Office review. For all items submitted by investigators to the IRB, Human Subjects Office (HSO) staff performs an initial review to ensure regulatory and institutional requirements for submission have been met before referring for IRB review. To fully participate in this process, investigators shall:

2.2.1 Ensure all pre-submission requirements have been met before the item is submitted for IRB review, such as conflict of interest disclosures, CITI training, GCP training (as applicable), SRC approval obtained, etc.

2.2.2 Ensure all required questionnaires are completed and documents are included such as recruitment materials, data collect instruments, etc.

2.2.3 Respond to HSO requests for additional information and/or clarification in a timely manner.

2.2.3.1 HSO staff will communicate with the investigator/research team if additional information is needed prior to IRB review.
2.2.3.1.1 A complete response is expected within two (2) weeks.

2.2.3.1.2 If a response is not received within two (2) weeks, the submission may be withdrawn. HSO staff will communicate with the investigator/research team prior to taking this action. The investigator may resubmit the item at any time.

2.2.3.2 For items reviewed at a convened IRB meeting, investigators have two (2) weeks to provide a complete response to the requested provisions (for all submissions other than expiring continuing reviews). If no response is received after two (2) weeks, the item will be withdrawn unless the investigator specifically requests an extension. HSO staff will communicate with the investigator/research team prior to taking this action.

2.3. **Study Status and Progress.** Investigators shall:

2.3.1 Prospectively request any changes to a research study in the appropriate manner, (i.e., submission of an amendment), and implement those changes only after receiving approval from the IRB, except where necessary to eliminate apparent immediate hazards to human subjects. If this occurs, the investigator must promptly report the exception to the IRB.

2.3.1.1 All amendments updating risks, benefits, or study procedures must be submitted to the IRB for review within 60 days of receipt of the amendment by the study team.

2.3.2 Promptly notify the IRB when a research study is to be withdrawn from further IRB review.

2.3.2.1 If this occurs prior to HSO review, the investigator should notify the HSO and may withdraw the IRB submission.

2.3.2.2 If this occurs after IRB approval, the investigator must notify the HSO, which will remove the protocol from active records.

2.3.3 Report study closure to the IRB for all FDA regulated and all greater than minimal risk studies within a reasonable time frame. At a minimum, this must be completed prior to study expiration.

2.3.3.1 Reporting study closure is optional for minimal risk, non-FDA regulated studies.

2.3.4 Report the progress of approved research (e.g., renewal) to the IRB and, if required, to the sponsor and/or monitor, as often as required and in a manner prescribed by the IRB on the basis of risks to subjects but not less than once per year for full review and expedited studies that are federally funded or regulated (e.g., FDA, VA). Federal funding includes pass-through funding. Expedited studies that are neither federally funded nor federally regulated are eligible for approval for two years.
2.3.4.1 Oversight by the IRB is required as long as investigators are either interacting or intervening with subjects or accessing identifiable private information for research purposes. This includes research studies that remain active only for data analysis or for long-term follow-up, even when the research is permanently closed to the enrollment of new subjects and all subjects have completed all research-related interventions. For multi-site research, the local investigator may close the study at the local site if investigators are neither interacting with subjects nor accessing subjects’ identifiable information.

2.3.4.2 The IU Human Subjects Office will notify investigators of the need to renew a study well in advance of a study’s expiration date. Upon notification, the investigator should complete and submit to the IRB the appropriate renewal submission and attach any necessary documents. It is ultimately the investigator’s responsibility to ensure that the research is reapproved prior to the study’s expiration date.

2.3.4.3 The regulations make no provisions for any grace period extending the conduct of the research beyond the expiration date of IRB approval. Thus, if a PI fails to provide renewal information to the IRB or the IRB has not reviewed and approved a research study by the expiration date, the research, including research interventions or interactions, enrollment of new subjects, and analysis of identified data, must stop, unless the IRB finds that it is in the best interests of individual subjects to continue participating in the research interventions or interactions. Enrollment of new subjects cannot occur after the expiration of IRB approval.

2.3.5 Promptly report to the IRB any promptly reportable event as defined in the IU SOP for Reportable Events and, if appropriate, to the sponsor and other appropriate regulatory agencies. The initial determination of the relationship of the event to the study and/or test article rests with the investigator.

2.3.6 Notify the IRB if the investigator is leaving the institution and either terminate active research studies or arrange for appropriate transfer of authority for all active research studies to another qualified investigator.

2.3.7 If a suspension or termination involves the withdrawal of current subjects from the research, the investigator must notify and withdraw subjects in a manner that considers their safety, rights, and welfare. Subjects must also be notified if follow-up for safety reasons is required or permitted. Events requiring prompt reporting to the IRB must continue to be reported as defined in the IU SOP for Reportable Events.

2.4. **Informed Consent.** Investigators shall:

2.4.1 Pursuant to 45 CFR 46.116 and 21 CFR 50.20, the PI must ensure that informed consent, unless waived or altered, is obtained from each research subject or
2.4.2 Although the PI is ultimately responsible for assuring that an appropriate informed consent process is approved and carried out, he/she is not required to personally conduct the consent interview. If permitted by the IRB, the PI may delegate the responsibility for conducting the consent interview, including obtaining informed consent, to appropriate members of the research team.

2.4.3 The consent document must be provided to the subject (or LAR) and the original signed consent document must be retained in the study records. The consent document should also be placed in the subject’s medical record, if appropriate. The consent provided to subjects does not need to be signed, although providing the signed and dated consent is preferred.

2.4.4 Upon identification of a potential study subject, the PI or appropriate member of the research team will be responsible for identifying who is legally authorized to give consent for the subject, if consent is required. The PI also needs to explain when informed consent will be obtained, including any waiting period (between informing the subject and obtaining consent) that will be observed. If the subject is physically or mentally unable to provide consent, then the LAR may be approached to give consent for the subject. Careful attention should be given to any potential impairment to informed consent.

2.4.5 The informed consent document(s) remain in effect until such time that a revision, if any, is approved by the IRB. As soon as IRB approval of the revised consent occurs, this consent becomes the current version and any previous consents may no longer be used to consent participants.

2.4.6 Research involving patients. Informed consent must be obtained from each patient prior to altering care for the purpose of research. Informed consent must be obtained prior to performing any non-routine procedures, such as testing for eligibility, if being done exclusively for the purpose of screening for, or participating in, the research study. This could be done using a specific screening informed consent document and/or the regular main study consent document.

2.5. Certification for Research Supported by a Federal Department or Agency

2.5.1 Pursuant to 45 CFR 46.103(f), the investigator is required to submit the certification of human subjects review and approval (“certification”) with the application or proposal or by such later date as may be prescribed by the department or agency to which the application or proposal is submitted. If the certification is not submitted within the appropriate time limits, the application or proposal may be returned to the institution.

2.5.2 Under no condition shall research covered by 45 CFR 46.103 be supported prior to receipt of the certification that the research has been reviewed and approved by an IRB, unless the investigator provides affirmation that IRB approval will be obtained prior to conducting human subjects portions of the research.
Section II: SOPs/Policies

3. ADDITIONAL POLICIES AND PROCEDURES

3.1 Research Subject to FDA Regulations

3.1.1 Investigators are responsible for following the additional responsibilities as outlined in the FDA Guidance for Industry, Investigator Responsibilities – Protecting the Rights, Safety, and Welfare of Study Subjects.

3.1.2 Additional Responsibilities for Research Involving Investigational Drugs

3.1.2.1 Pursuant to 21 CFR 312.53(c)(1), before participating in an investigation, the PI must provide a commitment (Form FDA-1572) to the sponsor.

3.1.2.2 In addition to the investigational plan, conditions of approval imposed by the IRB, and applicable regulations, the PI is also responsible for ensuring that an investigation is conducted according to the signed investigator statement and any conditions of approval imposed by the FDA.

3.1.2.3 The PI 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.

3.1.2.3.1 Case histories include the case report forms and supporting data such as signed and dated consent forms and medical records including, for example, progress notes of the physician, the individual’s hospital chart(s), and the nurses’ notes.

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

3.1.2.4 The PI is required to retain records required to be maintained under 21 CFR 312 for a period of two (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 two (2) years after the investigation is discontinued and the FDA is notified.

3.1.2.5 Investigator Reports

3.1.2.5.1 Progress Reports. The PI is required to furnish all reports to the sponsor of the drug who is responsible for collecting and evaluating the results obtained.

3.1.2.5.2 Safety Reports. The PI is required to 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 shall report the adverse effect immediately.

3.1.2.5.3 **Final Report.** The PI is required to provide the sponsor with an adequate report shortly after completion of the investigator’s participation in the investigation.

3.1.2.5.4 **Financial Disclosure Reports.** The PI is required to provide the sponsor with sufficient accurate financial information to allow an applicant to submit a complete and accurate certification or disclosure statement as required under 21 CFR 54.4. The investigator is required to promptly update this information if any relevant changes occur during the course of the investigation and for one (1) year following the completion of the study.

3.1.2.6 **Inspection of Investigator Records and Reports**

3.1.2.6.1 The investigator is required, upon request from any properly authorized officer or employee of FDA, at a reasonable time, to permit such officer or employee to have access to and copy and verify any records or reports made by the investigator pursuant to 21 CFR 312.62, Investigator Recordkeeping and Record Retention.

3.1.2.6.2 The investigator is not required to divulge participant names unless the records of particular individuals require a more detailed study of the cases, or unless there is reason to believe that the records do not represent actual case studies, or do not represent actual results obtained.

3.1.3 **Additional Responsibilities for Research Involving Investigational Devices**

3.1.3.1 Pursuant to 21 CFR 812.43(c)(4), the PI must provide the sponsor with a signed agreement.

3.1.3.2 Pursuant to 21 CFR 812.140(a), the PI shall maintain the following accurate, complete, and current records relating to his/her participation in an investigation:

3.1.3.2.1 All correspondence with another investigator, the IRB, the sponsor, a monitor, or FDA, including required reports.

3.1.3.2.2 Records of receipt, use, or disposition that relate to:

3.1.3.2.2.1 The type and quantity of the device, the dates of its receipt, and the batch number or code mark;
3.1.3.2.2.2 The names of all persons who received, used, or disposed of each device; and

3.1.3.2.2.3 Why and how many units of the device have been returned to the sponsor, repaired, or otherwise disposed of.

3.1.3.2.3 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 chart(s), and the nurses’ notes. Such records shall include:

3.1.3.2.3.1 Documents showing evidence of 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. The case history for each individual shall document that informed consent was obtained prior to participation in the study;

3.1.3.2.3.2 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; and

3.1.3.2.3.3 A record of the exposure of each subject to the investigational device, including the date and time of each use, and any other therapy.

3.1.3.2.4 The protocol, with documents showing the dates of reasons for each deviation from the protocol.

3.1.3.2.5 Any other records that FDA requires to be maintained by regulation or by specific requirement for a category of investigations or a particular investigation.

3.1.3.3 Investigator Reports. Pursuant to 21 CFR 812.150(a), the PI shall prepare and submit the following complete, accurate, and timely reports:

3.1.3.3.1 Unanticipated Device Effect. The PI shall submit to the sponsor and to the reviewing IRB a report of any unanticipated adverse device effect occurring during an
investigation per the reporting requirements described in the IU SOP for Reportable Events.

3.1.3.3.2 **Withdraw of IRB Approval.** The PI shall report to the sponsor within five (5) working days any withdrawal of approval by the reviewing IRB of the investigator’s part of an investigation.

3.1.3.3.3 **Progress Reports.** The PI shall submit progress reports on the investigation to the sponsor, the monitor and the IRB at regular intervals, but in no event less often than yearly. For reporting to the IRB, this is done at the time of continuing review.

3.1.3.3.4 **Protocol Deviation.** The PI shall notify the sponsor and the IRB of any deviation from the investigational plan to protect the life or physical well-being of a subject in an emergency. Such notice shall be given as soon as possible, but in no event later than five (5) working days after the emergency occurred. Except in such an emergency, prior approval by the sponsor is required for changes in or deviations from a plan, and also, if these changes or deviations may affect the scientific soundness of the plan or the rights, safety, or welfare of human subjects, by FDA and the IRB, in accordance with §812.35(a). For reporting requirements, see the IU SOP for Reportable Events.

3.1.3.3.5 If the PI uses a device without obtaining informed consent, the PI shall report such use to the sponsor and IRB within five (5) working days after the use occurs. For reporting requirements, see the IU SOP for Reportable Events.

3.1.3.3.6 **Final Report.** The PI shall, within three (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 IRB.

3.1.3.3.7 **Financial Disclosure Reports.** The PI is required to provide the sponsor with sufficient accurate financial information to allow an applicant to submit a complete and accurate certification or disclosure statement as required under 21 CFR 54.4. The investigator is required to promptly update this information if any relevant changes occur during the course of the investigation and for one (1) year following the completion of the study.
3.1.3.3.8 The PI shall, upon request by the IRB or FDA, provide accurate, complete, and current information about any aspect of the investigation.

3.1.3.4 **Device Risk Assessment.** The PI must provide to the IRB the sponsor’s initial assessment of whether a device study is considered significant risk (SR) or nonsignificant risk (NSR).

3.1.3.5 If the IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in the exception provided 21 CFR 50.24(a) or because of other relevant ethical concerns, the IRB will document its findings and provide them promptly in writing to the PI, who is required to notify the sponsor of the clinical investigation.

3.1.3.6 **Inspection of Investigator Records and Reports**

3.1.3.6.1 The PI (or other investigator who has authority to grant access) shall 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.

3.1.3.6.2 The PI shall permit authorized FDA employees, at reasonable times and in a reasonable manner, to inspect and copy all records relating to an investigation.

3.1.3.6.3 The PI shall permit authorized FDA employees to inspect and copy records that identify participants, upon notice that FDA has reason to suspect that adequate informed consent was not obtained, or that reports required to be submitted by the PI to the sponsor or IRB have not been submitted or are incomplete, inaccurate, false, or misleading.

3.1.4 **Additional Responsibilities for Both Investigational Drug and Device Studies**

3.1.4.1 The PI is responsible for informing any patient or subject, or any person used as a control, that the drug(s) or device(s) are being used for investigational purposes and assuring that the requirements relating to obtaining informed consent and IRB approval, as required by federal regulations, are followed.

3.1.4.2 If applicable, the PI must ensure that the toxicology and pharmacokinetics/pharmacodynamics or safety data of a test article (e.g., device, drug, biologic) to be given to a human subject have been fully evaluated such that it is safe for use in human subjects.
3.1.4.3 If the research involves an investigator-held IND or IDE, the investigator assumes all of the responsibilities of the sponsor per 21 CFR 312, Subpart D or 21 CFR 812, Subpart C, including adverse event reporting to the FDA and participating sites (multi-center trials) and submission of annual reports. Because of the additional responsibilities of a sponsor, the PI must meet with individuals within the Office of Research Compliance to discuss the responsibilities prior to study approval.

3.1.4.4 The PI must maintain compliance with institutional, hospital, clinic, OSHA, and other special committee regulations and policies (e.g., radiation safety, Scientific Review Committee, or other institutional committees) as well as Medicare/Medicaid billing, and HIPAA requirements (see IU SOP for Confidentiality and Privacy).

3.1.4.5 The PI must provide to the IRB the IND and/or IDE number issued by the FDA, if applicable for investigational drugs or devices, before final IRB approval can be granted.

3.1.4.6 The PI is responsible for reading and understanding all of the information, including the potential risks and side effects, of any drug(s) and/or device(s) used in a research study.

3.1.4.7 If applicable, the PI must submit updated clinical investigators brochures to the IRB as they occur. In addition, any progress or final reports must be provided to the IRB with the PI’s written assessment.

3.2. **Research Subject to HIPAA Regulations**

3.2.1 Ensure that a release for health information authorization form is obtained from each subject at the time of consent, unless the authorization requirement has been waived by the IRB.

3.3. **Research Subject to VA Regulations**

3.3.1 Investigators must hold a current VA appointment to conduct VA research.

3.3.2 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:

3.3.2.1 The type of safety information to be collected, including AEs;

3.3.2.2 Frequency of safety data collection;

3.3.2.3 Frequency or periodicity of review of cumulative safety data;
3.3.2.4 Statistical tests for analyzing the safety data to determine if harm is occurring; and

3.3.2.5 Conditions that trigger an immediate suspension of the research, if applicable.

3.3.3 The investigator must submit the protocol for initial review and obtain written approvals from the IRB, other applicable committees, and 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.

3.3.4 If research is conducted at the VA and expires because the IRB did not grant re-approval by the study’s expiration date, either because the IRB did not receive the required materials or because the IRB received the materials but did not grant re-approval, the following additional requirements must be met:

   3.3.4.1 Stop all research activities except where stopping could be harmful to subjects; and

   3.3.4.2 The PI must submit immediately to the IRB Chair a list of research subjects for whom stopping research procedures would cause harm. The Chair must determine within two (2) business days whether such interactions or interventions may continue.

3.3.5 The investigator must obtain and document legally effective informed consent prospectively.

   3.3.5.1 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.

   3.3.5.2 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 engage 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 PI must determine that there is appropriate authority to allow the disclosure of individual names and other information to the contracted firm.

3.3.6 The investigator must create or update a VHA health record and a progress note 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., nursing homes).
3.3.7 The VA does not permit the conduct of classified research involving human subjects

3.4. Research Subject to Other Regulations

3.4.1 Research Subject to Department of Defense (DoD) Regulations

3.4.1.1 There may be additional DoD educational requirements or certification required, including DoD-specific CITI modules.

3.4.2 Research Subject to Department of Education (ED) Regulations

3.4.2.1 All instructional material (teacher manuals, films, tapes, or other supplementary material) that will be used in connection with any research or experimentation program or project designed to explore or develop new or unproven teaching methods or techniques must be available for inspection by the parents or guardians of subjects who have not reached the age of majority as defined by state law.

3.4.3 Research Subject to Department of Justice (DOJ) Regulations. For research conducted within the Bureau of Prisons:

3.4.3.1 The researcher must have academic preparation or experience in the area of study of the proposed research.

3.4.3.2 When submitting a research protocol, the applicant must provide the following information:

3.4.3.2.1 A summary statement that includes

3.4.3.2.1.1 Name and current affiliations of the researchers

3.4.3.2.1.2 Title of the study

3.4.3.2.1.3 Purpose of the study

3.4.3.2.1.4 Location of the study

3.4.3.2.1.5 Methods to be employed

3.4.3.2.1.6 Anticipated results

3.4.3.2.1.7 Duration of the study

3.4.3.2.1.8 Number of participants (staff or inmates) required and amount of time required from each

3.4.3.2.1.9 Indication of risk or discomfort involved as a result of participation
Section II: SOPs/Policies

3.4.3.2.2 A comprehensive statement that includes

3.4.3.2.2.1 Review of related literature

3.4.3.2.2.2 Detailed description of the research method

3.4.3.2.2.3 Significance of anticipated results and their contribution to the advancement of knowledge

3.4.3.2.2.4 Specific resources required from the Bureau of Prisons

3.4.3.2.2.5 Description of all possible risks, discomforts, and benefits to individual participants or a class of participants, and a discussion of the likelihood that the risks and discomforts will actually occur

3.4.3.2.2.5.1 Description of steps taken to minimize any risks

3.4.3.2.2.6 Description of physical or administrative procedures to be followed to:

3.4.3.2.2.6.1 Ensure the security of any individually identifiable data that are being collected for the study

3.4.3.2.2.6.2 Destroy research records or remove individual identifiers from those records when the research has been completed

3.4.3.2.2.7 Description of any anticipated effects of the research study on organizational programs and operations.

3.4.3.2.2.8 Relevant research materials such as vitae, endorsements, sample consent statements, questionnaires, and interview schedules

3.4.3.2.3 A statement regarding assurances and certification required by federal regulations, if applicable.

3.4.3.3 The investigator must assume responsibility for actions of any person engaged to participate in the research project as an associate, assistant, or subcontractor to the investigator.
3.4.3.4 At least once a year, the investigator shall provide the Chief, Office of Research and Evaluation, with a report on the progress of the research.

3.4.3.5 At least twelve (12) working days before any report of findings is to be released, the investigator 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 investigator shall include an abstract in the report of findings.

3.4.3.6 In any publication of results, the investigator shall acknowledge the Bureau’s participation in the research project.

3.4.3.7 The investigator shall expressly disclaim approval or endorsement of the published material as an expression of the policies or views of the Bureau.

3.4.3.8 Prior to submitting for publication the results of a research project conducted pursuant to DOJ regulations, the investigator shall provide two copies of the materials, for information purposes only, to the Chief, Office of Research and Evaluation, Central Office, Bureau of Prisons.

3.4.3.9 For research funded by the National Institute of Justice, 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.
IRB Executive Committee

1.0 Scope
This policy applies to the Indiana University (IU) Human Research Protection Program (HRPP).

2.0 Policy Statement
The institutional review board (IRB) Executive Committee provides oversight function to the IU HRPP by making both binding decisions and offering advisory considerations regarding matters related to research involving human subjects.

2.1. Membership
The membership of the IRB Executive Committee consists of the chairs and vice chairs of each IU IRB. Other individuals may be included as voting members to achieve diversity and expertise to carry out the activities of the Committee, as needed.

The Chair is the Associate Vice President for Research Compliance. She/he may appoint another member to perform the functions of the Chair, as necessary.

2.2. IRB Executive Committee Meetings
The Committee has periodic meetings as required to perform its duties and responsibilities. There is at least one meeting per year.

The majority of the Committee members present at a meeting constitutes a quorum. Members may attend meetings in person or via telephone or video conference.

Committee decisions are made by a majority vote of the members present at the meeting. Members having a conflict of interest in a matter may not vote, but will be counted toward quorum. Voting occurs only after there has been a full, open discussion.
3.0 **Reason for the Policy**
The IRB Executive Committee was established to coordinate IRB policy and procedural matters at IU involving the use of human subjects in research.

4.0 **Procedures**
4.1. **Non-members at the IRB Executive Committee Meetings**
The Chair may invite or allow a non-member to attend a meeting, as needed.

4.2. **Subcommittees**
The Chair may appoint subcommittees to execute various duties related to the objectives and policies of the Committee. Findings and recommendations by subcommittees are considered advisory in nature and are not binding unless accepted by a formal vote of the IRB Executive Committee.

5.0 **Sanctions**
IRB members and HRPP staff that are found to be in violation of this policy may be subject to sanctions relating to their participation in review of research with human subjects.

6.0 **History**
Replaces portions of the previous IU SOP for IRB Operations (v02/2017)

7.0 **Related Information**
AAHRPP Standards
- N/A

IU HRPP Documents
- N/A

KC IRB Questionnaires
- N/A

Regulatory References
- N/A
IRB Meetings and Minutes

About This Policy

Effective Date:
03/29/2018

Last Updated:
03/29/2018

Policy Contact:
IU Human Subjects Office
(317) 274-8289
irb@iu.edu

1.0 Scope
This policy applies to all Indiana University (IU) institutional review boards (IRBs).

2.0 Policy Statement
IU has seven (7) IRBs that are charged with understanding and applying their obligation to protect the rights and welfare of human research subjects recruited to participate in research activities and to ensure compliance with applicable institutional policies and federal and state regulations.

2.1 IRB Meetings
IRB Meeting Schedules
Each IRB ordinarily meets at least once per month, with the exception of IRB 07, which is an ad hoc IRB that meets only when called by the Chair. Meeting schedules are provided to IRB members well in advance of the meetings. The IRB Chair may, however, call additional meetings at any time if necessary.

IRB Meeting Quorum
Quorum must be present at the IRB meeting to conduct business, take action, or vote. Quorum is constituted of a majority of voting IRB members, or their designated alternates, present at the IRB meeting, including at least one member whose primary concerns are in nonscientific areas. Members who attend remotely, such as by phone or video conference, are counted toward quorum. Members who leave the meeting or are absent for discussion and voting on an item due to a conflict of interest do not count toward quorum; however, members who leave temporarily, such as to take a phone call, are counted toward quorum.

A nonaffiliated member and a member who represents the general perspective of
research subjects should be present at IRB meetings. These roles can be filled by the same person. Meetings may be held without the nonaffiliated and subject representative members, if necessary; however, frequent absences are not acceptable.

Prisoner representatives attend only as needed and only affect quorum when present at a meeting.

Committee decisions are made by a majority vote of the members present at the meeting. Voting occurs only after there has been a full, open discussion.

**IRB Meeting Attendees**
An IRB may, in its discretion, invite individuals with competence in special areas (e.g., consultants) to assist in the review of issues that require expertise beyond or in addition to that available on the IRB. These individuals may not vote with the IRB or be counted toward quorum. The IRB cannot delegate to consultants its responsibility to determine whether the criteria for approval are met.

When the IRB reviews research that affects the risk to pregnant women, human fetuses, neonates of uncertain viability, or nonviable neonates; children; or individuals lacking consent capacity, at least one individual (IRB member or consultant) who is knowledgeable about or experienced in working with such subjects must be present at the meeting or provide written comments. When the IRB reviews research involving prisoners as subjects, at least one individual (IRB member) who is knowledgeable about or experienced in working with prisoners must be present at the meeting. When the IRB reviews research that is regulated by the VA, at least one VA voting member (as defined by the IU HRPP Policy on IRB Membership) must be present.

Any IRB member or consultant present at a meeting who has a conflicting interest in a matter cannot vote on that matter and must be absent from the meeting during the deliberation and voting. He/she can, however, be in attendance to present information or answer questions as requested by the IRB. Examples of conflicting interests include:
- Participation in the project
- Financial interest as defined by the IU Policy on Financial Conflicts of Interest in Research
- Certain non-financial interests, including having supervision over the investigator of the project or participating in a project that is in direct competition with the project
- Any other real or perceived conflict

**IRB Meeting Materials**
Meeting materials are made available to all members of the IRB in advance of the meeting. The following items are included at minimum, as applicable:
- Agenda
- Minutes from the most recent meeting for review and approval

2.2. **IRB Minutes**
IRB meetings are documented by the IRB minutes, which include the following:
- Attendance at the meeting
- Names of IRB members who leave the meeting due to a conflict of interest
- Reviewers submitting written comments in lieu of attendance at the meeting
• Actions taken by the IRB, including votes for, against, or abstaining, and the names of IRB members who abstain, if any
• Accounting of deliberations for each item, including a summary of the discussion of controverted issues and their resolution, the basis for requiring changes in research, and the basis for disapproving research
• The approval period (for initial approval and renewals)
• Determinations required by the regulations and research-specific findings justifying determinations for waiver or alteration of the consent process or documentation
• Determinations that the study has appropriate plans for research involving vulnerable populations, including children, prisoners, pregnant women, fetuses, neonates of uncertain viability or nonviable neonates, and individuals lacking consent capacity
• For VA research:
  o Determination and documentation of the level of risk and the rationale for the IRB’s determination
  o A summary of the justification for including nonveterans as participants
  o A summary of the discussion when real, scrambled, or partial Social Security numbers will be used in the study and what security measures are in place to protect them
  o Notice of the approval of research by the IRB Chair contingent on specific minor conditions, documented in the minutes of the first IRB meeting that takes place after the date of the approval
  o Determination of the expedited review eligibility category, if applicable

IRB minutes are approved by the convened IRB at a subsequent IRB meeting. Once approved, they may not be altered by anyone, including a higher authority.

IRB minutes and decisions may be made available, upon request, to relevant individuals or institutional officials at IU and/or its affiliates.

3.0 Reason for the Policy
To facilitate IRB review of human subjects research at convened IRB meetings.

4.0 Procedures
4.1. Convened IRB Reviewer System
A primary reviewer system is used for items requiring review by the convened IRB. This includes amendments, renewals, and general information, including reportable events. For new, greater-than-minimal-risk studies requiring review by the convened IRB, a secondary reviewer is also assigned. Human Subjects Office (HSO) staff evaluate each study and assign a primary and/or secondary reviewer with appropriate scientific expertise to conduct the in-depth review. Additionally, for these same submissions, a nonscientist or non-affiliated member may be assigned as a tertiary reviewer.

4.1.1. If an IRB member feels the item they have been assigned to review is outside of their area of expertise and/or if they have or believe they have a conflict with the item, the IRB member should contact the HSO as soon as possible so the item may be reassigned to another IRB member to review and/or an additional reviewer can be identified.
4.1.2. Complete submission information is made available for review by any IRB member at the meeting, and any member may, upon request, review the full research study.

4.1.3. A minimum of the following items, as applicable, are provided to all IRB members:
   - Applicable forms, questionnaires, and protocol summary containing the relevant information to determine whether the proposed research fulfills the criteria for approval;
   - Proposed consent/assent document(s);
   - Recruitment materials;
   - Protocol and investigator’s brochure;
   - For federally-funded research, the grant proposal, HHS sample informed consent form(s), and HHS sample protocol

4.1.4. Except for life-threatening emergencies that meet very specific requirements as outlined in the IU SOP on Emergency Use of Investigational Test Articles, review of all research that qualifies for full IRB review is performed at a convened IRB meeting.

5.0 **Sanctions**

IRB members and Human Research Protection Program (HRPP) staff that are found to be in violation of this policy may be subject to sanctions relating to their participation in review of research with human subjects.

6.0 **History**

Replaces portions of the previous IU SOP for IRB Operations (v02/2017)

7.0 **Related Information**

**AAHRPP Standards**
- Standard II-1, Elements II.1.D, II.1.E,
- Standard II-2, Elements II.2.C, II.2.D
- Standard II-5, Element II.5.B

**IU HRPP Documents**
- IRB Agenda Template
- IRB Minutes Template

**KC IRB Questionnaires**
- N/A

**Regulatory References**
- 21 CFR 56
- 45 CFR 46
- OHRP Guidance: Written Institutional Review Board (IRB) Procedures
- OHRP/FDA Guidance: Minutes of Institutional Review Board (IRB) Meetings; Guidance for Institutions and IRBs
- VHA Handbook 1200.05, Requirements for the Protection of Human Subjects in Research, especially section 14
IRB Membership

About This Policy

Effective Date:
03/29/2018

Last Updated:
03/29/2018

Policy Contact:
IU Human Subjects Office
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irb@iu.edu

1.0 Scope
This policy applies to all Indiana University (IU) institutional review boards (IRBs).

2.0 Policy Statement

2.1 IRB Membership
Members are appointed to the IU IRBs to ensure the following requirements are met:

- Each IRB has at least five members with varying backgrounds to promote complete and adequate review of research activities commonly conducted by IU and its affiliates.
- Each IRB is sufficiently qualified, through the experience, expertise, and diversity of its members, including consideration of race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects.
- Each IRB possesses the professional competence necessary to review specific research activities.
- Each IRB is able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice.
- Consideration is given to the inclusion of one or more individuals who are knowledgeable about and experienced in working with children; pregnant women, fetuses, neonates of uncertain viability, or nonviable neonates; prisoners; or individuals lacking consent capacity on IRBs that regularly review research involving these categories of subjects.
- Every nondiscriminatory effort is made to ensure that no IRB consists entirely of men or entirely of women, including consideration of qualified persons of both sexes; however, no selection is made to the IRB on the basis of gender.
• No IRB consists entirely of members of one profession.
• Each IRB includes at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are unambiguously in nonscientific areas (i.e., little or no scientific or medical training or experience).
• Each IRB includes at least one member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution.
  o Retired VA employees who are receiving VA retirement benefits are considered to be affiliated when they are members of a VA IRB, but veterans who receive their care at the facility, but have never been employed by VA, would not be considered affiliated.
• Each IRB includes at least one member who represents the perspective of research subjects.
• Each IRB that reviews VA research:
  o has at least two VA–compensated staff appointed as voting members, appointed in writing for a period of three years;
  o is able to ascertain the acceptability of proposed research in terms of VA requirements and standards of government ethics;
  o gives consideration to including a Veteran or Veteran’s representative.

The following may not serve as voting members of the IRB:
• Individuals responsible for business development for IU and its affiliates
• Individuals who own equity in the institution
• VA facility research staff including, but not limited to, the Associated Chief of Staff for Research & Development (R&D) and the Administrative Officer for R&D
• VA Research Compliance Officers; however, these individuals may act as consultants to the IRB
• VA Facility Directors, their administrative staff, Chief of Staff, other facility senior administrators such as Associate or Assistant Directors or Chief Nurse, and NPC Administrative Staff

The VA Privacy Officer and the Information Security Officer serve in an advisory capacity to the IRB as consultants.

2.2. Membership Rosters
IRB membership rosters are maintained which list IRB members identified by name, earned degrees, representative capacity, indications of experience such as board certifications, licenses, etc., sufficient to describe each member’s primary anticipated contributions to each IRB deliberation, and any employment or other relationship between each member and the institution (e.g., full time employee, member of governing panel or board, paid or unpaid consultant).

For alternates, the roster identifies by name the primary member(s) for whom each alternate member may substitute. Alternates must have qualifications similar to the member they replace.

Pursuant to Indiana University’s Federalwide Assurance, changes in IRB membership are reported to the Office for Human Research Protections (OHRP) quarterly.
3.0  Reason for the Policy
To ensure compliance with 45 CFR 46.107, 21 CFR 56.107, and the VA Handbook 1200.05(2) and to facilitate IRB review of human subjects research by assuring each IRB has the appropriate expertise to review research under its oversight.

4.0  Procedures
4.1.  IRB Appointment
The Vice President for Research or his/her designee appoints IRB members, including Chairs and Vice Chairs, based on recommendations from IU department chairs and following a careful review of candidate qualifications to ensure adequate representation. IRB members may be appointed for terms of up to three years, and may be reappointed for an unlimited number of terms. At the time of appointment and at reappointment, as requested, IRB members are required to:

- read the Belmont Report
- complete the required IRB member modules of the Collaborative Institutional Training Initiative (CITI) course
- review the IRB Member Education website
- disclose potential conflicts of interest.

IRB members cannot serve as voting members until these requirements are met.

A reasonable number of alternates who may serve in place of absent members are also appointed. Alternates must also complete the appointment requirements listed above.

4.2.  IRB Member Responsibilities
All IRB members and alternates are expected to fulfill the following responsibilities:

- Attend monthly IRB meetings (Alternates attend only upon request)
- Serve as primary reviewer for IRB submissions assigned to them
  - Conduct an in-depth review of all materials
  - Be prepared for discussion at the meeting, including presenting the submission to the IRB and making a recommendation regarding IRB action
  - Complete Reviewer Checklist(s)
- Be familiar with all other submissions included on the meeting agenda
- Be knowledgeable about the local research context in order to make appropriate determinations
- Be knowledgeable of the community from which the subjects are drawn to ensure the protection of subjects’ rights and the appropriateness of the informed consent process
- As applicable, review the storage and control plans for investigational drugs and devices to ensure that they are used only in approved research and under the direction of approved investigators
- Review expedited submissions on an ad hoc basis
  - Complete Reviewer Checklist(s)
- Complete annual membership evaluation
- Disclose potential conflicts of interest

In addition, IRB Chairs and Vice Chairs are responsible for the following:
• Attend IRB Executive Committee Meetings
• Conduct IRB meetings, including:
  o Call meetings to order
  o Facilitate discussions
  o Provide counsel to IRB Members
  o Call for motions and votes
  o Adjourn meetings
• Work with Human Subjects Office (HSO) staff to coordinate resolution of compliance issues, including discussion and mediation with study teams
• Review and provide comments on requests for study suspensions
• Evaluate IRB Members annually, in conjunction with HSO staff

4.3. Evaluation of IRB Members
IRB members, including Chairs and Vice Chairs, are evaluated annually using the IRB Member Evaluation Form by the Assistant Vice President for Research Compliance, in collaboration with the Director of the Human Research Protection Program (HRPP) and selected IRB members. Feedback may be provided individually or in aggregate either electronically or in a meeting setting. Information from the evaluation is maintained by the HSO. The Evaluation Tool addresses attendance, quality of reviews, contributions at IRB meetings, timeliness of reviews, and evidence of understanding of applicable regulations, policies, and procedures.

Concerns with any IRB member’s performance are resolved in consultation with the IRB Chair or Vice Chair (when appropriate), department Chair, Associate Vice President for Research Compliance, and/or the IRB member directly, as appropriate. Potential outcomes can range from further education for the IRB member to removal from the IRB.

When IRB members are considered for reappointment, evaluations that occurred during their service on the IRB are considered along with input from members of the HRPP staff, IRB Chairs and/or Vice Chairs, and department Chairs.

5.0 Sanctions
IRB members and HRPP staff that are found to be in violation of this policy may be subject to sanctions relating to their participation in review of research with human subjects.

6.0 History
Replaces portions of the previous IU SOP for IRB Operations (v02/2017)

7.0 Related Information
AAHRPP Standards
- Standard I-1, Element I.1.E

IU HRPP Documents
- IRB Member Information Sheet
- IRB Member Evaluation Form

KC IRB Questionnaires
• N/A

Regulatory References
• 21 CFR 56, especially § 56.107
• 45 CFR 46, especially § 46.107 and Subpart E
• VHA Handbook 1200.05, Requirements for the Protection of Human Subjects in Research, especially section 6
IRB Review Process

About This Policy

Effective Date:
03/29/2018

Last Updated:
03/29/2018

Policy Contact:
IU Human Subjects Office
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1.0 Scope
This policy applies to all non-exempt human subjects research, and exempt human subjects research requiring limited institutional review board (IRB) review, conducted by Indiana University (IU) faculty, staff, students, or others which falls under the jurisdiction of the IU IRBs.

2.0 Policy Statement
2.1 Guiding Principles
The IU IRBs are charged with protecting the rights and welfare of human research subjects, specifically ensuring that those individuals participating in research are not subject to undue or inappropriate risks, that participation remains a voluntary right, and that the conduct of research is upheld as a privilege.

IU follows the ethical principles established by the Belmont Report to ensure the ethical conduct of research. These principles - autonomy/respect for persons, beneficence, and justice – form the cornerstone of federal regulations involving human subjects.

IU applies the federal regulations for protection of human subjects (45 CFR 46, Subpart A, Protection of Human Subjects, also known as “the Common Rule”) when research is sponsored or overseen by a federal agency.

When studies do not receive funding from or are not otherwise regulated by a federal agency, IU has adopted policies and procedures to accommodate differences in types of research and to reduce unnecessary administrative burdens. In these instances, IU has adopted equivalent protections for subjects.
Additional federal, state, and local laws, regulations, and requirements may apply. When laws or regulations differ or conflict, the stricter requirements will be followed.

Pursuant to 45 CFR 46.103(a), each institution engaged in research that is governed by the Common Rule (45 CFR 46) and conducted or supported by a federal department or agency shall provide written assurance satisfactory to the department or agency head that it will comply with the requirements set forth in the regulations. IU and their affiliates provide this assurance in the form of a Federalwide Assurance approved by the Office for Human Research Protections (OHRP).

2.2. Authority of IU Institutional Review Boards

Authority to develop, implement, and monitor all human subjects protection programs has been designated by the President of Indiana University to the Vice President for Research, who serves as the institutional official (IO) for research. The IU IRBs are authorized by the IO to review human subjects research in accordance with the IU Policy on Research with Human Subjects. The IRB functions independently of other organizational entities in protecting research subjects.

Prior to research initiation, the IRB review must find that all criteria for IRB approval outlined below are met, or grant exemption, as applicable. The IRB evaluates whether resources are adequate to protect subjects’ rights and welfare.

The IRB may approve, require modification to secure approval (“provisionally approve” or “table”), or disapprove research proposals covered by this policy, including exemptions requiring the IRB conduct a limited IRB review to make the determination required by the IU Human Research Protection Program (HRPP) Policy on Exempt Research.

No official or office of the institution may approve a research activity that has been disapproved by the IRB, and no external body or official may override IRB disapprovals, nor apply undue pressure on the IRB to approve a research study or reverse a decision. IRB members or Human Subject Office (HSO) staff who feel they are being unduly influenced should report this to the University Director, HRPP or to the Research Integrity Officer. Either of these officials may investigate and take corrective action, as necessary.

Research which is approved by the IRB may be disallowed by the institution. If research is approved by the IRB but not permitted by the institution, the appropriate institutional authority will promptly notify the investigator and the IRB that the research cannot be conducted, including the reasons for that determination.

The IRB may suspend, place restrictions upon, or terminate approval of research activities falling within its jurisdiction that are not being conducted in accordance with IRB requirements or that have been associated with unexpected serious harm to subjects.

The IRB may have the consent process or the research procedures of any research study under its jurisdiction observed by a third party if the IRB determines that such observation is indicated. This is typically done by the IU Quality Improvement Office.

Deliberations, decisions, findings, and actions of the IRB associated with research activities are considered confidential, except as appropriate. This information is
reported to appropriate institutional officials as required by law and/or policies of the IRB. Failure to adhere to this provision may be cause for removal of a member from the IRB. See the Indiana Public Access Counselor (http://in.gov/pac/) for additional information regarding the Open Door Law and Public Records Act.

2.3. **Criteria for IRB Approval**

Based on the IRB’s review of information provided by the investigator, and in accordance with appropriate regulations and IU and IU HRPP policies and procedures, the IRB may grant approval of research, including initial review, continuing review, and modifications to previously approved research, if it determines that all of the following requirements are satisfied:

- Risks to subjects are minimized by using procedures which (1) are consistent with sound research design and which do not unnecessarily expose subjects to risk, and (2) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.
- Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies/procedures/activities subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.
- Selection of subjects is equitable. In making this assessment, the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, or individuals lacking consent capacity.
- Unless waived by the IRB, informed consent will be sought from each prospective subject or the subject’s legally authorized representative in accordance with and to the extent required by relevant regulations and IU HRPP Policies and procedures.  
- Unless waived by the IRB, informed consent will be appropriately documented in accordance with and to the extent required by relevant regulations and IU HRPP Policies and procedures.  
- When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects. See IU SOP on Safety Monitoring.  
- When appropriate, there are adequate provisions to protect the privacy of participants and to maintain the confidentiality of data.  
- When some or all the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, or individuals lacking consent capacity, additional safeguards have been included in the research proposal to protect the rights and welfare of these subjects.

2.4. **Expedited Review**

The IRB may use an expedited review procedure to review any of the following:

- Research which (1) presents no more than minimal risks to human subjects, and (2) involves only procedures listed in one or more of the Expedited Research Categories below.
• Renewals or modifications to research previously-approved under expedited procedures provided the research continues to meet the Expedited Research Categories below and any modifications do not substantially increase risk to subjects.
• Minor changes in research previously-approved by the convened IRB
• Research granted exemption but requiring a limited IRB review under the IU HRPP Policy on Exempt Research.

The IRB may not use an expedited review procedure to review any of the following:
• Research in which identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to their financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal
• Classified research involving human subjects
• Studies involving randomized use of drugs, devices, or biologics. All such studies are reviewed by the convened IRB.

2.5. Expedited Research Categories

Category 1
Clinical studies of drugs and medical devices only when either condition below is met:
• Research on drugs for which an investigational new drug application (21 CFR 312) is not required. Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review; or
• Research on medical devices for which (1) an investigational device exemption application (21 CFR 812) is not required; or (2) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

Category 2
Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:
• From healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or
• From other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

Category 3
Prospective collection of biological specimens for research purposes by noninvasive means. Examples include:
• Hair and nail clippings in a nondisfiguring manner;
• Deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction;
• Permanent teeth if routine patient care indicates a need for extraction;
• Excreta and external secretions (including sweat);
• Uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue;
• Placenta removed at delivery;
• Amniotic fluid obtained at the time of rupture of the membrane prior to or during labor;
• Supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques;
• Mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; or
• Sputum collected after saline mist nebulization.

Category 4
Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared / approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications). Examples include:
• Physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject’s privacy;
• Weighing or testing sensory acuity;
• Magnetic resonance imaging;
• Electrocardiography; electroencephalography, thermography detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography;
• Moderate exercise, muscular strength testing, body composition assessment and flexibility testing where appropriate given the age, weight and health of the individual.

Category 5
Research involving materials (data, documents, records, or specimens) that have been collected or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis). Note that some research in this category may be exempt from the federal regulations or IU HRPP Policy and procedure. This listing refers only to research that is not exempt.

Category 6
Collection of data from voice, video, digital, or image recordings made for research purposes.

Category 7
Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. Note that some research in this category may be exempt from federal regulations or IU HRPP Policy and procedure. This listing refers only to research that is not exempt.
Category 8
Continuing review (i.e. renewal) of research previously approved by the convened IRB as follows:

- where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions, and (iii) the research remains active only for long-term follow-up of subjects; or
- where no subjects have been enrolled and no additional risks have been identified; or
- where the remaining research activities are limited to data analysis.

Category 9
Continuing review (i.e. renewal) of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

2.6. Renewals
The IRB conducts continuing review of research at intervals appropriate to the degree of risk, but not less than once per year for:

- Non-exempt studies that are federally funded or regulated (e.g., FDA, VA);
- Renewals requiring review by the convened IRB.

The IRB may require review more frequently than annually as it deems appropriate.

The IRB is not required to conduct renewal for the following:

- Research that is not federally funded or FDA- or VA-regulated and is eligible for expedited review per this policy
- Research granted exemption, including exempt research requiring a limited IRB review per the IU HRPP Policy on Exempt Research
- Research that is not federally funded or FDA- or VA-regulated and required review by the convened IRB, but has progressed to the point that it involves only one or both of the following:
  - Data analysis, including analysis of identifiable private information or identifiable biospecimens (i.e., data analysis only)
  - Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care (i.e., clinical follow-up)

The IRB may require renewal for this research on a case-by-case basis as it deems appropriate. If renewal is required, the IRB must document the rationale for such requirement.

2.7. Amendments to Previously Approved Research
Any proposed changes in approved research must be reviewed and approved by the IRB prior to implementation to ensure that the modified research continues to meet the criteria for approval, except when it is necessary to implement changes to eliminate apparent immediate hazards to the subjects. In this situation, the changes must be promptly reported in accordance with the IU SOP on Reportable Events.

2.8. Study Closure
Closure of all non-exempt research must be reported to the IRB within a reasonable time frame (i.e., prior to study expiration, when applicable).
• For FDA-regulated research and greater than minimal risk research, investigators must provide a final accounting of subject recruitment, withdrawals, adverse events, deviations, and changes to risk/benefit ratio. The closure is approved by an IRB member via the expedited review process and is reported to a convened IRB.

• Minimal risk research which is not FDA-regulated may be closed by an HSO staff member and does not require reporting to a convened IRB.

2.9. IRB Review of Investigational Test Articles

2.9.1 Devices

When the principal intent of the medical device (or other product regulated as a device) is to develop information about the product's safety or efficacy, submission of an Investigational Device Exemption application (IDE) is ordinarily required. However, in certain circumstances, the FDA does not require an IDE.

Investigations of devices fall into one of three categories: exempt from IDE requirements, studies of nonsignificant risk (NSR) devices subject to abbreviated IDE requirements, or significant risk (SR) devices subject to full IDE requirements. The assessment of whether a device is exempt from IDE requirements, NSR subject to abbreviated IDE requirements, or SR subject to full IDE requirements is initially made by the investigator and/or the sponsor. The IRB must agree with the assessment based on the proposed use of the device in the research and not on the device alone; however, the FDA has the ultimate decision in determining if a device is IDE exempt, NSR, or NSR.

• Exempt from IDE Requirements: The IRB must agree with the justification of exemption; otherwise, the investigator will be required to follow the full or abbreviated IDE requirements. Review the full FDA regulations at 21 CFR § 812 for applicability for exemption.

• NSR Device: If the investigator and/or sponsor determines that a device is NSR, the convened IRB considers the explanation of its determination and any other information that may assist in evaluating the risk of the device. The convened IRB may agree or disagree with the assessment of NSR.

• SR Device: In deciding if a device poses a SR, the IRB considers the nature of the harm that may result from use of the device. If the IRB determines that the device is SR, the investigator is notified and the study cannot be approved and/or conducted until the investigator has provided the IRB with documentation of FDA approval of an IDE application, FDA determination that the device is NSR, or FDA IDE exemption determination.

Drugs or biological products

If the study involves a drug or biological product used in humans in any way other than in the course of medical practice, an IND is required unless certain exemptions apply. The assessment of whether a drug or biological product requires an IND or is exempt from IND requirements is initially made by the investigator and/or the sponsor. The IRB must agree with the assessment based on the proposed use of the drug or biological product in the research; however, the FDA has the ultimate decision in determining if the study of the drug or biological product requires an IND. Review the full FDA regulations at 21 CFR § 312 for applicability for exemption.
2.10. Research Subject to VA Regulations

Criteria for Approval

Relevance of the research to the mission of VA and the veteran population that it serves is considered by the IRB. If non-veterans will be included, the protocol and related materials must justify the inclusion of non-veterans.

Scientific Review
The VA Research and Development Committee defers the scientific review for research conducted at or funded by the VA to the IRB.

Amendments
Amendments to VA research involving issues related to biosafety or radiation safety must first be approved by the appropriate committee or subcommittee prior to granting final IRB approval.

Renewals
In addition to the information provided to the IRB when conducting renewal, status reports for research conducted at or funded by the VA must also include the investigator’s assessment based on research results, the gender and minority status of those entered into the research, number of subjects considered as members of specific vulnerable populations, and an assurance that all serious or unexpected adverse events had been reported as required.

Study Expirations
Pursuant to the VHA Handbook 1200.05, research conducted at or on behalf of the VA that does not receive renewal within the time frame set by the IRB is automatically suspended. Only if the IRB or IRB Chair, in consultation with the Chief of Staff (COS), finds that it is in the best interest of individual subjects can already enrolled subjects continue with research interventions or interactions.

Once the investigator is notified of the suspension by the local VA research office, he/she must immediately submit to the IRB Chair a list of research subjects for whom suspension of the research would cause harm. The IRB Chair, with appropriate consultation with the COS, determines if the subjects may continue in the research. If the research is FDA-regulated, the COS and IRB Chair must follow FDA requirements in 21 CFR 56.1018(b)(3) in making their decision. Additionally, any sponsoring agency, private sponsor, Office of Research & Development (ORD), Office of Research Oversight, or other federal agencies will be informed, as appropriate, by the local VA research office.

Recruitment of Human Subjects for Research
Subject consent and authorization or, alternatively, waivers of consent for recruitment and of authorization for recruitment must be approved by the IRB prior to accessing, obtaining, and/or utilizing protected health information for VA research recruitment activities.
Institutional Review
IRB-approved research activities may be disapproved by the IU or VA IO, the Research & Development (R&D) Committee, or ORD.

IRB disapprovals or required modifications to the research cannot be overruled by any other entity.

The R&D Committee must provide the final approval before the research can be initiated.

2.11. Research Subject to Other Regulations

Research Subject to Department of Defense (DoD) Regulations
When conducting DoD sponsored survey research or survey research conducted within the DoD, review and approval is typically required by the DoD, and when appropriate, the research should be reviewed and approved by the IRB prior to DoD approval.

Research Subject to Department of Justice (DOJ) Regulations
Research conducted within the Bureau of Prisons must have an adequate research design and contribute to the advancement of knowledge about corrections.

3.0 Reason for the Policy
This policy ensures that human subjects research conducted under the oversight of the IU IRB protects human subjects and is conducted in accordance with all applicable federal, state, and local laws and regulations and institutional policy.

4.0 Procedures

4.1. IRB Administration and Support
The day-to-day operations of the IRB are administered and supported by the IU Human Subjects Office (HSO). No individual responsible for business development at IU or its affiliates may participate in the day-to-day operations of the IRB review process.

The IRB has given HSO staff the authority to conduct preliminary review of all research submitted to the IRB in order to ensure that it is in an acceptable form for the IRB to review.

The IU HSO certifies the review and approval of human subjects research to external funding agencies, as required.

The IRB has delegated authority to HSO staff to provide guidance to investigators as to whether an activity requires IRB review. However, HSO staff may consult with members of the IRB with any questions.

HSO staff notify investigators in writing of IRB actions taken on research.

4.2. Submission to the IRB
Submission of proposed research is made through the online KC IRB system. Investigators complete a series of questionnaires, and, depending on the nature of the research, may also be required to provide the following additional materials, as applicable:
- Data collection instruments, including surveys, questionnaires, interview questions, etc.;
- Recruitment materials, including flyers, advertisements, letters, e-mail scripts, etc.
- Informed consent or assent documents, unless a waiver of consent or assent is being requested.
- Grant proposal, if the research is funded by a Health and Human Services (HHS) agency such as NIH, and the IU investigator is the direct recipient of the funds.

4.3. **IRB Actions**

The IRB may approve, provisionally approve, table, or disapprove a research study or submission, including new studies, amendments, and renewals. All actions and determinations made by the IRB are conveyed to the investigator in writing.

**Approval**
No changes are needed. The investigator may proceed with the research.

**Provisional Approval**
Specific revisions, stipulated by the convened IRB and requiring simple concurrence by the investigator need to be made. After revisions have been made, final approval may be granted by the IRB Chair or designee. In the event of extensive changes or questions, reviewers may request subsequent review at a convened IRB meeting. The approval of research contingent on specific minor revisions is documented in the minutes of the first IRB meeting that takes place after the date of approval.

**Table**
Major concerns exist that impact the protection of human subjects, or clarifications or modifications regarding the research or consent process that are directly relevant to the determinations required by the convened IRB are necessary. This action can be taken only by the convened IRB, and the investigator’s response must be reviewed by the convened IRB at a subsequent meeting.

**Disapprove**
Significant study concerns exist such that the IRB does not feel the project can be conducted as currently proposed. Specific reasons for disapproval are included in meeting minutes and communicated to the investigator in writing. The study cannot be resubmitted in the same format. This action can be taken only by the convened IRB.

The IRB may, upon the request of an investigator or on its own initiative, reconsider any proposal and reverse its own determination. An investigator may appeal a decision made by the IRB by responding in writing to concerns posed by the IRB. These appeals should be addressed to the HSO, which will provide this information to the IRB. The IRB may choose to invite the investigator to a meeting to address the concerns or may reject the investigator’s appeal based on initial concerns with the research.

Research studies that are tabled or disapproved by the IRB cannot be resubmitted to a different IRB in an attempt to bypass the original IRB’s decision.

Research that is not being conducted in accordance with the IRB’s requirements or has been associated with unexpected serious harm to participants may also be suspended.
(temporary cessation of some or all research activities) or terminated (permanent
withdraw of IRB approval for all research activities).

4.4. Expedited review
Although investigators make a preliminary determination about whether research
meets the criteria for expedited review procedures, the IRB makes the final
determination. If the IRB does not concur with the investigator’s determination, it may
request modification to the research or require that the research be submitted for
convened IRB review.

Individuals who are appointed as regular or alternate members of an IRB may be
designated by the Chair to review research that qualifies for review under expedited
procedures when at least one of the following criteria have been satisfied:

• Minimum of two (2) years’ service as a regular member of the IRB
• Minimum of twenty (20) full board reviews with mentorship from experienced
IRB members
• Minimum of eight (8) new expedited study reviews in collaboration with an
experienced IRB member
• In the case of HSO staff IRB members, having attained Certified IRB Professional
(CIP) certification and completed the applicable training per the HSO staff
manual.

In conducting an expedited review, the IRB reviewer may exercise all of the authorities
of the convened IRB, except that he/she may not disapprove the research. Research
may only be disapproved by the convened IRB.

Consultants with specific expertise may be utilized to assist in the review of expedited
research, when appropriate. Their comments are documented and forwarded to an IRB
member for review and final approval.

Approval of research under the expedited review procedure is reported to the convened
IRB.

4.5. Scientific Review
Scientific review, which addresses whether the research uses procedures consistent
with sound research design that will yield the expected knowledge, is conducted on all
non-exempt human subjects research submitted to the IRB. Scientific review may be
conducted by external committees as described below. When scientific review is not
conducted by one of these committees, the IRB conducts scientific review as part of
determining that the research meets the criteria for IRB approval.

IU Simon Cancer Center (IUSCC) Scientific Review Committee (SRC)
This committee provides scientific review for prospective cancer-related research
utilizing IUSCC patients or resources. Documentation of the IUSCC SRC approval must
be obtained before IRB approval is granted.

Indiana Clinical and Translational Science Institute (CTSI)
New studies which are greater than minimal risk, require review by the convened
biomedical IRB, and have not undergone a peer-review process must be submitted to
the CTSI SRC for scientific review. Documentation of CTSI SRC approval must be
obtained before IRB approval is granted.
• Peer review may include review of the protocol by an external funder, such as
a federal agency or established not-for-profit research foundation, or protocol development by a commercial sponsor, such as a pharmaceutical or medical device company.

- When deemed necessary by an IRB Chair or HSO Associate Director, other protocols requiring convened IRB review may be required to obtain CTSI SRC approval prior to IRB approval.

The CTSI-sponsored Project Development Teams (PDTs) assist investigators in developing ideas/hypotheses into well-designed translational research projects. This goal is accomplished by helping investigators with protocol development (including scientific review); provision of pilot funding; facilitation of collaboration with other investigators; and access to certain CTSI Core Resources. Investigators may request scientific review from the PDTs.

4.6. Renewal and expiration

If renewal is required, KC IRB reflects the current expiration date for the protocol. The HSO notifies investigators of the need to renew a study well in advance of the expiration date.

- Upon notification, the investigator should submit for IRB review the appropriate renewal information, including any necessary protocol attachments.
- Submission for renewal is made through the online KC IRB system. Investigators complete a questionnaire and, depending on the nature of the research, may also be required to provide additional materials for the IRB’s review.

Review of Renewals

The following information must be provided by the investigator at time of renewal and is reviewed by the IRB, as applicable:

- The number of subjects accrued, including a summary of any withdrawal of subjects from the research since the last IRB review and the reasons for withdrawal, if known
- Summary of unanticipated problems, minor deviations, and/or noncompliance since the last IRB review
- Statement whether adverse events have occurred in excess of the expected frequency and level of severity as documented in the research protocol, the informed consent document, and investigator’s brochure and, if so, a summary
- Most recent data safety monitoring results, if applicable
- Summary of the progress of the research
- Any relevant information, published or unpublished, since the last IRB review, especially information about risks associated with the research. Relevant information may include literature publications, audits, subject complaints, interim findings.
- The latest version of the IRB-approved protocol and informed consent document(s)
- A brief summary of any amendments to the research approved by the IRB since the last IRB review (compiled by the HSO on the investigator’s behalf)
- Any proposed modifications to the informed consent document or protocol
- For VA studies, the investigator’s assessment based on research results, the gender and minority status of those entered into the research, number of subjects considered as members of specific vulnerable populations, and an
assurance that all serious or unexpected adverse events had been reported as required

When the IRB reviews the current informed consent/assent documents at the time of renewal, it ensures that they are still accurate and complete. If any significant new findings are identified that may relate to the subject’s willingness to continue participation in the research, the IRB requires that the information be provided to subjects in accordance with regulations.

The IRB determines whether additional verification from sources other than the investigator are necessary to ensure that no material changes have occurred since the last review based upon the type of research, risks to subjects, and/or previous noncompliance concerns.

Expiration
When renewal is required, there are no provisions for any grace period extending the conduct of the research beyond the expiration date of IRB approval. Additionally, where the convened IRB issues a provisional approval, renewal must occur no more than one year after the date the research was reviewed by the convened IRB. It is the investigator’s responsibility to ensure that the research is reapproved prior to the study’s expiration date.

- If the investigator fails to submit a renewal to the IRB or the IRB has not reviewed and approved a research study by 11:59 p.m. on the last date the protocol is approved, research activities must cease, including enrollment of new subjects, interventions on/interactions with current subjects, and analysis of identified data.
- However, if the investigator is actively pursuing renewal with the IRB and the IRB believes that an overriding safety concern or ethical issue exists such that it is in the best interest of individual subjects for the research to continue, the IRB may permit this while the review process is completed. Enrollment of new subjects, however, cannot occur after the expiration of IRB approval.
- Lapse in IRB approval need not be reported to OHRP as a suspension of IRB approval under HHS regulations.

4.7. Amendments to Previously Approved Research
Submissions for amendment are made through the online KC IRB system. Investigators complete a questionnaire and attach any revised IRB-approved documents and any applicable new documents.

Amendments to Expedited Research
Amendments to research previously approved under expedited procedures are reviewed under expedited procedures provided the changes continue to meet the expedited category(ies). If the proposed changes to the research involve addition of procedures which are not described by the expedited category(ies) or involve greater than minimal risk, the research must be reviewed by the convened IRB.

Amendments to Research Previously Approved by the Convened IRB
Pursuant to 45 CFR §46.110(b)(2), minor changes in research previously approved by the convened IRB may be reviewed and approved under an expedited review procedure. Major changes (e.g., those that involve increased risks or discomforts to subjects or decreased potential benefit) are reviewed and approved by the convened IRB. Refer to the IU HSO website for additional information and examples.
Personnel Changes
Changes in key personnel are considered amendments to previously approved research which require prospective IRB approval; however, investigators may make changes to the list of non-key research personnel by prospectively submitting a notification of the change to the HSO. These notifications are not considered amendments and do not require prospective IRB review and approval. See the IU HSO website for additional information.

4.8. Reopening Research
The investigator may request the IRB reopen a research study that was prematurely closed/expired. In reviewing this request, the IRB may require modifications to the research prior to reopening and/or enrolling subjects, as necessary. The investigator may need to submit a new research application to restart/continue the previously closed/expired research study at the discretion of the HSO.

5.0 Sanctions
University faculty, staff, and students that are found to be in violation of this policy may be subject to sanctions relating to their participation in research with human subjects, up to and including permanent suspension or bar from engaging in research with human subjects at IU.

6.0 History
Replaces portions of the previous IU SOP for IRB Operations (v02/2017)

7.0 Related Information
AAHRPP Standards
- Standard II-2, II.2.D, II.2.E, II.2.G,
- Standard II-4, Elements II.4.A

IU HRPP Documents
- Forms:
  - Drug or Biological Product Form
  - Medical Device Form
- Guidance:
  - Additional Review by Non-IRB Committees
  - Data Safety Monitoring
  - Expedited Research
  - Seeking Opinion from FDA Regarding Drug Exemption
- Policies/Procedures:
  - Recruitment of Human Subjects
  - Safety Monitoring
- Staff Manual - Training

KC IRB Questionnaires
- KC Crosswalk (http://researchcompliance.iu.edu/hso/hs_guidance.html)
Regulatory References

- 21 CFR 56
- 21 CFR 312
- 21 CFR 812
- 45 CFR 46
- FDA Information Sheet Guidance for IRBs, Clinical Investigators, and Sponsors: Significant Risk and Nonsignificant Risk Medical Device Studies
- FDA Guidance for Clinical Investigators, Sponsors, and IRBs
  - Investigational New Drug Applications (INDs) – Determining Whether Human Research Studies Can Be Conducted Without an IND
  - IRB Responsibility for Reviewing the Qualifications of Investigators, Adequacy of Research Sites, and the Determination of Whether an IND/IDE is Needed
- OHRP Guidance:
  - Approval of Research with Conditions
  - Continuing Review
  - Expedited Review Procedures
  - Written Institutional Review Board (IRB) Procedures
- VHA Handbook 1200.05, Requirements for the Protection of Human Subjects in Research
KC IRB

1.0 Scope
This policy applies to all Indiana University (IU) faculty, staff, and students, or others who are engaged in human subjects research which falls under the jurisdiction of the Indiana University Human Research Protection Program (HRPP).

2.0 Policy Statement
Kuali Coeus (KC) is one of multiple Kuali software modules IU has implemented for electronic research administration. The Human Subjects Office (HSO) implemented KC IRB, which stands for Kuali Coeus Institutional Review Board, in August 2013. KC IRB is a web-based system to manage the complexities of research administration needs for faculty, staff, and institutional affiliates. KC IRB was implemented to manage the submission, processing, and review of human subjects research studies at IU. All IU faculty, staff, and students must submit all proposed research studies involving human subjects in the KC IRB system. This system provides a high level of accountability as it allows for tracking the research, including initial submission, amendments, renewals and general information items, and systematic administration of reviews by the HSO staff and the IRBs. KC IRB does not purport to meet the standards for electronic signature set forth in the FDA’s 21 CFR 11.

3.0 Reason for the Policy
To ensure that members of the research community understand and use KC IRB in a consistent manner that facilitates compliance with IU HRPP Policies and procedures and federal regulations.

4.0 Procedures
4.1 KC IRB System Controls
4.1.1 System Access
KC IRB is an IU-hosted system protected by Central Authentication Service (CAS)
and can be accessed only with an IU computing account (username and passphrase). Anyone with an IU computing account can access KC IRB; however, only certain individuals (or groups) can access the study-specific KC IRB Protocol.

The level of access to the KC IRB Protocol is determined by roles and permissions given to individuals. Some roles and permissions are automatically assigned by KC IRB, while some are manually assigned.

4.1.2. **Roles and Permissions**

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<tr>
<th>Role</th>
<th>Permission</th>
<th>Create &amp; Submit</th>
<th>View</th>
<th>Edit</th>
<th>Review &amp; Approve</th>
<th>Query &amp; Report</th>
<th>Design &amp; Maintain</th>
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<td><strong>Baseline:</strong> Anyone with access to KC IRB via CAS authentication, including faculty, staff, students, and affiliates</td>
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<tr>
<td><strong>Unit Administrator Advanced:</strong> Persons requesting access to protocols whose lead unit belongs to a particular unit or set of units for purposes of administrative management or reporting</td>
<td>✔</td>
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<tr>
<td><strong>Unit Administrator Protocol View:</strong> Persons requesting access to protocols whose lead unit belongs to a particular unit or set of units</td>
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<tr>
<td><strong>Organization Correspondent:</strong> Persons requesting access to protocols that include a particular organization</td>
<td>✔</td>
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<tr>
<td><strong>Principal Investigator (PI):</strong> PI, Site-specific PI, Student, Fellow, Resident PI</td>
<td>✔</td>
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<tr>
<td><strong>Co-Investigators/Research Personnel:</strong> Key and Non-Key Personnel</td>
<td>✔</td>
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</tr>
<tr>
<td><strong>Study Manager, Correspondent, Aggregator:</strong> Persons making submissions on behalf of the PI or requiring receipt of study correspondence, delegates, and study contacts</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
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</tr>
</tbody>
</table>

1 Definitions of permissions are as follows:
- **Create:** Initiate a submission within KC IRB
- **Submit:** Take the “Submit for Review” or “submit” action
- **View:** Read-only access to a protocol submission
• **Edit**: Make changes to a protocol submission  
• **Review**: Perform as a Reviewer; view protocol submission and take certain reviewer actions  
• **Approve**: Take the “Approve” action (or other determination [e.g., Grant Exemption]; Close) in KC IRB  
• **Query**: Search using specific protocol/submission criteria  
• **Report**: Design and carry out reporting functions  
• **Design**: Manipulate system functionality/user interface for KC IRB  
• **Maintain**: Assign users to roles and edit tables for display to users

4.1.3. **Role Management**  
Requests for and assignments of roles are the responsibility of HSO management.

The HSO maintains a list of personnel assigned to roles.

4.1.4. **Change History**  
An audit trail of changes made to a protocol is maintained in the Protocol History. The history contains the following in regard to the altered record:

- Description of action
- Date of action
- Date of modification
- Comments/explanation
- Username of person performing action
- Time/date of action

Protocols are editable based on the status of the protocol and/or submission. Changes may be made to protocols/submissions only in accordance with the following:

- **Administrative Correction** - Available only to the following roles:
  - HSO Management
  - HSO Staff
- **Edit** - Available only in the following protocol statuses:
  - Pending / In Progress
  - Amendment in Progress
  - Renewal in Progress
  - FYI in Progress
  - Returned to PI
  - Withdrawn
  - Tabled
  - Provisionally Approved

4.1.5. **Sequencing**  
KC IRB assigns numbers to amendment, renewal, and FYI actions in a sequential order (i.e., A002, R005). The protocol history displays sequence number in order.

4.1.6. **Record Retrieval**  
KC IRB is equipped with search functionality as follows:

- Anyone with access to KC IRB can utilize the search functionality; however, the results returned are dependent on the roles as outlined above.
- Some search results may be configured to return “active” and/or
“inactive” protocols.
  o In general, protocol statuses that are considered “inactive”
    include “Deleted,” “Abandoned,” and “Amendment or
    Renewal Incorporated into Protocol”.

4.1.7. **Person Signature**

KC IRB is equipped with electronic signature capabilities, which the system
refers to as “person signature”.

The HSO utilizes the person signature functionality as follows:
- When the following actions are taken, the correspondence generated
  includes the person signature of the HSO staff member taking the
  action.
  o Review Not Required
  o Exemption Granted*
    *When a limited IRB review is required, the correspondence
     includes the person signature of the IRB Chair of the Board to
     which the item is assigned.
- When the following actions are taken, the correspondence generated
  includes the person signature of the IRB Chair of the Board to which the
  item is assigned.
  o Approve
  o Close
  o Disapprove
  o Expedited Approval
  o Response Approval
  o Specific Minor Revisions (Provisional Approval)
  o Substantive Revisions Required (Table)
  o Suspend
  o Terminate
- The HSO prints (see below) and continues to apply an ink (physical)
  signature to all non-exempt human subjects research (HSR) submissions
  that are subject to VA or FDA regulations. All other non-exempt HSR
  submissions may utilize an electronic signature (via Adobe Acrobat
  secure signature functionality or another acceptable secure electronic
  signature program).

4.1.8. **Printing**

KC IRB protocol data may be printed directly from the system via the “Print”
panel, which is displayed on the Protocol Actions tab of the KC Protocol.

4.1.9. **Protocol Expiration Date**

Protocols assigned expiration dates expire at 11:59 p.m. on the IRB-approved
expiration date. For example, if the protocol was approved for 1 year on July
20, 2015, the investigator can conduct study activities through 11:59 p.m. July
19, 2016.

4.2. **KC IRB Submission Process**

This section describes the type of information needed and the mechanism used by
faculty, staff, students, and others when preparing to submit a protocol through KC
IRB.
Investigators and research teams create protocols electronically in the KC IRB system. There are two ways information about a research study is provided within the system: 1) entering data directly into data fields and 2) uploading pertinent documents into the system.

The main protocol description is described in smart-form Questionnaires housed within the KC Protocol. For detailed information about the questionnaire logic and specific questionnaire questions, refer to the KC Crosswalk located on the HSO Policies & Guidance webpage.

KC IRB accommodates various types of submissions that may occur during the active life of a research study, including:

- New Protocol Application:
  - Exempt, Expedited, and Full Board
  - Not-Human Subjects Research (Research Not Subject to Human Subjects Regulations)
  - Reliance Request
  - Emergency Use
  - Humanitarian Use Device
- Amendment
- Renewal with or without an Amendment
- Notify IRB of a Reportable Event
- Request to Close an IRB Protocol

Once a submission has been prepared within the KC IRB system, it must be officially submitted for IRB review. When the “Submit for Review” action is taken on the Protocol Actions tab of the KC Protocol, the protocol is locked to additional editing and notifications are generated for the following individuals/groups:

- Aggregator (a KC role granted to the initiator of a protocol)
- PI
- Site Specific PI
- Student, Fellow, Resident PI
- Study Manager/Correspondent
- IRB Admin “Intake” Group
- Radiation Safety Office, if the protocol involves the use of radiation/radioactivity in addition to what is used for standard clinical treatment
- University Director, HRPP and Executive Director, RIICE, if study involves gene therapy

Notifications received by the IRB Admin “Intake” Group initiate the intake process within the HSO. No further action is required from the other recipients.

4.3. **KC IRB Screening and Pre-Review Process**

Upon submission, a preliminary review (“pre-review”) by an HSO staff member is conducted. If the pre-review results in needed clarifications or revisions, these are communicated to the research team within KC IRB.

HSO staff take the “Return to PI” action in KC, which unlocks the KC Protocol for editing, and prompts notifications for the above-listed individuals (4.2).
Once the research team has addressed the items identified in the pre-review, the protocol must be resubmitted for IRB review. When the “Submit for Review” action is taken on the Protocol Actions tab of the KC Protocol, the protocol is again locked to additional editing and notifications are generated for the above-listed individuals/groups (4.2).

4.4. **KC IRB Review and Approval Process**

Once pre-review is complete, submissions are reviewed and approved in the following manner:

- **Not Human Subject Research and Reliance Requests**
  - Qualified HSO staff member reviews directly within the KC IRB system.
  - Reviewer takes “Review Not Required” action, which indicates confirmation that IRB review and approval are not required.
  - “Review Not Required” action generates an approval letter containing the reviewer’s signature.
  - Above-listed individuals (4.2) except the IRB Admin “Intake” Group receive notification of approval.

- **Exempt Submissions**
  - The KC Protocol, including Questionnaires and attached documents, is reviewed by a qualified HSO staff member directly within the KC IRB system.
  - Reviewer takes “Grant Exemption” action, which indicates confirmation that the study is exempt from the requirements of 45 CFR 46 per the criteria set forth in 45 CFR 46.101(b) or IU HRPP Policy on Exempt Research.
  - “Grant Exemption” action generates a notice of exemption letter containing the reviewer’s signature, which can be retrieved from the KC Protocol.
  - Above-listed individuals (4.2) except the IRB Admin “Intake” Group receive notification of approval.
  - PI and Student, Fellow, Resident PI receive notification, if the study intends to include children

- ** Expedited and Full Board Submissions (including HUD, Amendments, Renewals, and FYI Submissions)**
  - For VA- and FDA-regulated submissions:
    - The KC Protocol, including questionnaires and attached documents, is printed and reviewed by a qualified IRB member.
    - The IRB member signs the printed signature page(s)* to indicate approval.
    - HSO staff uploads scanned, signed signature page(s) to the KC Protocol.
    - HSO staff takes the appropriate approval action, such as expedited approval, response approval, or approval in KC IRB, which indicates confirmation that the study meets the criteria for IRB approval set forth in 45 CFR 46.111 and/or 21 CFR 56.111.
    - The approval action generates the approval letter containing the IRB Chair’s signature and listing any protocol-specific determinations made by the IRB.
    - The approval letter and all signed signature pages can be
For all other research submissions:

- The KC Protocol, including Questionnaires and attached documents, is reviewed (within the KC IRB system, via email, and/or from an internal electronic file server) by a qualified IRB member.
- The IRB member electronically signs the signature page(s)* to indicate approval.
- HSO staff uploads the digitally signed signature page(s) to the KC Protocol.
- HSO staff takes the appropriate approval action, such as expedited approval, response approval, or approval in KC IRB, which indicates confirmation that the study meets the criteria for IRB approval set forth in 45 CFR 46.111.
- The approval action generates the approval letter containing the IRB Chair’s signature and listing any protocol-specific determinations made by the IRB.
- The approval letter and all signed signature pages can be retrieved from the KC Protocol.

4.4.1. **Electronic Stamping of Informed Consent Documents**

KC IRB applies an electronic stamp to unsecured PDF informed consent documents when they are viewed or downloaded from the system. This electronic stamp is based on the status of the protocol at the time the document is viewed or downloaded. Electronic stamps appear as follows:

- For studies that are **Open to Enrollment** → Protocol XXXXXXXXXXX IRB Approved
- For studies that are **Closed to Enrollment** → Protocol XXXXXXXXXXX IRB Approved for re-consenting only
- For studies in **Data Analysis Only** → Protocol XXXXXXXXXXX IRB Approved – Do Not Enroll Subjects

* List of Signature Pages printed from the KC Protocol and signed by qualified IRB member:

- Non-Exempt New Studies → Protocol Summary
- Amendments → Protocol Summary + Amendment Questionnaire
- Renewals → Protocol Summary + Renewal and Changes & Amendments Questionnaires
- Reportable Events → Protocol Summary + Reportable Events Questionnaire
- Study Closures → Closeout Report Questionnaire
- HIPAA Authorization Waivers → HIPAA Questionnaire
- VA HIPAA Authorization Waivers → VA Research Questionnaire
• For *disapproved* studies → Protocol XXXXXXXXXX Disapproved
• For *expired* studies → IRB Approval of Protocol XXXXXXXXXX Expired DD-Month-YYYY
• For *closed* studies → Protocol XXXXXXXXXX Closed

While the electronic stamp is required to be applied only to the informed consent document, the system will apply it to ANY unsecured PDF document viewed or downloaded from the Notes & Attachments tab of the KC Protocol.

4.4.2. **IRB Approval Documentation**
Approval documents vary based on the type of submission and level of review provided. Please note the combination of documentation noted below constitutes the “IRB approval document”.

<table>
<thead>
<tr>
<th>Type of Submission</th>
<th>Approval Documents</th>
</tr>
</thead>
<tbody>
<tr>
<td>New Study – Full Board or Expedited</td>
<td>Approval Letter</td>
</tr>
<tr>
<td></td>
<td>Signed Protocol Summary</td>
</tr>
<tr>
<td></td>
<td>Informed Consent with Watermark</td>
</tr>
<tr>
<td></td>
<td>(if applicable)</td>
</tr>
<tr>
<td>New Study – Exempt</td>
<td>Notice of Exemption Letter</td>
</tr>
<tr>
<td>Amendment – Exempt</td>
<td>Notice of Exemption Letter</td>
</tr>
<tr>
<td>Amendment - Full Board or Expedited</td>
<td>Approval Letter</td>
</tr>
<tr>
<td></td>
<td>Signed Protocol Summary**</td>
</tr>
<tr>
<td></td>
<td>Amendment Questionnaire**</td>
</tr>
<tr>
<td>Renewal – Full Board or Expedited</td>
<td>Approval Letter</td>
</tr>
<tr>
<td></td>
<td>Signed Protocol Summary**</td>
</tr>
<tr>
<td></td>
<td>Renewal Questionnaire**</td>
</tr>
<tr>
<td></td>
<td>Changes &amp; Amendments Questionnaire**</td>
</tr>
<tr>
<td>Reportable Event</td>
<td>Approval Letter</td>
</tr>
<tr>
<td></td>
<td>Signed Protocol Summary**</td>
</tr>
<tr>
<td></td>
<td>Reportable Events Questionnaire**</td>
</tr>
<tr>
<td>Closure</td>
<td>IRB Closure Notice/Letter</td>
</tr>
<tr>
<td></td>
<td>Signed Closeout Report Questionnaire</td>
</tr>
<tr>
<td>Reliance Request</td>
<td>Notice of Reliance</td>
</tr>
<tr>
<td>Not Human Subject Research</td>
<td>Notice of Determination - Administratively Reviewed</td>
</tr>
<tr>
<td>(Research Not Subject to Human Subjects Regulations)</td>
<td></td>
</tr>
<tr>
<td>Waiver – Informed Consent / Parental Consent</td>
<td>Approval Letter</td>
</tr>
<tr>
<td>Waiver – HIPAA Authorization</td>
<td>Approval Letter</td>
</tr>
<tr>
<td></td>
<td>Signed Protocol Summary**</td>
</tr>
<tr>
<td></td>
<td>Signed KC IRB Questionnaire K and/or L**</td>
</tr>
</tbody>
</table>

**Collated together into a single document**

4.5. **KC IRB Maintenance of Research Submissions**
All actions related to a specific submission, including information entered, documents attached, post-approval submissions, correspondence generated, HSO or IRB notes,
and history and status are stored together electronically within the KC IRB Protocol for each research study.

For VA- and FDA-regulated research submissions, a physical file of the same above-listed information is also maintained, which includes the ink signature pages of approved actions.

Actions taken and protocol attachments are clearly labeled with the username of the individual who took the action and the date and time that action was taken.

5.0 Sanctions
University faculty, staff, and students that are found to be in violation of this policy may be subject to sanctions relating to their participation in research with human subjects, up to and including permanent suspension or bar from engaging in research with human subjects at IU.

6.0 History
Replaces the previous IU SOP for KC IRB (v02/2017)

7.0 Related Information
AAHRPP Standards
• N/A

IU HRPP Documents
• N/A

KC IRB Questionnaires
• KC Crosswalk (http://researchcompliance.iu.edu/hso/hs_guidance.html)

External References
• www.kuali.org
1. INTRODUCTION

The FDA regulations for the protection of human subjects in research, 21 CFR 50, stipulate requirements for obtaining (§50.25) and documenting (§50.27) informed consent. They also provide a narrow exception to the requirement for informed consent from each human subject, or his or her legally authorized representative (LAR) prior to initiation of an experimental intervention (§50.24). The exception applies to a limited class of research activities involving human subjects who are in need of emergency medical intervention but cannot give informed consent because of their life-threatening medical condition and do not have an LAR to represent them. The intent of these regulations is to allow research on life-threatening conditions for which available treatments are unproven or unsatisfactory and where it is not possible to obtain informed consent, while establishing additional protections to provide for safe and ethical studies.

The FDA recognizes that persons with life-threatening conditions who can neither give informed consent nor refuse enrollment are a vulnerable population. The FDA recognizes that the lack of autonomy and inability of subjects to give informed consent requires additional protective procedures in the review, approval, and operation of this research. The exception from the informed consent requirement permitted by the rule is conditional upon documented findings by an Institutional Review Board (IRB).

2. POLICY AND ASSOCIATED PROCEDURES

2.1. Exception from Informed Consent for Studies Conducted in Emergency Settings

2.1.1 Pursuant to 21 CFR 50.24, the IRB may approve research (clinical investigation) without requiring that informed consent of all research subjects be obtained if the IRB (with the concurrence of a licensed physician who is a member of or consultant to the IRB and who is not otherwise participating in the clinical investigation) finds and documents each of the following:

2.1.1.1 The human subjects are in a life-threatening situation, available treatments are either unproven or unsatisfactory; and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.

2.1.1.2 Obtaining informed consent is not feasible because:

5.7.1.2.1 The subjects will not be able to give their informed consent as a result of their medical condition;
5.7.1.2.2 The intervention under investigation must be administered before consent from the subjects’ LAR is feasible; and

5.7.1.2.3 There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation.

2.1.1.3 Participation in the research holds out the prospect of direct benefit to the subjects because:

5.7.1.3.1 Subjects are facing a life-threatening situation that necessitates intervention;

5.7.1.3.2 Appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence supports the potential for the intervention to provide a direct benefit to the individual subjects; and

5.7.1.3.3 Risks associated with the investigation are reasonable in relation to what is known about the medical condition of the potential class of subjects, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.

2.1.1.4 The clinical investigation could not practicably be carried out without the waiver.

2.1.1.5 The proposed investigational plan defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact an LAR for each subject within that window of time and, if feasible, to asking the LAR contacted for consent within that window rather than proceeding without consent. The investigator will summarize efforts made to contact LARs and make this information available to the IRB at the time of continuing review.

2.1.1.6 The IRB has reviewed and approved informed consent procedures and an informed consent document consistent with §50.25. These procedures and the informed consent document are to be used with subjects or their LARs in situations where use of such procedures and documents is feasible. The IRB has reviewed and approved procedures and information to be used when providing an opportunity for a family member to object to a subject’s participation in the clinical investigation consistent with §50.24(a)(7)(v).

2.1.1.7 Additional protections of the rights and welfare of the subjects will be provided, including, at least:
5.7.1.7.1 Consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the clinical investigation will be conducted and from which the subjects will be drawn;

5.7.1.7.2 Public disclosure to the communities in which the clinical investigation will be conducted and from which the subjects will be drawn, prior to initiation of the clinical investigation, of plans for the investigation and its risks and expected benefits;

5.7.1.7.3 Public disclosure of sufficient information following completion of the clinical investigation to apprise the community and researchers of the study, including the demographic characteristics of the research population, and its results;

5.7.1.7.4 Establishment of an independent data monitoring committee to exercise oversight of the clinical investigation; and

5.7.1.7.5 If obtaining informed consent is not feasible and a legally authorized representative is not reasonably available, the investigator has committed, if feasible, to attempting to contact within the therapeutic window the subject’s family member who is not an LAR, and asking whether he/she objects to the subject’s participation in the clinical investigation. The investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review.

2.1.1.8 The IRB is responsible for ensuring that procedures are in place to inform, at the earliest feasible opportunity, each subject, or if the subject remains incapacitated, an LAR of the subject, or if such a representative is not reasonably available, a family member, of the subject’s inclusion in the clinical investigation, the details of the investigation, and other information contained in the informed consent document. The IRB shall also ensure that there is a procedure to inform the subject, or if the subject remains incapacitated, an LAR of the subject, or if such a representative is not reasonably available, a family member, that he/she may discontinue the subject’s participation at any time without penalty or loss of benefits to which the subject is otherwise entitled. If an LAR or family member is told about the clinical investigation and the subject’s condition improves, the subject is also to be informed as soon as feasible. If a subject is entered into a clinical investigation with waived consent and the subject dies before an LAR or family member can be contacted, information about the clinical
investigation is to be provided to the subject’s LAR or family member, if feasible.

2.1.1.9 The IRB determinations required by 21 CFR 50.24(a) and the documentation required by 21 CFR 50.24(e) are to be retained by the IRB for at least three (3) years after completion of the clinical investigation, and the records shall be accessible for inspection and copying by FDA in accordance with 21 CFR 56.115(b).

2.1.1.10 Protocols involving an exception to the informed consent requirement under 21 CFR 50.24 must be performed under a separate investigational new drug application (IND) or investigational device exemption (IDE) that clearly identifies such protocols as protocols that may include subjects who are unable to consent. The submission of those protocols in a separate IND/IDE is required even if an IND for the same drug product or an IDE for the same device already exists. Applications for investigations under 21 CFR 50.24 may not be submitted as amendments under 21 CFR 312.30 or 21 CFR 812.35.

2.1.1.11 If an IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in the exception provided under §50.24(a) or because of other relevant ethical concerns, the IRB must document its findings and provide these findings promptly in writing to the clinical investigator and to the sponsor of the clinical investigation. The sponsor of the clinical investigation must promptly disclose this information to the FDA and to the sponsor’s clinical investigators who are participating or are asked to participate in this or a substantially equivalent clinical investigation of the sponsor, and to other IRB’s that have been, or are, asked to review this or a substantially equivalent investigation by that sponsor.

2.2. Emergency Research Consent Waiver Subject to HHS Regulation. The regulations for the protection of human research subjects (45 CFR 46) stipulate requirements for obtaining (§46.116) and documenting (§46.117) informed consent, and give the IRB authority to alter or waive informed consent in certain circumstances (§46.116(c)-(d)). In addition, pursuant to §46.101(i), the Secretary, HHS, has waived the general requirements for informed consent at §46.116(a) and (b) and §46.408 (to be referred to as the “Emergency Research Consent Waiver”) for a class of research consisting of activities, each of which have met the following strictly limited conditions:

2.2.1 Research Subject to FDA Regulations

2.2.1.1 The IRB has approved both the activity and a waiver of informed consent and found and documented that:

2.2.1.1.1 the research activity is subject to 21 CFR 50 and will be carried out under an FDA investigational new drug (IND) application or an FDA investigational device
2.2.2 **Research Not Subject to FDA Regulations.** The IRB has approved both the research and a waiver of informed consent and has (a) found and documented that the research is not subject to 21 CFR 50 and (b) found, documented and reported to OHRP that the conditions outlined in 2.1 above have been met relative to the research.

3. **ADDITIONAL POLICIES AND PROCEDURES**

3.1 **Research Subject to FDA Regulations**

3.1.1 The research plan must be approved in advance by the FDA and the IRB, and publicly disclosed to the community in which the research will be conducted.

3.2 **Research Subject to HIPAA Regulations**

N/A

3.3 **Research Subject to VA Regulations**

3.3.1 VHA does not conduct planned emergency research.

3.4 **Research Subject to Other Regulations**

3.4.1 **Research Subject to Department of Defense (DoD) Regulations**

3.4.1.1 An exception from consent in emergency medicine research is prohibited unless a waiver is obtained from the U.S. Secretary of Defense.

3.4.2 **Research Subject to Department of Education (ED) Regulations**

N/A

3.4.3 **Research Subject to Department of Justice (DOJ) Regulations**

N/A
1. INTRODUCTION

A criterion for approval of research is that selection of subjects is fair and equitable. As such, the IRB must evaluate this by considering both the selection (inclusion and exclusion) criteria and the proposed plans for recruitment of subjects for each research study.

Identifying, approaching, selecting, recruiting, and enrolling subjects in research must be done in a planned fashion. If not done properly, research can fail due to improper subject selection with subsequent withdrawal of subjects who did not meet entry criteria. There must be fair procedures and outcomes in the selection of research subjects.

A sound recruitment plan should be described and justified and should consider the following points: (a) number of subjects; (b) identification of potential subjects; (c) how best and who to approach for community projects; (d) whether subjects may be employees or students of the research staff; (e) plan for contacting potential subjects (e.g., methods, medium, communication, advertisement); (f) compensation; (g) whether there is need for approval from treating health care providers, if applicable; and (h) whether other approvals are needed.

2. POLICY AND ASSOCIATED PROCEDURES

2.1 Recruitment

2.1.1 Recruitment methods and advertisements represent the beginning of the consent process. Therefore, the IRB must review and approve proposed recruitment methods and advertisement material to judge whether they fulfill the requirements of consent. When approaching or recruiting subjects, information must be presented in a language that is understandable to the subject or the subject’s representative.

2.1.2 Methods, materials, and modes used to approach or recruit subjects must be submitted to the IRB for review and cannot be used until IRB approval is given. Additionally, the study sponsor may require approval of the recruitment process. The final versions of any printed, audio, or video advertisements or other recruitment information to be seen or heard by prospective subjects to solicit participation in research must be included with an explanation of the mode of communication at the time of study submission. Methods of recruitment may include but are not limited to print, radio, or television advertisements; personal contact; database searches; letters to potential subjects; Internet listings; newsletters; and community talks or exhibit booths.

2.1.3 Should recruitment or advertising methods be changed or added, the methods and materials to be used must be submitted to the IRB via an amendment. These recruitment methods and materials must be reviewed and approved by the IRB prior to their use. When advertisements are easily compared to an approved informed consent document,
they may be reviewed and approved using an expedited procedure. However, if the IRB reviewer has doubts or other complicating issues are involved, he/she may request that the advertisement be reviewed at a convened IRB meeting.

2.1.4 Materials given to others (e.g., health care providers, teachers, or schools) intended for use to solicit research subjects and not given to or seen by the potential subjects do not require IRB approval. However, the process (e.g., contacting health care providers or teachers for referrals) must be explained in the IRB application and be approved by the IRB.

2.1.5 Contacting potential subjects should be carefully considered. If a potential subject is to be identified by protected or confidential information (e.g., medical records or legal files), the procedures for identifying and contacting them and the methods for disclosing this information should be clearly delineated in the IRB application and reviewed by the IRB on a case-by-case basis.

2.1.6 When doing research within a community group or organization, the person authorized to speak for the group should be approached for permission to recruit from that group or organization.

2.1.7 When appropriate, a potential subject should be encouraged to consult his/her physician prior to enrollment. Before any study findings are reported to a subject’s physician, permission for information to be released must be obtained from the subject.

2.1.8 Recruiting or approaching subjects may not begin until IRB approval has been obtained for the study as well as the recruitment process, method, mode, and material(s). Additionally, there can be no more subject recruitment if a study is suspended or terminated by the IRB or the IRB approval of the study has expired.

2.1.8.1 Selection of subjects must be based on the IRB approved inclusion and exclusion criteria. Any change in these criteria must first be approved by the IRB.

2.1.8.2 Subjects may be considered for a research study (prescreened) prior to obtaining full informed consent as long as no procedures are performed.

2.1.8.3 If subjects are purposely placed into different study groups, the method of assignment (or randomization) must be predetermined.

2.1.8.4 Screening procedures (if applicable) that are not the standard of care but instead are being conducted solely for the purposes of the research project must be completed only after the consent has been fully executed. The subject must meet the inclusion and exclusion criteria before he/she is enrolled into the study. If the subject is screened but he/she does not meet the inclusion and exclusion criteria, then this is considered a screen failure. However, an exception may occur when permission of the sponsor is obtained as a waiver on a case-by-case basis to include the subject in the study.
Section II: Recruitment of Human Subjects

2.2. Additional Sites and/or Sponsoring Organizations

There may be additional approvals necessary depending on where subjects will be recruited (e.g., from Bloomington Hospital or the VA Hospital). It is the obligation of the Principal Investigator to secure these approvals.

2.3. Media Relations

2.3.1 Use of official IU or department logos may require special approval through the school or department. See IU’s Brand Guidelines, [http://brand.iu.edu](http://brand.iu.edu) for more information.

2.3.2 Investigators in the School of Medicine should refer to the School of Medicine’s Office of Public and Media Relations website, [http://communications.medicine.iu.edu](http://communications.medicine.iu.edu), or contact the office at 317-274-7722 for additional guidance.

2.4. Advertisements

2.4.1 Advertisements should include information prospective subjects need to determine their eligibility and interest. At a minimum, advertisements should include:

   2.4.1.1 The name and address of the investigator and/or research facility;
   2.4.1.2 The location of the research and person or office to contact for further information;
   2.4.1.3 The purpose of the research or condition under study;
   2.4.1.4 In summary form, the criteria that will be used to determine eligibility for the study;
   2.4.1.5 A brief list of participation benefits, if any; and
   2.4.1.6 The time or other commitment required of subjects (e.g., number of visits and total duration of participation).

2.4.2 The IRB will review advertisements to assure that they do not:

   2.4.2.1 Promise free medical treatment when the intent is only to say that subjects will not be charged for taking part in the study;
   2.4.2.2 State or imply certain favorable outcomes or other benefits beyond what is outlined in the informed consent document and the protocol;
   2.4.2.3 Include any exculpatory language.
   2.4.2.4 Emphasize the payment or payment amount by such means as larger or bold type.
2.4.2.5 Include a coupon or other incentive from the sponsor for a discount on the purchase price of the test article once it has been approved for marketing.

2.4.2.6 There are additional requirements for advertisements for FDA-regulated research. See Section 3.1 for additional information.

2.4.3 Advertisements submitted to the IRB must be indicative of the size of type and other visual effects that will be employed in the final product.

2.4.4 IRB review and approval of web-based listings of clinical trials is not required when the information listed is limited to the basic trial information, such as the title, purpose of the study, protocol summary, basic eligibility criteria, study site location(s), and how to contact the site for further information.

2.5. Payment Arrangements and Recruitment Incentives to Subjects

2.5.1 Payment arrangements also represent a part of the consent process and can place subjects at risk of coercion or undue influence or cause inequitable selection. Therefore, the IRB must review and approve proposed payment arrangements to judge whether they fulfill the requirements of consent, and determine that:

2.5.1.1 Payment for participation is not considered a benefit, but a recruitment incentive.

2.5.1.2 The payment amount and the proposed method and timing of disbursement is neither coercive nor presents undue influence.

2.5.1.3 Credit for payment accrues as the study progresses and is not contingent upon the subject completing the entire study. However, payment of a small proportion as an incentive for completion of the study is acceptable, providing that such incentive is not coercive.

2.5.1.4 Unless it creates undue inconvenience or a coercive practice, payment to subjects who withdrew from the study should be made at the time they would have completed the study or a phase of the study had they not withdrawn. For example, in a study lasting only a few days, the IRB may find it permissible to allow a single payment date at the end of the study, even to subjects who withdrew before that date.

2.5.1.5 Any amount paid as a bonus for completion is reasonable and not so large as to unduly induce subjects to stay in the study when they would otherwise have withdrawn.

2.5.1.6 All information concerning payment, including the amount and schedule, is explained in the informed consent document.

2.5.1.7 Subject recruitment incentives that involve drawings must conform to the IU Policy on Drawings, Games, and Prizes, linked from http://policies.iu.edu/policies/index.shtml.
Section II: SOPs/Policies

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2.6. Tracking

The number of subjects screened and the number of subjects consented should be tracked for reporting purposes. The IRB Continuing Review form requires this reporting and, for VA and NIH-sponsored studies, reporting of gender and race is also required.

2.7. Recruitment Incentives to Investigators

2.7.1 Research staff may not personally accept payments, gifts, or any other types of compensation for recruitment or enrollment that may constitute an inducement to modify standard practice, benefit a single employee, or give preferential treatment to one research sponsor over another. In contrast, compensation offered as acknowledgment for legitimate additional work or effort required by a specific project possibly unanticipated during initial budget negotiations may be accepted; however, it must be appropriately reported as a budget revision for the project. This does not preclude the receipt of gifts from research sponsors (unrelated to a specific research project); however, the institution has clear policy distinguishing gifts from sponsored research projects.

2.7.1.1 Gifts are unrelated to a specific research project are unconditional and voluntary, impose no contractual requirements, are awarded irrevocably, and the donor does not directly benefit.

2.7.1.2 Sponsored research projects have a particular intent and the recipient incurs specific obligations. Sponsored research projects involve legal agreements or legal duties related to expectations, risks, rights, indemnifications, and/or time limits. Legal and financial management is different for grants versus gifts.

See IU’s policy on Sponsored Programs (Grant and Contracts) and Gifts, linked from http://policies.iu.edu/policies/index.shtml, for more information.

2.7.2 The IRB shall review payments to determine that

2.7.2.1 The amount of payment and the proposed method and timing of disbursement is neither coercive nor presents undue influence;

2.7.2.2 Credit for payment accrues as the study progresses and is not so large as to unduly induce subjects to stay in the study when they would otherwise have withdrawn; and

2.7.2.3 All information concerning payment, including the amount and schedule of payments, is set forth in the consent document.

2.7.3 Referring health care providers are not allowed to be given financial incentives such as finder’s fees.

2.8. Employee, Colleague, or Student Recruitment
2.8.1 If recruitment among employees, colleagues, or students is anticipated, it must be explained and justified. It is recommended the persons with the following study-related responsibilities **not** participate as subjects in the research study: data collection or other direct access to study data; direct subject contact and/or care; distribution and/or monitoring of investigational agents or study interventions.

2.8.2 The investigator should consider and address the possibility of coercion or undue influence and any equivalent alternatives (such as for classroom research).

3. **ADDITIONAL POLICIES AND PROCEDURES**

3.1. **Research Subject to FDA Regulations**

3.1.1 **Advertisements.** In addition to the items listed above in Section 2, advertisements for FDA-regulated research **cannot:**

3.1.1.1 Make claims, either explicitly or implicitly, about the drug, biologic, or device that are inconsistent with FDA labeling.

3.1.1.2 Allow compensation for participation in a trial offered by a sponsor to include a coupon good for a discount on the purchase price of the product once it has been approved for marketing.

3.1.1.3 Use terms such as “new treatment,” “new medication,” or “new drug” without explaining that the test article or treatment is investigational.

3.1.2 For additional information, see the FDA Information Sheet on Recruiting Study Subjects, [http://www.fda.gov/RegulatoryInformation/Guidances/ucm126428.htm](http://www.fda.gov/RegulatoryInformation/Guidances/ucm126428.htm).

3.2. **Research Subject to HIPAA Regulations**

3.2.1 In addition to the items listed above in Section 2, identifying, contacting, and/or recruiting potential subjects for research purposes must also abide by HIPAA regulations if recruitment will involve a covered entity (e.g., by care providers, review of medical records, or referral from a covered entity).

3.2.2 In general, recruitment described in the following scenarios **does not require** obtaining an authorization from the patient or a waiver of authorization approved by the IRB:

3.2.2.1 Recruitment by a physician, dentist, nurse, or other licensed practitioner who has provided care to the patient;

3.2.2.2 Recruitment by someone who didn’t provide care to the patient but who is part of the same department or practice plan of the patient’s treatment provider.

3.2.2.3 Patient’s treatment provider (who is not the researcher) directs patient to contact the researcher.
3.2.2.4 Subject contacts the researcher (or IU) directly in response to an advertisement. Also, it is acceptable to gather *minimal* information during this contact to determine the potential subject’s eligibility. For example, obtaining the individual’s contact information and explaining two or three major inclusion/exclusion criteria. It is not acceptable to communicate the entire informed consent or an exhaustive list of inclusion/exclusion criteria, unless authorization is first obtained from the subject or the IRB approves a waiver of authorization for this process.

3.2.3 In general, recruitment described in the following scenarios **does** require either an authorization from the patient or a waiver of authorization approved by the IRB.

3.2.3.1 The treatment provider will obtain an authorization from the potential subject to release the subject’s information to the researcher.

3.2.3.2 Subject contacts the researcher (or IU) directly in response to an advertisement, but detailed information (more than *minimal* as described above) about the individual’s health is needed to determine eligibility.

3.2.3.3 Adding an individual’s information to an IRB-approved recruitment database for recruitment into future studies.
3.3. **Research Subject to VA Regulations**

3.3.1 Pursuant to the VHA Handbook 1200.05 §24, non-veterans may be entered into VA-approved research studies only when there are insufficient veterans available to complete the study, in accordance with 38 CFR 17.45 and 38 CFR 17.92. All regulations pertaining to the participation of veterans as research subjects, including requirements for indemnification in case of research-related injury pertain to non-veteran subjects enrolled in VA-approved research.

3.3.2 Subject consent and authorization must be obtained or, alternatively, waivers of consent for recruitment and of authorization for recruitment must be approved by the IRB, prior to accessing, obtaining, and/or utilizing protected health information for recruitment activities involving VA subjects.

3.3.3 Researchers are required to ensure appropriate telephone contact with participants.

3.3.3.1 Researchers ensure that initial contact with prospective subjects is made in person or by letter prior to initiating any telephone contact, unless there is written documentation that a prospective subject is willing to be contacted by telephone about the study in question or a specific kind of research. The initial contact must provide a telephone number or other means the prospective subject can use to verify that the study constitutes VA research.

3.3.3.2 Researchers ensure that in subsequent contact, the research team begins telephone calls to subjects by referring to previous contacts and, when applicable, to the information provided in the consent document, and that the scope of telephone contacts is limited to topics outlined in IRB-approved protocols and consent documents.

3.3.3.3 Research team members are prohibited from requesting Social Security numbers by telephone.
3.4. **Research Subject to Other Regulations**

3.4.1 **Research Subject to Department of Defense (DoD) Regulations**

3.4.1.1 **Protections to Minimize Undue Influence.** For research involving U.S. military personnel, the following additional protections for subjects are necessary to minimize undue influence:

3.4.1.1.1 Officers are not permitted to influence the decision of their subordinates;

3.4.1.1.2 Officers and senior non-commissioned officers may not be present at the time of recruitment;

3.4.1.1.3 Officers and senior non-commissioned officers have a separate opportunity to participate; and

3.4.1.1.4 When recruitment involves a percentage of a unit, an independent ombudsman is present.

3.4.1.2 **Limitations on Dual Compensation.** U.S. military personnel, including temporary, part-time, and intermittent appointments, are prohibited from receiving pay or compensation for participation in research during duty hours. The following are exceptions:

3.4.1.2.1 A subject may be compensated if he/she participated when not on duty.

3.4.1.2.2 Federal employees while on duty and non-federal employees may be compensated for blood draws for research up to $50 per draw.

3.4.1.2.3 Non-federal employees may be compensated for participation other than blood draws in a reasonable amount as approved by the IRB according to prevailing rates and the nature of the research.

3.4.2 **Research Subject to Department of Education (ED) Regulations**

N/A

3.4.3 **Research Subject to Department of Justice (DOJ) Regulations**

3.4.3.1 Research that is conducted within the Bureau of Prisons has the following additional requirements:

3.4.3.1.1 The selection of participants within any one organization must be equitable;
3.4.3.1.2 Incentives may not be offered to help persuade inmate subjects to participate. However, soft drinks and snacks to be consumed at the test setting may be offered.

3.4.3.1.3 Reasonable accommodations such as nominal monetary compensation for time and effort may be offered to non-confined research subjects who are no longer in Bureau of Prisons custody and participating in authorized research being conducted Bureau employees or contractors.
Reliance

About This Policy

Effective Dates:
10/26/2017

Last Updated:
01/19/2018

Policy Contact:
IU Human Subjects Office
(317) 274-8289
irb@iu.edu

Scope
This policy applies to all Indiana University (IU) faculty, staff, and students, or others who are engaged in non-exempt human subjects research which falls under the jurisdiction of the Indiana University Human Research Protection Program (HRPP).

Policy Statement
Where appropriate, IU may enter into reliance arrangements, under which IU-affiliated investigators utilize the services of and rely on an external, reviewing Institutional Review Board (IRB) for IRB review and oversight. Alternatively, the IU IRBs may provide IRB review and oversight for non-affiliated investigators. Reliance may be appropriate for any of the following reasons, among others:

- Sponsor or funding agency request or requirement
- Study is part of an existing network, consortium, or agency which encourages or mandates single IRB review
- Proposed external IRB has already reviewed this study or a similar study
- IRB expertise concerns (e.g. special subject population, untypical research design, sensitive topics)
- Efficiency considerations, especially for collaborating research
- Feedback or request from Institutional Official, HRPP staff, IRB, etc.
- Conflict of interest concerns (e.g. institutional conflict of interest)

Reliance is generally not considered appropriate for the following types of research, unless a compelling reason for reliance exists:
• **Research previously approved by the IU IRBs**: When research has already been approved by the IU IRBs, arguments for potential efficiencies to be gained by use of a single IRB are difficult to make. Transfer of oversight between IRBs places additional burden on both IRB and study staff for little benefit and may give the perception of forum-shopping. In addition, institutional knowledge about a protocol created through multiple IRB reviews is likely to be lost during the transfer process.

• **Research for which an IU investigator holds the IND or IDE**: As the IND or IDE holder, the investigator assumes the responsibilities of the sponsor, resulting in additional responsibility and oversight which make reliance on an external IRB inappropriate.

• **Compassionate use protocols when approval of each patient is required by the FDA, IRB, or sponsor in order to provide treatment at the participating institution**: Since treatment is specific to the local institution, local IRB review is required.

• **Comparative effectiveness research**, as identified by the IU Human Subjects Office (HSO), unless an IRB Chair or member with expertise in the relevant specialty agrees to the reliance. This type of research often compares standard-of-care methodologies which can vary by location and require specific knowledge of local context.

• **Planned emergency research**: Planned emergency research requires a community consent plan which would require specific knowledge of local context; as such, reliance on an external IRB would not be sufficient to protect subjects.

• **VA research**, unless the reviewing IRB is the VHA Central Office IRB, an IRB of another VA facility, or an IRB of another federal agency, pursuant to VHA Handbook 1200.05(5)(d)(1).

When reliance is accepted, the relying institution may not approve the research if not approved by the reviewing IRB and vice versa.

When reliance on an external IRB is requested for research which is greater than minimal risk, the reviewing IRB must be deemed qualified by HRPP and Office of Research Compliance (ORC) leadership. Qualification of the reviewing IRB is not required when the reviewing IRB will review only (1) minimal risk research or (2) greater than minimal risk research when IU-affiliated investigators are only engaged in minimal risk research activities.

**Reason for the Policy**

To facilitate efficient conduct of human subjects research by allowing IRB review to be performed by one institution when multiple institutions are engaged in the research.

**Procedures**

**Reliance on external IRBs**

Investigators may request reliance on an external IRB for any of the above reasons by submitting a Reliance Request to the HSO. HSO staff evaluate the request, ensure all institutional responsibilities are met, and determine on a case-by-case basis whether reliance on the external IRB is acceptable. If the HSO determines that reliance is not appropriate, the study must be submitted to the IU IRB for review.

**Qualification of external IRBs**

Reviewing, external IRBs are evaluated and deemed qualified based on a balance of the following factors:

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• IRB has been granted AAHRPP-accreditation
• IRB’s membership satisfies the requirements of 45 CFR 46.107 and 21 CFR 56.10 and documentation has been provided
• Policies and procedures for the IRB are publicly available for review, or the IRB has an appropriate process in place for making policies and procedures available to investigators
• IRB has a process for notifying ORC of determinations of UPIRTSO, serious and/or continuing noncompliance, suspensions, and terminations
• IRB has a process for ensuring ORC has access to IRB approvals, determinations, and documentation, either in real-time or upon request

Insufficiency in one of the above factors may be outweighed by consideration of the other factors and does not automatically deem the external IRB unqualified. Qualification requests are approved by the HRPP Director and Associate Vice President for Research Compliance and documented via the IRB Qualification Request.

Updates/modification of reliance information
Once the reliance request has been accepted and approval obtained from the external IRB, study teams must notify the HSO of any of the following:

• PI change and, when required by the reliance agreement, personnel changes
• Any changes which require revisions to the HIPAA authorization
• Potential conflicts of interest, including institutional and potential financial interests, which could affect or be affected by the research
• Study closure, when the project is complete and closed with the reviewing IRB

Reliance on IU IRB
Investigators may request that the IU IRB provide IRB approval for non-affiliated investigators. Such requests should be made via amendment after initial approval for the research protocol has been granted by the IU IRB, but may be done at time of initial approval upon request. The study team must provide a plan for management and communication of IRB-related information, including ensuring non-affiliated investigators are familiar with and will follow IU HRPP policies and procedures. The study team must also ensure all required reporting and requests for amendments by non-affiliated investigators are submitted to the IU IRB, and IRB decisions and approved documents are communicated to sites and/or non-affiliated investigators. HSO staff evaluate the request, ensure all institutional responsibilities are met, and determine on a case-by-case basis whether reliance is acceptable. If the HSO determines that reliance is not appropriate, the non-affiliated investigators must obtain IRB approval from an appropriate, external IRB for their participation in the research.

When non-affiliated investigators are conducting the research on behalf of an external institution, the external institution must agree to rely upon the IU IRB for IRB review and approval of the investigators’ participation.

Reliance Documentation
When the IU HRPP agrees to rely on an external IRB, or when an external institution agrees to rely on the IU IRB, the responsibilities of the reviewing IRB and the relying institution are documented through a written agreement between the reviewing IRB and the relying institution (e.g. reliance agreement).
Alternatively, the HSO may determine that an agreement is unnecessary and that responsibilities may be documented in institutional policy or the specific research protocol.

When the IU IRB provides approval for non-affiliated investigators who are not conducting research on behalf of an institution, or when IU extends its Federalwide Assurance to cover a non-affiliated investigator, the responsibilities of the reviewing IRB and the non-affiliated investigator are documented through a Non-Affiliated Investigator Agreement.

**Responsibilities**
Responsibilities are governed by the relevant reliance agreement, where applicable, and the reviewing IRB and relying institution shall comply with all terms and conditions of the reliance agreement. At a minimum, responsibilities should include those listed below.

**Reviewing IRB responsibilities:**
Unless otherwise dictated by the written reliance agreement, the reviewing IRB shall:

- Perform initial and continuing review and review amendments and reportable events for all sites
- Ensure criteria for approval are met for all research and all sites, taking into account local context information provided by relying institution
- Review consent forms, when applicable
- Make Privacy Board determinations per HIPAA, when applicable
- Consider conflict of interest determinations, including any management plans, relating to the research and ensure plans are incorporated into IRB review as applicable
- Notify investigators of IRB decisions, etc., and ensure appropriate communication plan for dissemination between sites
- Maintain appropriate IRB records and documents relating to the IRB review, and make records available to relying institution upon request
- Notify the relying institution of any of the following which relate to the conduct of research at the relying institution:
  - Serious and/or continuing noncompliance, suspensions, and/or terminations
  - Audits, including findings and corrective actions
  - Reporting to a federal agency
  - Communication with regulatory agencies

**Relying Institution responsibilities:**
Unless otherwise dictated by the written reliance agreement, the relying institution shall:

- Ensure investigators are appropriately qualified and meet relying institution standards for eligibility to conduct research, including but not limited to human subjects protection training and collection and maintenance of conflict of interest disclosure forms
- Provide local context information to the reviewing IRB and ensure required information is incorporated into IRB-approved documents
- Ensure investigators are notified of their responsibilities when conducting research pursuant to a reliance agreement
- Ensure compliance with the reviewing IRB determinations and requirements, applicable federal regulations, and all applicable state and local laws and institutional requirements
• Ensure appropriate monitoring of research and perform reviewing IRB-directed audits upon request
• Establish a process for reviewing conflicts of interest and creating management plans when appropriate
• Notify the reviewing IRB of any of the following which relates to research under the oversight of the reviewing IRB:
  o Serious and/or continuing noncompliance
  o Restriction/suspension of research activities
  o Audits, including findings and corrective actions
  o Communication with regulatory agencies
  o Legal claims
  o Research misconduct
• Receive notifications of issues from the reviewing IRB and take additional local action, if applicable

IU IRB responsibilities:
Unless otherwise dictated by written agreement, the IU IRB retains the following responsibilities even when IU has relied upon an external IRB for review:

  • Provide IRB review upon request by the HSO or the institution. This may include local review of reviewing IRB determinations of unanticipated problem involving risks to subjects or others, serious/continuing noncompliance, suspensions and terminations.
  • Review reports of audits conducted by the ORC Human Subjects Auditors

Investigator responsibilities
IU-affiliated investigators conducting research for which an external, reviewing IRB has provided approval must fulfill all responsibilities outlined by the IU HRPP Policy on Investigator Responsibilities, plus the following:

  • Submit Reliance Request to the HSO
  • Obtain IRB approval for conduct of the research by IU-affiliated investigators from the reviewing IRB, including ensuring all IU-affiliated investigators are listed on the IRB documentation as required by the reviewing IRB
  • Ensure the IRB-approved documents are accurate and consistent with conduct of the research by IU-affiliated investigators
  • Conduct research in accordance with the reviewing IRB’s policies and procedures, the IRB-approved documents and conditions of approval, and any applicable laws and regulations
  • Ensure all IU-affiliated investigators are appropriately qualified and have met IU or IU-affiliate standards for eligibility to conduct research, including but not limited to human subjects protection training and disclosure of conflict of interest disclosure forms

Definitions
IU-affiliated investigator: Indiana University faculty, staff, and students engaged in human subjects research, and employees and staff of IU- affiliate institutions which have contracted with the IU IRBs for review and oversight of human subjects research. IU- affiliate institutions include Eskenazi Health, Indiana State Department of Health, IU Health, Purdue Pharmacy Practice, Regenstrief Institute, and
Roudebush VAMC.

Non-affiliated investigator: Investigators who are not faculty, staff, or students of IU, or employees or staff of IU- affiliate institutions.

Reliance: An instance of IRB review when one or more relying institutions choose to accept IRB review and oversight for a research project from another institution’s reviewing IRB. In these situations, the reviewing IRB provides IRB review and oversight for conduct of the research at the relying institution(s).

Relying Institution: An institution engaged in human subjects research which relies on an external reviewing IRB for review and oversight of human subjects research.

Reviewing IRB: The IRB responsible for review and oversight of a research project. Also known as the “IRB of record.”

Sanctions
University faculty, staff, and students that are found to be in violation of this policy may be subject to sanctions relating to their participation in research with human subjects, up to and including permanent suspension or bar from engaging in research with human subjects at Indiana University.

History
Revised for minor editorial, formatting, and terminology updates and to remove a repetitive sentence.

Related Information
AAHRPP Standards
- Standard I-9 for Organization Implementing Shared Oversight of Research

HRPP Documents
- HRPP Reliance Form:
  - IRB Qualification Request
  - Investigator Responsibilities
  - Relying Site Local Context Checklist
  - Relying Site Personnel List
- IU-PU-ND Request for Deferral Form
- Non-Affiliated Investigator Agreement

KC IRB Questionnaires
- Reliance Request
- Questionnaire C – Sites & Collaborations

External References
- 45 CFR 46, especially 45 CFR 104(e) (effective January 19, 2018) and 45 CFR 114(b) (effective January 20, 2020)
- VHA Handbook 1200.05, Requirements for the Protection of Human Subjects in Research, especially 1200.05(5)(d)(1)
• SMART IRB master reliance agreement and online reliance system (https://smartirb.org/)
1. INTRODUCTION

All members of the IU research community involved in human subjects research are expected to comply with the highest standards of ethical and professional conduct in accordance with federal and state regulations and institutional policies governing the conduct of research involving human subjects.

Federal regulations at 45 CFR 46.103(b)(5) and 21 CFR 56.108(b) require the IU Institutional Review Boards (IRB) to have written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and the federal department or agency head of any unanticipated problems involving risks to subjects or others (hereafter referred to as “unanticipated problems”), any serious or continuing noncompliance with the federal regulations or the requirements or determinations of the IRB, and any suspension or termination of IRB approval. In keeping with this regulatory requirement, investigators are required to promptly report to the IRB unanticipated problems, serious or continuing noncompliance, and suspensions or terminations. The IRB will review these events and fulfill reporting requirements to the appropriate institutional officials, federal departments or agencies, and appropriate other entities. This document focuses on the reporting responsibilities of the investigator. Additional reporting responsibilities required by federal regulations can be found in the IU SOP for Reporting.

2. POLICIES AND PROCEDURES

2.1. In accordance with federal regulations, the IRB has established the following policies and procedures for the reporting of reportable events as a means of ensuring (a) the relationship of the risks and benefits to subjects participating in research studies remains acceptable throughout the conduct of the study; and (b) the consent document contains the information necessary for subjects to make an informed decision about their participation or continuation in the study.

2.2. Reportable events, including unanticipated problems or noncompliance, can come from a number of different sources, including investigators, members of the research team, the study sponsor, the regulatory body (e.g., OHRP, FDA), subjects and/or their families, institutional personnel or committees, the media, the public, or anonymous sources. Additionally, the IRB can identify reportable events during its review of research studies.

2.3. Unanticipated Problems and Adverse Events. HHS regulations (45 CFR 46) do not define or use the term adverse event, nor is there a common definition of this term across government and non-government entities. However, the regulations do address the need to report unanticipated problems. Only a small subset of adverse events occurring in human subjects participating in research will meet the definition of an unanticipated
problem. Because federal regulations require that the IRB have written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and any supporting department or agency head of any unanticipated problems, and not adverse events, not all adverse events will require prompt reporting. In fact, the vast majority of adverse events occurring in human subjects are not unanticipated problems. Only if the adverse event meets the three criteria of an unanticipated problem (i.e., unexpected, related or possibly related to participation, and suggests that the research places subjects or others at a greater risk of harm than was previously known or recognized) does it require prompt reporting.

Diagram taken from OHRP Guidance on Unanticipated Problems and Adverse Events (January 15, 2007)

The diagram illustrates three key points:

1. The vast majority of adverse events occurring in human subjects are not unanticipated problems (Area A).
2. A small portion of adverse events are unanticipated problems (Area B).
3. Unanticipated problems include other incidents, experiences, and outcomes that are not adverse events (Area C).

2.3.1. **Assessing whether an adverse event is unexpected.** See the definition of unexpected adverse event in IU SOP III Definitions. Consider that the vast majority of adverse events occurring in the context of research are expected in light of (a) the known toxicities and side effects of the research procedures; (b) the expected natural progression of subjects’ underlying diseases, disorders, and conditions; and (c) subjects’ predisposing risk factor profiles for the adverse event. Thus, most individual adverse events do not meet the first criterion for an unanticipated problem and do not require prompt reporting to the IRB.

2.3.2. **Assessing whether an adverse event is related or possibly related to participation.** See the definition of related or possibly related to participation in IU SOP III Definitions. In general, adverse events that are determined to be at least partially caused by the procedures involved in the research would be considered related to participation in the research, whereas adverse events...
determined to be solely caused by an underlying disease, disorder, or condition of
the subject or other circumstances unrelated to either the research or any
underlying disease, disorder, or condition of the subject would be considered
unrelated to participation in the research. Many individual adverse events
occurring in the context of research are not related to participation in the research
and therefore do not meet the second criterion for an unanticipated problem and
do not require prompt reporting to the IRB.

2.3.3. Assessing whether an adverse event suggests that the research places subjects
or others at a greater risk of harm than was previously known or recognized.
The first step in assessing whether an adverse event meets the third criterion for
an unanticipated problem is to determine whether the adverse event is serious.
See the definition of serious adverse event in IU SOP III Definitions. Adverse
events that are unexpected, related or possibly related to participation in research,
and serious are considered to be the most important subset of adverse events
representing unanticipated problems. Such events suggest that the research places
subjects or others at a greater risk of physical or psychological harm than was
previously known or recognized and routinely warrant consideration of
substantive changes in the research protocol or informed consent
process/document or other corrective actions in order to protect the safety,
welfare, or rights of subjects. However, other adverse events that are unexpected
and related or possibly related to participation in the research but not serious
would also be unanticipated problems if they suggest that the research places
subjects or others at a greater risk of physical or psychological harm than was
previously known or recognized.

2.4 Promptly Reportable Events

2.4.1 The following events must be reported to the IRB within five (5) business
days of the study team becoming aware of the event, regardless of the level
of review of the study (i.e., Full Board, Expedited, Exempt):

2.4.1.1 Conduct of human subjects research without IRB approval, including:

2.4.1.1.1 Conduct of research without submitting for IRB review.

2.4.1.1.2 Conduct of research prior to receiving IRB notification of
final approval.

2.4.1.1.3 Initiation of substantive changes (i.e., changes that would
affect the subjects’ willingness to participate, such as
changes to study procedures, risks and/or benefits) to the
research protocol without prior IRB approval, including
changes necessary to eliminate apparent immediate
hazards to the subject.

NOTE: “IRB-approved protocol” refers to all study
information, including that contained in the KC IRB
Questionnaires, formal protocol document, consents,
etc.
2.4.1.4 Inclusion of vulnerable subject populations without specific IRB approval.

2.4.1.5 Conduct of research when IRB approval has expired or been suspended or terminated.

**NOTE:** Expiration of IRB approval in itself is not promptly reportable, but conduct of research activities after expiration is reportable.

2.4.1.6 Subject interactions or review of identifiable research data by individuals who have not completed appropriate investigator requirements (e.g., COI disclosure and CITI training).

2.4.1.2 Adverse events (either locally or at an external site) assessed by the principal investigator (PI) as (1) unexpected, (2) related or possibly related to study participation, AND (3) suggests that the research places subject(s) or others at greater risk of harm than was previously known.

2.4.1.3 Unanticipated adverse device effects.

2.4.1.4 Major protocol deviations/protocol noncompliance that occurred and may, in the opinion of the PI, (1) impact subject safety and/or (2) affect the integrity of the data, such as:

2.4.1.4.1 Dosing errors.

2.4.1.4.2 Enrolling a subject who does not meet eligibility criteria.

2.4.1.4.3 Study visits outside of the protocol-specified timeframe or missed study visits.

**NOTE:** Study visit deviations that do not meet either criteria 2.4.1.4.1 or 2.4.1.4.2 above should be reported with the next Renewal submission.

2.4.1.5 Consent and/or authorization issues, including:

2.4.1.5.1 Failure to obtain consent and/or authorization from subjects, including obtaining consent from someone who cannot legally consent for the subject.

2.4.1.5.2 Failure to obtain the subject’s signature on the informed consent and/or authorization (unless a waiver of documentation of consent has been granted) prior to the subject starting study procedures.
2.4.1.5.3 Enrolling subjects using a consent which does not include all known risks, or continuation of subject participation without notification of newly identified risks.

2.4.1.5.4 Other major deficiencies in the informed consent or HIPAA authorization process or documentation (e.g., substantive outdated informed consent or HIPAA content, such as missing study procedures information, that may affect subjects’ willingness to participate).

2.4.1.5.5 Minor deficiencies in the informed consent or HIPAA authorization process or documentation affecting ten (10) or more subjects (e.g., outdated informed consent or HIPAA content that is not substantive, such as change in number of subjects to be enrolled, or lack of signature of individual obtaining consent).

NOTE: Generally the IRB would not expect subjects to be re-consented for this type of event.

2.4.1.6 Subject complaints that indicate an unexpected risk and/or that affect the rights and welfare of human subjects.

2.4.1.7 Study suspensions or holds related to risk, safety, or compliance issues.

2.4.1.8 Incidents that may compromise information security, subject privacy, and/or confidentiality (e.g., subject data breach).

2.4.1.9 Local audit reports (i.e., Human Subjects/Quality Improvement Office audits, VA audits).

2.4.1.10 Follow-up information for a previous reportable event.

2.4.1.11 Failure to submit amendments which update risks, benefits, or procedures within sixty (60) days of receipt, or promptly report events when required per IU IRB SOPs.

NOTE: Receipt of an external auditing/monitoring report, such as an FDA Form 483, in itself does not require prompt reporting. However, the study team must evaluate each finding in any such report and assess whether the events require reporting to the IRB and, if so, whether the event(s) meet prompt reporting criteria.

2.5 Discovery of Reportable Event(s) After Study Closure

2.5.1 Promptly reportable events must be reported to the IRB even after the study is closed, regardless of the length of time since study closure.

2.5.2 If an event does not meet prompt reporting criteria, submission of a report is not required.
Section II: SOPs/Policies

2.6. **IRB Responsibilities When Reviewing Promptly Reportable Events.** As part of its oversight responsibilities, the IRB must establish procedures for the evaluation of reportable events with human subject protection regulations and the prompt reporting of serious or continuing noncompliance with federal regulations and institutional policies.

2.6.1. IU Human Subjects Office staff will verify whether the event represents a promptly reportable event (e.g., represents a potential unanticipated problem involving risks to subjects or others [UPIRTSO] or possible serious or continuing noncompliance). Only the convened IRB can make a determination of unanticipated problem or serious or continuing noncompliance.

2.6.1.1. Promptly reportable events (e.g., represents potential unanticipated problem or possible serious or continuing noncompliance) will be reviewed at a convened IRB meeting for possible action.

2.6.1.2. Events which are not promptly reportable do not have the potential to be determined to be a potential unanticipated problem or possible serious or continuing noncompliance (i.e., minor noncompliance) and will be reviewed at the time of next renewal or by a qualified IRB member-reviewer via expedited processes, if applicable.

2.6.2. When the IRB receives a promptly reportable event, it must review the report to determine whether the affected research protocol still satisfies the requirements for IRB approval under §46.111. In particular, the IRB shall consider whether risks to subjects are still minimized and reasonable in relation to the anticipated benefits, if any, to the subjects and the importance of the knowledge that may reasonably be expected to result.

2.6.3. Pursuant to §46.109(a), the IRB has the authority to require, as a condition of continued approval by the IRB, submission of more detailed information by the investigator(s), the sponsor, the study coordinating center, or the Data Safety Monitoring Board or Committee about any unanticipated problem or noncompliance occurring in a research protocol.

2.6.4. If the IRB determines that a report does in fact represent a UPIRTSO or serious or continuing noncompliance, it must report it to appropriate institutional officials, regulatory agencies (e.g., OHRP, FDA), and others, as applicable. (For additional information regarding the IRB’s reporting requirements, please see the IU SOP on Reporting). If the IRB determines that the report does not represent an unanticipated problem or serious or continuing noncompliance, no further reporting is required.

2.6.5. Upon review of a reportable event, the IRB will determine if any action must be taken as a result of the report. The IRB will consider the rights and welfare of subjects when taking any action or imposing any sanction. Possible actions or sanctions include but are not limited to:

2.6.5.1. No action taken, protocol continues as previously approved.
2.6.5.2. No further action required, investigator’s proposed corrective action plan is adequate.

2.6.5.3. Refer to or consult with other institutional entities (Dean, University Counsel, Ethics Committee, IRB Executive Committee, subcommittee appointed by the IRB).

2.6.5.4. Restrict use of or destroy research data collected.

2.6.5.5. Audit the research study(ies).

2.6.5.6. Modify the research protocol and/or informed consent process/document.

2.6.5.7. Notify or re-consent past and/or current subjects if the report may relate to their willingness to continue to take part in the study.

2.6.5.8. Withdraw currently enrolled subjects if it is determined to be in their best interest.

2.6.5.9. Require additional training of the investigator and/or research team.

2.6.5.10. Modify the continuing review schedule.

2.6.5.11. Require increased reporting by the investigator and/or increased monitoring of the research and/or informed consent process.

2.6.5.12. Restrict privileges of the investigator to conduct human research.

2.6.5.13. Suspend or terminate research or suspend specific research activities (e.g., recruitment, enrollment, interaction/intervention, and/or follow-up).

2.6.5.14. Other actions deemed appropriate.

2.7. **IRB-Imposed Suspensions and Terminations Due to Reportable Events**

2.7.1. Pursuant to §46.113, the IRB has the authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB’s requirements, institutional policies, and/or federal or state regulations, or has been associated with unexpected serious harm to subjects. Any suspension or termination of approval shall include a statement of the reasons for the IRB’s action and shall be reported promptly to the investigator, appropriate institutional officials, and the department or agency head. (For additional information regarding the reporting of suspensions and terminations, please see the IU SOP on Reporting).

2.7.2. Suspensions and terminations cannot be overturned by Institutional Officials.
2.7.3. Suspensions of research are typically made at a convened IRB meeting; however, they can also be made on an urgent basis by either an IRB Chair or designee, if necessary. Suspensions can be lifted only by the convened IRB. If an IRB Chair or designee suspends research, it will be reported to the full IRB for consideration and possible action. Termination of research can be made only by the convened IRB.

2.7.4. When an IRB Chair or designee suspends or the convened IRB suspends or terminates a research study, any unanticipated problems or outcomes resulting from the suspension or termination must be reported to the IRB in accordance with this policy.

2.7.5. When the IRB suspends or terminates a research study, it will consider whether the suspension or termination requires that subjects be withdrawn from the study and/or places them at risk of harm.

2.7.5.1. When subjects must be withdrawn from a study, the IRB will consider the safety, rights, and welfare of subjects and determine necessary termination procedures (e.g., drug tapering, final visit, lab tests, other follow-up, and/or arrangements for continued care).

2.7.6. If the IRB determines that the suspension or termination will place subjects at risk of harm and/or follow-up of subjects for safety reasons is permitted or required, the IRB will determine which subjects are to be notified (e.g., current or past subjects) and the manner in which they are to be notified (e.g., in writing or by telephone). Depending upon the reasons for the suspension or termination and the design of the study, the IRB may require that any of the following individuals be notified of the suspension or termination:

2.7.6.1. All subjects who have been or who are currently enrolled;

2.7.6.2. Only subjects who are currently enrolled and active; or

2.7.6.3. Only subjects who participated in a certain aspect of the study.

2.7.7. Investigators may request to attend an IRB meeting to discuss a suspension or termination in order to provide clarification of the issues. Additionally, investigators may request in writing that the IRB reconsider a suspension or termination within 10 days of such action.

3. ADDITIONAL POLICIES AND PROCEDURES

3.1. Research Subject to FDA Regulations

N/A

3.2. Research Subject to HIPAA Regulations

N/A
3.3. **Research Subject to VA Regulations**

3.3.1 **Local Research Deaths.** VA personnel, including WOC and IPA appointees, must ensure oral notification of the IRB immediately upon becoming aware of any local research death that is both unanticipated and related to the research.

3.3.1.1 The IRB must alert ORO by email or telephone within 2 business days after receiving such notification and provide relevant information as requested. The VA facility Director and the ACOS/R&D must receive concurrent notification.

3.3.1.2 VA personnel, including WOC and IPA appointees, must ensure written notification of the IRB within 5 business days of becoming aware of the death.

3.3.1.3 Within 5 business days after receiving written notification of the death, the IRB Chair or a qualified IRB member-reviewer must determine and document whether any actions are warranted to eliminate apparent immediate hazards to subjects.

3.3.1.4 The IRB must review the death and the determination of the IRB Chair or qualified IRB member-reviewer at its next convened meeting and must determine and document that:

3.3.1.4.1 The death was both unanticipated and related to the research; or

3.3.1.4.2 There is insufficient information to determine whether the death was both unanticipated and related to the research; or

3.3.1.4.3 The death was not unanticipated and/or the death was not related to the research.

3.3.1.5 Regardless of the determination under paragraph 3.3.1.4, the convened IRB must also determine and document whether any protocol or informed consent modifications are warranted. If modifications are warranted, the convened IRB must determine and document whether or not investigators must notify or solicit renewed/revised consent from previously enrolled subjects; and if so, when such notification or consent must take place and how it must be documented.

3.3.1.6 The IRB must notify the VA facility Director and the ACOS/R&D of its determinations under paragraphs 3.3.1.4 and 3.3.1.5 within 5 business days of the determinations.

3.3.1.7 The VA facility Director must report the determinations to ORO within 5 business days after receiving the IRB’s notification.

3.3.2 **Local SAEs.** VA personnel, including WOC and IPA appointees, must ensure written notification of the IRB within 5 business days after becoming aware of any local SAE that is both unanticipated and related to the research.
Section II: SOPs/Policies

3.3.3 **Serious Problems.** VA personnel, including WOC and IPA appointees, must ensure written notification of the IRB within 5 business days after becoming aware of any serious problem that is both unanticipated and related to the research.

3.3.4 **IRB Review of SAEs and Serious Problems.** Within five (5) business days after receiving written notification of an SAE or serious problem, the IRB Chair or a qualified IRB member-reviewer must determine and document whether any actions are warranted to eliminate apparent immediate hazards to subjects.

3.3.4.1 The IRB must review the incident and the determination of the IRB Chair or qualified IRB member-reviewer at its next convened meeting and must determine and document that:

3.3.4.1.1 The incident was serious and unanticipated and related to the research; or
3.3.4.1.2 There is insufficient information to determine whether the incident was serious and unanticipated and related to the research; or
3.3.4.1.3 The incident was not serious, and/or the incident was not unanticipated, and/or the incident was not related to the research.

3.3.4.2 Regardless of the determination under paragraph 3.3.4.1, the convened IRB must also determine and document whether any protocol or informed consent modifications are warranted. If modifications are warranted, the convened IRB must determine and document whether or not investigators must notify or solicit renewed/revised consent from previously enrolled subjects; and if so, when such notification or consent must take place and how it must be documented.

3.3.4.3 The IRB must notify the VA facility Director and the ACOS/R&D in writing within 5 business days after its convened meeting if:

3.3.4.3.1 Actions were taken to eliminate apparent immediate harm to subjects; or
3.3.4.3.2 The IRB determined that the incident is serious and unanticipated and related to the research, or there was insufficient information to make the determination; or
3.3.4.3.3 Protocol or informed consent modifications were warranted.

3.3.4.4 The VA facility Director must report the situation to the ORO within 5 business days after receiving the IRB’s notification.

3.3.5 **Other AEs, SAEs, and Problems.** The IRB must be notified of, and review, other AEs, SAEs, and unanticipated problems involving risks to subjects or others (i.e., not covered by paragraphs 3.3.1 – 3.3.3) in accordance with Section 2 of this SOP.
Section II: SOPs/Policies

3.3.6 **Apparent Serious or Continuing Noncompliance.** VA personnel, including WOC and IPA appointees, must ensure that the IRB is notified, in writing, within 5 business days after becoming aware of any apparent serious or continuing noncompliance with IRB or other human research protection requirements.

**NOTE:** HIPAA Privacy Rule deficiencies, including uses and disclosures of PHI for research without legal authority (e.g., without a valid authorization or waiver of authorization), are to be reported in accordance with this paragraph. Such deficiencies should also be reported to the facility Privacy Officer (PO).

3.3.6.1 The convened IRB must review any such notifications at the earliest practicable opportunity, not to exceed 30 business days after the notification. The IRB Chair may take interim action as needed to eliminate apparent immediate hazards to subjects.

3.3.6.2 The convened IRB must determine and document whether or not serious or continuing noncompliance actually occurred.

3.3.6.3 If the IRB determines that serious or continuing noncompliance occurred:

3.3.6.3.1 A documented IRB determination is also required as to whether remedial actions are needed to ensure present and/or future compliance.

3.3.6.3.2 IRB must notify the VA facility Director and the ACOS/R&D within 5 business days after making its determinations.

3.3.6.3.3 The VA facility Director must report the determination to ORO within 5 business days after receiving the IRB’s notifications.

3.3.6.3.4 If the apparent serious or continuing noncompliance was identified by an RCO audit, the IRB must notify the RCO within 5 business days after its determinations under paragraphs 3.3.6.2 and 3.3.6.3.1, regardless of outcome.

3.3.6.3.5 The IRB must track the determinations required under paragraphs 3.3.6.2 and 3.3.6.3 for use in the VA facility Director Certification.

3.3.7 **Other Apparent Noncompliance.** The IRB must be notified of, and review, other apparent noncompliance (not covered by paragraph 3.3.6) in accordance with Section 2 of this SOP.

3.3.8 **Suspensions and Terminations of Research by the VA Facility.** VA facility officials and research review committees must notify the VA facility Director, the ACOS/R&D, and the RCO within 5 business days of suspending or terminating any VA human research study. The VA facility Director must report the suspension/termination to ORO within 5 business days after receiving the notification.

3.3.9 **External Suspensions/Terminations of Research.** VA personnel, including WOC and IPA appointees, must ensure that the IRB is notified, in writing, within...
5 business days after becoming aware of any suspension or termination of VA research by, or at the direction of, any entity external to the facility.

3.3.9.1 The convened IRB must review the suspension/termination at the earliest practicable opportunity, not to exceed 30 business days after notification, to determine whether it:

3.3.9.1.1 Resulted from a local adverse event(s), local noncompliance, or other local issue(s); or
3.3.9.1.2 Requires local action (in addition to the suspension/termination) to ensure the safety, rights, or welfare of local human research subjects, personnel, or others or the effectiveness of the local HRPP.

3.3.9.2 If the IRB determines that either 3.1.2.1.1 or 3.1.2.1.2 applies,

3.3.9.2.1 The IRB must notify the VA facility Director and the ACOS/R&D within 5 business days after the determination;
3.3.9.2.2 The VA facility Director must report the suspension/termination to ORO within 5 business days after receiving the IRB’s notification.

3.3.10 **Program Changes.** The VA facility Director must report to ORO as follows.

3.3.10.1 Any change in the status (e.g., expiration, restriction, suspension, or termination) of the facility’s Federalwide Assurance (FWA) must be reported within 5 business days.

3.3.10.2 Any proposed changes to the FWA, including changes in designated IRB(s) and changes in IRB membership, must be reported prior to submission to the Office for Human Research Protections (OHRP).

**NOTE:** VA facilities designating VHA-approved Central IRBs need not report Central IRB membership changes to ORO.

3.3.10.3 New or substantially revised MOUs related to human research protections or oversight must be reported within 5 business days after the final concurrence/signature. ORO strongly encourages contacting ORO early in the development of new or revised MOUs.

3.3.10.4 Failure of a VA facility to achieve or maintain the HRPP accreditation required under VHA Handbook 1200.05 must be reported to ORO within 5 business days.

**NOTE:** For more information, see VHA Handbooks 1058.03 and 1058.05.

3.4. **Research Subject to Other Regulations**

3.4.1 **Research Subject to DoD Regulations**
3.4.1.1 Any unanticipated problems involving risks to participants or others for any DoD-supported research must be promptly (within at least 30 days) reported to the DoD HRPP officer.

3.4.2 Research Subject to Department of Education (ED) Regulations

N/A

3.4.3 Research Subject to DOJ Regulations

N/A
### Reporting

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<th>Current Version: 07/2015</th>
<th>Previous Versions: 07/14, 10/10, 07/09, 02/05, 05/06, 03/08</th>
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#### 1. INTRODUCTION

Pursuant to 45 CFR 46.103(b)(5) and 21 CFR 56.108(b), IRB must establish procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and the department or agency head of (a) any unanticipated problems involving risks to subjects or others; (b) any serious or continuing noncompliance with the regulations or the requirements or determinations of the IRB; (c) any suspension; or (d) termination of IRB approval.

#### 2. POLICIES AND PROCEDURES

2.1. Pursuant to 45 CFR 46.103(b)(5) and 21 CFR 56.108(b), the IRB will review reports of unanticipated problems and serious or continuing noncompliance. If the IRB determines that a report does in fact represent an unanticipated problem involving risks to subjects or others, or serious or continuing noncompliance, or if the IRB suspends or terminates approval of research, appropriate institutional officials, regulatory agencies, and others will be notified. Such individuals and entities will also be notified of subsequent actions and information, such as responses to significant provisions, as appropriate. Please note this policy does not apply to administrative holds, events occurring off-site, or suspensions not initiated by the IRB.

2.2. IRB staff will prepare minutes from the IRB meeting in which the report and the IRB’s determination of the report was discussed. Included in the minutes will be all of the following information:

- **2.2.1.** Description of the event/circumstance.
- **2.2.2.** Summary of the IRB’s deliberations, including any provisions.
- **2.2.3.** Actions taken by the IRB.
- **2.2.4.** Reasons for the IRB’s actions.
- **2.2.5.** Plans for continued investigation or action.

2.3. After review and approval by an HSO Director or designated HSO staff member, a copy of the minutes will be distributed to:

- **2.3.1.** the Principal Investigator; and
- **2.3.2.** the IRB.

- **2.3.3.** Unless already made aware of the report, a copy of the minutes will also be distributed to the following individuals, as applicable:
2.3.3.1. The Chair of the VA Research and Development Committee (or designee), if the research is conducted at or funded by the VA. The Chair will in turn forward the report to the VA Office of Research Oversight Regional Office.

2.3.3.2. Director of Grant Services or Director, Clinical Trials Office, who will forward the report to the sponsor or contract organization, if the research is funded and the study was suspended or terminated.

2.3.3.3. Department chair or supervisor of the Principal Investigator, as appropriate.

2.3.3.4. IU General Counsel, if the report raises issues of legal liability or there is a threat or perceived threat of a lawsuit.

2.3.3.5. The Privacy Officer of the covered entity, if the event involved unauthorized use, loss, or disclosure of PHI from that covered entity.

2.3.3.6. The Information Security Officer of the organization, if the event involved violations of information security requirements of that organization.

2.4. A formal report will be prepared by an HSO Director or designated HSO staff member, signed by an HSO Director and sent, as applicable, to the:

2.4.1. Office of Research and Development (ORD), if the study is funded by the VA.

2.4.2. Office for Human Research Protections (OHRP), if the study is subject to HHS regulations.

2.4.3. Food and Drug Administration (FDA), if the study is subject to FDA regulations.

2.4.4. Other federal agencies, such as NIH or DoD.

2.4.5. Vice President for Research, Indiana University.

2.5. Reports of serious or continuing noncompliance may be brought to the IRB Executive Committee if it is determined that information regarding the noncompliance could benefit the group.

2.6. All reports will be completed within 30 days of the IRB’s action.

3. ADDITIONAL POLICIES AND PROCEDURES

3.1. Research Subject to FDA Regulations

N/A

3.2. Research Subject to HIPAA Regulations
3.3. Research Subject to VA Regulations

3.3.1. Determinations of serious unanticipated problems, unanticipated SAEs, serious noncompliance or continuing noncompliance must be reported in writing by the IRB Chair or designee directly (without intermediaries) to the IO within five (5) business days after the determination. A simultaneous copy must be sent to the Associate Chief of Staff for Research, the Research and Development Committee, and any other relevant research review committee. An initial report of an IRB determination that serious noncompliance or continuing noncompliance occurred is required even where the determination is preliminary or disposition of the matter has not been resolved at the time of the report.

3.3.2. Any termination or suspension of research related to concerns about the safety, rights, or welfare of human research subjects, research staff, or others must be reported directly (without intermediaries) to the IO within five (5) business days after the termination or suspension occurs. The report must be made in writing with simultaneous copies, as applicable, to the Associate Chief of Staff for Research, the Research and Development Committee, the IRB, and any other relevant research review committee.

3.3.3. The IU Human Subjects Office must report the following directly to ORO:

3.3.3.1. Suspensions or terminations of IRB approval. Any suspension or termination of approval must be promptly reported to ORO in accordance with VHA Handbook 1058.01.

3.3.3.2. IRB Changes. The proposed addition or removal of the IRB(s) of record designated in a facility’s FWA must be submitted to ORO Central Office prior to submission to OHRP and in accordance with VHA Handbook 1058.03. Any change in IRB membership rosters must be reported to ORO Central Office in accordance with VHA Handbook 1058.03.

3.3.3.3. Substantive Memorandum of Understanding (MOU) Changes. Any substantive change in an MOU with an affiliate institution or other entity related to the designation of IRB(s) or other human research protection arrangements must be reported to ORO Central Office within five (5) business days.

3.3.3.4. Accreditation Problems. Failure of the VA facility to achieve the accreditation status required by ORD for human research protections, any change in the facility’s accreditation status, or any change in the accreditation status of an affiliate involved in the facility’s human research protection program must be reported to ORO Central Office within five (5) working days.

3.4. Research Subject to Other Regulations
3.4.1. **Research Subject to Department of Defense (DoD) Regulations**

3.4.1.1. The following must be reported promptly (no longer than within thirty (30) days) to the DoD human research protection officer:

3.4.1.1.1. Significant changes to the research protocol approved by the IRB.

3.4.1.1.2. Results of the IRB continuing review.

3.4.1.1.3. Change of reviewing IRB.

3.4.1.1.4. Notification by any federal department, agency, or national organization that any part of an HRPP is under investigation for cause involving a DoD-supported research protocol.

3.4.1.2. Surveys performed on DoD personnel must be submitted, reviewed, and approved by the DoD after the research protocol is reviewed and approved by the IRB.

3.4.2. **Research Subject to Department of Education (ED) Regulations**

N/A

3.4.3. **Research Subject to Department of Justice (DOJ) Regulations**

N/A
1. **INTRODUCTION**

The Code of Federal Regulations (CFR) Title 21 describes the procedures and requirements governing the use of investigational new drugs (§312) and clinical investigations of devices (§812). This SOP describes the policies at Indiana University for conducting research with these test articles, including the responsibilities of clinical investigators and sponsors when a clinical investigator assumes the sponsor function for an investigational test article.

Pursuant to FDA regulations, investigators are responsible for ensuring that an investigation is conducted according to the signed investigator statement or agreement, 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 and devices under investigation.

2. **POLICIES AND PROCEDURES**

2.1. **Research Involving Investigational Drugs**

2.1.1 Pursuant to 21 CFR 312.53(c)(1), an investigator must sign an investigator statement (Form FDA 1572).

2.1.2 When the principal intent of the investigational use of a test article is to develop information about the product’s safety or efficacy, submission of an Investigational New Drug (IND) application ordinarily must be submitted. However, in certain circumstances, FDA does not require an IND.

2.1.3 **Control of Investigational Drug.** The investigator shall administer the drug only to subjects under the investigator’s personal supervision or under the supervision of a sub-investigator responsible to the investigator. The investigator shall not supply the investigational drug to any person not authorized to receive it.

2.1.4 **Recordkeeping and Record Retention**

2.1.4.1 **Disposition of Drug.** The investigator is required to maintain adequate records of the disposition of the drug, including dates, quantity, and use by subjects. If the investigation is terminated, suspended, discontinued, or completed, the investigator shall return the unused supplies of the drug to the sponsor, or otherwise provide for disposition of the unused supplies of the drug under §312.59. Unused study drug must not be passed on to other investigators, used for animal research, or dispensed to non-study subjects.

2.1.4.2 **Case Histories.** The 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. 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 chart(s), and the nurses’ notes. The case history for each individual shall document that informed consent was obtained prior to participation in the study.

2.1.4.3 Record Retention. The investigator shall retain records required to be maintained for a period of two (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 two (2) years after the investigation is discontinued and FDA is notified.

2.1.5 Investigator Reports

2.1.5.1 Progress Reports. The investigator shall furnish all reports to the sponsor of the drug who is responsible for collecting and evaluating the results obtained.

2.1.5.2 Safety Reports. The investigator shall 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 shall report the adverse effect immediately.

2.1.5.3 Final Report. The investigator shall provide the sponsor with an adequate report shortly after completion of the investigator’s participation in the investigation.

2.1.5.4 Financial Disclosure Reports. The investigator shall 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. The investigator shall promptly update this information if any relevant changes occur during the course of the investigation and for one (1) year following the completion of the study.

2.1.6 Inspection of Investigator’s Records and Reports. The investigator shall, 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, Investigator Recordkeeping and Record Retention. 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.
2.1.7 **Handling of Controlled Substances.** If the investigational drug is subject to the Controlled Substances Act, the investigator shall 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.

2.2. **Investigational Drug Services**

2.2.1 All **inpatient** studies conducted at an IU Health, Eskenazi Health, or Roudebush VA facilities should use the services of the Investigational Drug Services (IDS) provided by the facility’s pharmacy department. The only exception is if the investigator, after consultation with the IDS, determines that he/she has adequate manpower, facilities, knowledge, and time to assume all the responsibilities the IDS would have provided.

2.2.2 **Outpatient** studies are not required to but may use the IDS, if they wish. Using the services of the IDS is strongly recommended for studies involving the use of an investigational drug that requires:

2.2.2.1 preparation in a sterile hood (all intravenous drugs);

2.2.2.2 admixing of any kind; and

2.2.2.3 third-party blinding.

2.2.3 **Receipt and Inventory of Study Drug.** Upon receipt of an investigational drug, the investigator or other designated individual should document that information on the packing slip matches what was sent to the site, including the amount, lot numbers, and quantity. Any discrepancies, damage, or tampering should be reported promptly to the sponsor.

2.2.4 **Prescribing and Dispensing of Study Drug.** Study drugs may only be dispensed by authorized individuals according to state and federal regulations and hospital/facility policies. If an investigator will be dispensing an investigational drug for an outpatient study, the following should be documented in the protocol and carried out during the study:

2.2.4.1 Individuals authorized to prescribe and/or dispense the study drug. These individuals must be listed on the Personnel tab of the KC Protocol and FDA Form 1572, as applicable. A record of authorized individuals’ signatures and initials should be maintained at all times.

2.2.4.2 Documentation of the order or prescription, such as order form or script signed by authorized individuals. The study drug should only be dispensed according to the dose, route, and frequency written in the order.

2.2.4.3 Documentation of any changes, titrations, or deviations made to dosing orders or protocol dosing, along with the signature(s) of
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authorized individuals. Dosing changes or deviations from the protocol should be made only to protect the subject and should be reported to the IRB according to the SOP on Reportable Events.

2.2.4.4 Each time a study drug is dispensed, documentation should be made of the amount and to whom it was dispensed, and the date and signature (or initials) of the individual dispensing the study drug. Subjects should be instructed in the proper storage, use, precautions, and potential risks of the study drug.

2.2.4.5 Subjects should be advised to return all study drug containers (used and unused) to the original study drug dispensing site, unless other means of disposition have been approved. Study personnel should record the amount (e.g., number of bottles/pills) and date of return. If a subject does not return study drug containers, study personnel should document attempts to retrieve them from the subject, including a certified letter, if necessary.

2.2.4.6 Discrepancies in amounts of study drug used and returned (actual and suspected) by the subject should be documented, along with the reason(s) for the discrepancy. Major discrepancies should be followed up with the subject and/or pharmacy to obtain an explanation.

2.2.4.7 Authorization from the sponsor is required for dispensing a study drug in special circumstances.

2.2.4.8 If the study drug is to be administered at a site that is not listed on the FDA Form 1572 and/or on the Personnel tab of the KC Protocol, approval must first be obtained from the sponsor and the IRB to do so.

2.2.5 Storage of the Study Drug. The study drug should be stored in a secure environment (e.g., locked cabinet in a locked area) with access limited to authorized research personnel. The study drug should be stored at the appropriate temperature and a temperature log should be maintained, if appropriate.

2.2.6 If a subject in an outpatient study requires hospitalization and the study drug needs to be administered during the subject’s hospital stay, a physician caring for the subject should write an order allowing the subject to continue taking the study drug from his/her own supply. The order should clearly document that the subject is enrolled in a study using an investigational drug. IDS should also be notified of the subject’s hospitalization, if its services are being used for the study.
2.3. **Research Involving Investigational Devices**

2.3.1 Pursuant to 21 CFR 812.43(c)(4), an investigator must sign an agreement, which commits him/her to certain requirements.

2.3.2 If the IRB determines that the device is a significant risk device, the investigator must confirm that the device has an investigational device exemption (IDE) issued by FDA, the device fulfills the requirements for an abbreviated IDE, or the protocol meets one of the FDA exemptions from the requirements to have an IDE.

2.3.3 **Receipt and inventory of study device.** This section applies to those study devices the investigator dispenses/administers to the study subject. The investigator (or designated research associate) is responsible for ensuring that:

2.3.3.1 Upon receipt (preferable within two (2) working days, but definitely prior to dispensing) of the study device, inventory the shipment, ensuring that the information on the packing slip matches exactly with what has been sent to the site, including the receipt date, lot numbers, device type, batch number, code mark, and quantity. Additionally, the identification of the person who received the shipment of devices should be noted. Documentation of this shipment inventory should be maintained.

2.3.3.2 Promptly (usually within two (2) to three (3) working days) bring any discrepancies to the attention of the sponsor/supplier of the device(s).

2.3.3.3 Retain a copy of the shipping inventory, packing slips, and document inventory in the study files.

2.3.3.4 Maintain an accountability log (most sponsors will issue/supply a device accountability log).

2.3.4 **Study Device Labeling**

2.3.4.1 Study devices from sponsor companies are pre-labeled and these should not be defaced, relabeled, or changed in any way without written permission of the sponsor. It is recommended that an additional label may be placed to include the study staff contact name/number, but only if the sponsor agrees.

2.3.4.2 If the Principal Investigator is responsible for labeling, he/she should be aware of applicable FDA regulations. Examples of what may appear on a label are: name of device, model number, serial number, and manufacturer.

2.3.4.3 When a study device is designated as investigational per FDA regulations, there should be a label with the following information:
• Name and place of business of the manufacturer, packer, or distributor.
• Quantity of contents if appropriate, and the following statement: “CAUTION–Investigational device. Limited by Federal (or United States) law to investigational use.”
• The label or other labeling shall describe all relevant contraindications, hazards, side effects, interfering substances or devices, warnings, and precautions.

2.3.5 **Storage of the Study Device (including devices that record data from automated instruments)**

2.3.5.1 Establish and maintain access controls for essential and appropriate research personnel.

2.3.5.2 Develop procedures for verifying physical access.

2.3.5.3 Store the study device in a secure environment that includes locks on doors and controlled access.

2.3.5.4 Establish equipment control both into and out of the research site.

2.3.5.5 Develop security incident procedures to report any privacy breaches.

2.3.5.6 Assess any privacy risks anticipated and develop methods to avoid those risks.

2.3.5.7 Develop data backup, storage, and emergency mode procedures, if applicable.

2.3.5.8 Ensure the study device is stored at the appropriate temperature, and maintain a storage area temperature log, if appropriate.

2.3.6 **Dispensing of Study Devices**

2.3.6.1 The use of an investigational device shall be permitted only with subjects under the investigator’s personal supervision or under the supervision of a co-investigator responsible to the investigator.

2.3.6.2 An investigational device shall not be supplied to any person not authorized to receive it.

2.3.6.3 Create an access log to document each time the study device is dispensed/used, where it is dispensed/used, to whom it is dispensed/used, and the date and signature or initials of the person dispensing/using the study device (plus any other information dictated by the study protocol).
2.3.7 Return/Destruction of Study Device (as applicable to the specific device)

2.3.7.1 At the conclusion of the study, ensure that all documentation regarding receipt, storage, dispensing, return of used containers, and accountability is complete and accurate.

2.3.7.2 An explanation of why and how many device units have been returned to the sponsor, repaired, or otherwise disposed of should be noted. When a device is disposed of, the identification of the person doing so should also be noted.

2.3.7.3 Devices obtained from a sponsor for the specific purpose of a research study must be returned to the sponsor. Only with the written authorization (i.e., in the protocol or other written correspondence) of the sponsor (and in compliance with federal regulations and institutional policies) may the investigator discard the device on site or retain the device.

2.3.7.4 Pursuant to 21 CFR 812.110, upon completion or termination of a clinical investigation or the investigator’s part of an investigation, or at the sponsor’s request, an investigator shall return to the sponsor any remaining supply of the device or otherwise dispose of the device as the sponsor directs.

2.3.7.4.1 Unused study devices that include individually identifiable health information must not be transferred to other investigators without IRB approval or an authorization from the study subject.

2.3.7.4.2 Unused study devices without individually identifiable health information must not be transferred to other investigators, used for animal research, or dispensed to non-study patients unless written consent is obtained from the sponsor/provider of the device.

2.3.7.5 Device study records must be kept for seven (7) years (according to federal regulations and the IU SOP on Data Management).

2.4. Research on FDA-Approved Devices for FDA-Approved Indications

2.4.1 Requires documentation of receipt, storage, dispensing, and return of the device as above.

2.4.2 The FDA-approved label is adequate, although including information specific to the study is recommended.

2.5. Radiologics

2.5.1 Radiation-emitting devices have similar requirements as above. However, there may be specific requirements based on the device and the study design and thus...
2.6. **Sponsor-Investigator Responsibilities.** Pursuant to §312.3(b), a Sponsor-Investigator is an individual who both initiates and conducts an investigation, and under whose immediate direction the investigational drug is administered or dispensed. When an investigator assumes the sponsor function, there are additional responsibilities.

The additional sponsor responsibilities that are assumed by a Sponsor-Investigator are outlined in 21 CFR 312 and 812, as well as ICH GCP E6 Section 5.

One of the most significant of these sponsor responsibilities relates to monitoring of the trial. This responsibility is distinct from Data Safety Monitoring and is performed to ensure adequate protection of the rights and welfare of human subjects, to confirm compliance with the currently approved protocol and applicable regulatory requirements, and to verify the quality of the clinical trial data submitted to FDA. In industry-sponsored studies, this is often delegated to a CRO. FDA expectations for trial monitoring are additionally discussed in the FDA’s Guidance for Industry: Oversight of Clinical Investigations — A Risk-Based Approach to Monitoring.

Additional sponsor responsibilities include applying to the FDA for use of the investigational drug or device.

2.6.1 **Investigational New Drug Application (IND)**

2.6.1.1 When the principal intent of the investigational use of a test article is to develop information about the product’s safety or efficacy, submission of an Investigational New Drug (IND) application ordinarily must be submitted. However, in certain circumstances, FDA does not require an IND.

2.6.1.2 The sponsor-investigator shall submit an IND to the FDA if he/she intends to conduct a clinical investigation with an investigational new drug that is subject to §312.40.

2.6.1.3 The sponsor-investigator shall not begin a clinical investigation subject to §312.2(a) until the investigation is subject to an IND in effect in accordance with §312.40.

2.6.2 **Investigational Device Exemption (IDE) Application**

2.6.2.1 When the intent is to determine the safety and effectiveness of an investigational device, submission of an IDE application may be required. However, in certain circumstances, the investigational use may be subject only to abbreviated IDE requirements or to an exemption.
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2.6.2.2 The sponsor-investigator shall submit an IDE to the FDA if he/she intends to conduct a clinical investigation with an investigational device that is subject to 812.20.

2.6.2.3 The sponsor-investigator shall not begin a clinical investigation subject to an IDE until the FDA has approved the application in accordance with 812.20.

2.6.3 IU Sponsor Investigators

2.6.3.1 Representatives from the Quality Improvement Office and Regulatory Knowledge Support/Clinical Translational Sciences Institute will be notified by HSO upon submission of a new protocol for which an IU investigator has submitted and holds the IND or IDE.

2.6.3.2 The investigator and applicable research support staff for the protocol are required to attend an educational session with QIO/CTSI representatives to review the additional Sponsor-Investigator responsibilities. This educational session is expected to occur within 30 days of IRB initial review. Please contact the Human Subjects Office – Indianapolis at 317-274-8289 to schedule this session.

2.6.3.2.1 An abbreviated process may be considered, in some circumstances, such as investigator and support staff attendance at a sponsor-investigator educational session within previous three years, absent revisions to applicable regulations and/or content of the session; demonstrated compliance with sponsor-investigator responsibilities via an audit or federal agency inspection of a Sponsor-Investigator project; or other dispensation from Institutional leadership, IRB Executive Committee or IRB Chair.

2.6.3.2.2 University faculty, staff, and students that are found to be in violation of this policy may be subject to sanctions relating to their participation in research with human subjects, up to and including permanent suspension or bar from engaging in research with human subjects at Indiana University.

3. ADDITIONAL POLICIES AND PROCEDURES

3.1 Research Subject to FDA Regulations

Preceding text is specific to FDA Regulations

3.2 Research Subject to HIPAA Regulations

N/A
3.3 **Research Subject to VA Regulations**

3.3.1 Research involving investigational drugs that is conducted at the VA must follow these additional requirements:

3.3.1.1 Inform the pharmacy service through the use of VA Form 10-1223 when IRB and VA Research & Development (R&D) approvals have been obtained.

3.3.1.2 Provide the pharmacy with a signed copy of VA Form 10-1086 to document each subject’s consent to participate in the study.

3.3.1.3 Inform the Chief, Pharmacy Service, and the R&D Committee when a study has been terminated.

3.4 **Research Subject to Other Regulations**

3.4.1 **Research Subject to Department of Defense (DoD) Regulations**

N/A

3.4.2 **Research Subject to Department of Education (ED) Regulations**

N/A

3.4.3 **Research Subject to Department of Justice (DOJ) Regulations**

N/A
1. INTRODUCTION

The federal regulations governing human subjects research state that (a) the research plan, when appropriate, shall make adequate provisions for monitoring of the collected data to ensure the safety of research subjects; and (b) there shall be adequate provisions to protect the privacy of subjects and to maintain the confidentiality of research data. The specifics of each study must be thoroughly evaluated and consideration given to a number of factors pertaining to each research study in order to determine the risk/benefit ratio for that study. Based on such assessed risk, safety checkpoint indicators should be built into the study protocol to continually monitor subjects’ safety. Periodic oversight should also be applied to assure that the safeguards built into the protocol are effective and followed and the research team is working effectively to maintain subject safety. Therefore, IU as well as other national organizations (e.g., NIH) require a safety/risk assessment and research oversight plan for every human subjects research study requiring full board (and in some cases, expedited) review.

In general, these research plans, also called data safety monitoring plans (DSMP), should provide for a regular review of accrued research data and other relevant information so as to ensure the validity and integrity of the data and that there is no change to the anticipated risk/benefit ratio of the research study. Additionally, there should be an ongoing review of study procedures so as to ensure that the privacy of research subjects and the confidentiality of their research data have not been violated.

2. POLICIES AND PROCEDURES

2.1. For the IRB to grant approval of a research project, it must ensure that the safety and welfare of human subjects are adequately protected. As part of its assessment, it shall determine that all of the criteria for IRB approval of research outlined in §46.111 are satisfied.

2.2. As part of the IRB’s review to assess whether the safety and welfare of subjects are adequately protected in a given research study, it may evaluate a research oversight plan outlined and submitted by the investigator.

2.3. PI Responsibilities for Developing a Safety/Risk Assessment and Research Oversight Plan

2.3.1 For all research studies that are considered greater than minimal risk, the PI will be responsible for developing a DSMP to assure that subject safety will be monitored. The IRB may also request that a minimal risk study develop a DSMP if it is felt to be necessary.
2.3.2 This plan will be required for all new research submissions meeting the criteria above before the IRB can grant final approval.

2.3.3 Because of the wide variety of research conducted within the IU system, risk assessment and research oversight plans can also vary widely. Rather than consulting only a specific policy, the investigator should consider the following when developing a safety/risk assessment and research oversight plan:

2.3.3.1 What is the nature of the research study? Does it involve the administration of a substance (e.g., drug or biologic) or an investigation device?

2.3.3.2 Is the subject population vulnerable (e.g., individuals lacking consent capacity, prisoners, pregnant women, children)? These populations require additional protections.

2.3.3.3 Where is the study being conducted (e.g., hospital, public area)?

2.3.3.4 How complex is the study (e.g., multi-dose, multi-drug dose-escalation, double-blinded, altered pharmacokinetics, early study phase, investigator-initiated, multi-site)?

2.3.3.5 How experienced is the research team (e.g., first study or experienced)?

2.3.3.6 What is the duration of the study (e.g., two days or two years) and duration of subject participation (e.g., one visit or many visits), and how many subjects will the research involve?

2.3.3.7 Is there any oversight by other organizations (e.g., pharmaceutical company, NCI)?

2.3.3.8 What kind of security safeguards exist for individually identifiable research data? Elements to consider:
   - Does the study involve sensitive information (e.g., HIV, mental health)?
   - Is it a multi-site study with sharing and/or accessing of data, video, or photography among many sites/individuals?
   - Will databases be accessed or developed?
   - How will subjects be recruited?

2.3.3.9 What kinds of safeguards exist for protecting the privacy of subjects? Elements to consider:
   - Where are interviews or other face-to-face encounters taking place and what measures have been taken to protect subjects’ privacy?
   - Are there any signs or other revealing information visible at the research site that might stigmatize subjects?
2.3.4 The oversight could be done using a variety of different individuals or entities, such as a pharmaceutical sponsor, contract research monitor, others within the department, Indiana Clinical Research Center (ICRC), or a granting organization (e.g., NCI). In some situations a DSMB may be required (e.g., NIH). For considerations in designing a safety monitoring plan, review process, safety reports, interim analysis, independence of review, steps emanating from review, statistical considerations, and stopping rules, see, for example, the National Institute of Diabetes and Digestive and Kidney Diseases guidance on DSMP, linked from http://www.niddk.nih.gov.

2.3.5 For some sponsored-research studies, the DSMP may already be explained within the protocol. This DSMP may even include an independent DSMB. If this is the case, the PI can simply reference that plan in response to this DSMP requirement.

2.3.6 If, however, the protocol does not contain its own DSMP, the PI is required to develop his/her own plan while taking into consideration the elements listed above. The PI should use the guidelines available in the Summary Safeguard Statement.

2.4. **IRB Responsibilities in Evaluating a Proposed Safety/Risk Assessment and Research Oversight Plan**

2.4.1 Based on the IRB’s review of required documentation provided by the investigator, including the safety/risk assessment and research oversight plan, in accordance with appropriate regulations and IU policies, and with consideration of the guidance provided in this SOP, the IRB will determine the adequacy of and have final approval authority regarding the research oversight plan. It may add, revise, or delete elements from the research oversight plan for each study, as necessary, to ensure the safety of subjects.

2.4.2 Evidence of execution of and adherence to the research oversight plan (e.g., dates of oversight checks, reports) will be requested by the IRB at interim or continuing updates. In some cases, the Human Subjects Research Auditor or other designee may perform an audit to determine adherence to the oversight plan. Also, based on new information on the safety aspects of the research the oversight process may be modified, according to the investigator’s or the IRB’s recommendation. This information should be retained and kept current. These documents will be useful during sponsor or regulatory agency inspections to show due diligence concerning subject safety.

2.4.3 As part of the research oversight plan, the IRB will determine the continuing review cycle for each study. Typically, the IRB reviews each study on an annual basis. However, for studies considered to be high-risk, the IRB may set the review cycle to occur more frequently (e.g., every 3 to 6 months or after 10 subjects have been enrolled). This review cycle may change during the course of the study if at any time the IRB determines that the risks to subjects have either increased or decreased.
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2.4.4 With information provided in continuing review reports or from other sources, the IRB will determine which studies require verification from sources other than the investigator that no material changes have occurred since the last continuing review and may result in a change to the research oversight plan. The following criteria will be used to make this determination:
- Randomly selected studies;
- Complex studies involving unusual levels and types of risk to subjects;
- Studies conducted by investigators who previously failed to comply with federal regulations and institutional policies; and
- Studies where concern about possible material changes occurring without IRB approval have been raised.

3. ADDITIONAL POLICIES AND PROCEDURES

3.1. Research Subject to FDA Regulations
N/A

3.2. Research Subject to HIPAA Regulations
N/A

3.3. Research Subject to VA Regulations
N/A

3.4. Research Subject to Other Regulations

3.4.1 Research Subject to Department of Defense (DoD) Regulations. A research monitor shall be appointed for research that is greater than minimal risk, and may be considered for research that is no more than minimal risk, when appropriate. In doing so, this individual will be appointed by name and have the authority to stop a research study in progress, remove individuals from a study, and take steps to protect the safety and well-being of subjects until the IRB can assess.

3.4.2 Research Subject to Department of Justice (DOJ) Regulations
N/A
1. INTRODUCTION

Safeguarding the confidentiality, integrity, and availability of research data is critically important to maintaining a successful research program. Good security ensures and builds research subject confidence that their personal information will be kept confidential, and also ensures that valuable research data is protected and accessible when needed.

Schools/departments/practice plans are responsible for managing the security of their systems, computers, networks, and other computer resources. Principal Investigators (PIs) also play an important role in addressing the security of research data. This SOP describes some of the key responsibilities that PIs and researchers have in safeguarding research data.

2. POLICIES AND PROCEDURES

2.1. Roles and Responsibilities of Principal Investigator and Research Team in Safeguarding Research Data

Policy References
- Protect IU: Public Safety & Institutional Assurance / Information Security & Privacy Program
- IU Guidelines for Handling Electronic Institutional and Personal Information
- IU Best Practices for Handling Electronic Institutional and Personal Information
- IU Policy on Security of Information Technology Resources

2.1.1 In general, all members of the research team are responsible for correctly and sufficiently using research computers, databases, and records to ensure security and confidentiality of the data stored and transmitted using those resources.

2.1.2 PIs are responsible for ensuring research data remains secure when under the research team’s control by:

- 2.1.2.1 Using appropriate safeguards to maintain the confidentiality, integrity, and availability of data that is collected, used, shared and/or stored for research purposes, including Protected Health Information (PHI);
- 2.1.2.2 Establishing appropriate security oversight for a research project and identifying whether certain aspects should be delegated and to whom.
- 2.1.2.3 Identifying all on-site and off-site research personnel who have or need access to research data in any form and ensuring they employ...
appropriate safeguards and follow all university policies regarding access to data.

2.1.2.4 Ensuring all members of the research team in contact with the data understand their responsibilities and that access to this data is appropriately restricted.

2.1.2.5 Ensuring that for human subject research, the Summary Safeguard Statement in the IRB application appropriately explains the safeguards used to protect the data, including the Data Source (i.e., the types of records that are used to gather the data) and the Data Recording/Collection method.

2.1.2.6 Immediately reporting any suspected or known security breaches that compromise research data to the University Information Security Office (UI SO) and the appropriate facility security office (e.g., IU School of Medicine, IU Health, VA, Eskenazi, IUMG). See Responding to Security Incidents below for details.

2.2. Security Plan

Each research project or center requires an appropriate security plan designed to safeguard the security of research data. This may be project specific, team specific, or lab or location specific.

2.2.1 This may be delegated to an appropriate person within a department, school, or division, but the PI is ultimately responsible for communicating needs and for ensuring an appropriate security organization plan exists. Note: in some situations, this could involve multiple organizations. As a result, this delegation may need to cross multiple organizational policies (e.g., IU Health, Eskenazi, VA).

2.2.1.1 The PI is responsible for identifying which security policies are applicable to their specific project and for oversight of the delegate.

2.2.1.2 The PI is responsible for identifying the need for the addition of any piece of equipment to the IU network (e.g., hardware, software, wireless devices).

2.2.1.3 The PI is responsible for coordinating security planning for the delegate and any third party outside the university (e.g., other institutions, investigators, companies, sponsors, labs) involved in supplying electronic resources used to collect, store, or share research data for a research project.

2.2.2 If the PI chooses not to delegate this responsibility, he/she is responsible for developing his/her own security plan that provides the following:

2.2.2.1 Description of the local environment, including:
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2.2.2.2 Explanation of the security controls that will be employed to ensure compliance with this policy.

2.3. Acceptable Use of Research Data and University Computer Resources

Policy References:
- Appropriate Use of Information Technology Resources
- IU SOP for Data Management

2.3.1 Research team members may access or use Computer Resources for approved research purposes only when:

2.3.1.1 They are authorized to access the resource for research purposes and the research is approved by the appropriate research oversight committee (e.g., IRB, IACUC, IBC, VA R&D); and

2.3.1.2 Use of the data is for legal and ethical purposes that comply with IU policies as well as state and federal laws and regulations.

2.3.2 Data should be collected, used, stored, shared, and disposed of only in accordance with the IU SOP for Data Management.

2.4. Secure Collection and Storage of Research Data

Policy References:
- IU Best Practices for Handling Electronic Institutional and Personal Information
- SEC-02, Disposition of IUSM Electronic Media

2.4.1 Collected data should be securely gathered and stored.

2.4.1.1 **Electronic data:** Data collected using a computer resource (e.g., laptop, hard drive, local shared drive, web-based system, CDs, USB drives, floppy disks) or a PDA should be stored in a secure location. Following are general guidelines:
- Keep all computer resources, including all removable media, in a secure location, such as a locked office, a locked cabinet, or a room with access limited only to authorized personnel.
- Ensure that security features on the computer resource or PDA are enabled, particularly if connected to a network or to the Internet. For example, access should require a password before allowing a user entry to a computer and/or electronic files.
- Secure electronic surveys or questionnaires. The survey should be restricted to authorized personnel only, such as by requiring a password to protect the survey and encrypting data when in
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2.4.1.2 Printed Data: Data referenced or collected from paper records must also be properly safeguarded. Following are general guidelines:
- Keep the records in a secure location, such as a medical records room or a locked private office.
- If practical, original records should not be removed from the source location or from an approved research location.
- If original records are removed from the source or from an approved research location to another approved research location, then records must be securely transported. Secure transport includes a fully enclosed folder, locked briefcase, U.S. Postal Service, or courier service. Reasonable measures should be taken to limit the amount of original data removed from the source location.
- Under no circumstances should paper records be left unattended in a public area.
- Paper surveys or questionnaires should be gathered and organized in a manner to minimize potential loss of the information. In addition, the data collection instruments should be stored in a secure location such as a locked cabinet or an office with limited access by unauthorized personnel (i.e., anyone who is not part of the research team).
- Paper records or data recorded in a researcher’s notes, on a case report form, or in other documents must be kept in a secure location, such as a locked office, a locked cabinet, or an area with limited access by unauthorized personnel.

2.4.1.3 Phone or In-Person Interviews: If data are collected during interviews (either phone interviews or those conducted in person), consider the physical proximity of the subject and interviewer and
the manner in which the data are collected during the interview:

- Interviews should be conducted in a private location when possible so that the subject’s information would not likely be overheard by individuals who are not members of the research team.
- In addition, records created from these interviews (e.g., notes, surveys, or other documentation or recordings) should be kept in a secure location or on a secure computer.

2.4.1.4 **Video and Audio Data:** Data collected using video, audio, or other media must be safeguarded when recorded and stored.

- Data should be collected in a private location when possible so that the subject’s information would not likely be overheard by individuals who are not members of the research team.
- Once the video or audio recording is completed, the storage media should be kept in a secure location (e.g., a locked cabinet or office).

2.4.1.5 **Long-Term Storage and Archival Companies:** Data that are archived or placed into long-term storage should be securely stored.

- Printed, audio, and video records or files should be securely stored off-site when possible, or at a minimum stored on-site in a locked room or cabinet. Access to the records should be limited to authorized personnel.
- Electronic files should be encrypted when possible.
- PIs should maintain an inventory of records or files maintained in long-term storage.
- When professional storage facilities or archival companies are utilized, contractual agreements should adequately protect the data.

2.5. **Secure Disposition, Disposal, or Destruction of Research Data and Electronic Media**

Policy References:
- **IU Best Practices for Handling Electronic Institutional and Personal Information**
- **SEC-02, Disposition of IUSM Electronic Media**

2.5.1 PIs must ensure that data transferred outside the immediate control of the research team are sent to authorized parties and that data are stored securely. This applies to organizations that handle storage or ongoing management of the data (e.g., off-site storage facilities or research sponsors.)

2.5.2 Printed records, removable storage media (such as CDs, USB drives, etc.) or computer equipment on which research data are stored, must be physically destroyed or sanitized according to the following guidelines before those resources are sold, donated, or discarded:
2.5.2.1 **Printed research data:** Printed data may be destroyed by burning, shredding, or other approved measures.
- The process for destruction should ensure that the information cannot be reconstructed; and
- If shredding is used, crosscut shredders are preferred.

2.5.2.2 **Data stored on computers and other electronic devices:**
Permanently delete or overwrite data stored on computers, laptops, PDAs, and other electronic devices before transferring the equipment, or destroy discarded equipment.
- Simply deleting data from a computer’s hard drive or a reusable storage device does not permanently delete the data. In other words, data must be removed at the physical level or appropriately over-written before transferring the equipment to someone else. This generally involves the use of special software designed to erase or overwrite the data. For assistance with permanently deleting or overwriting data, please contact the Information Technology support person for your department or school.
- Within the IU School of Medicine, you may contact the Clinical Affairs Information Technology Services (CAITS) for additional support, [https://caits.iu.edu](https://caits.iu.edu).

2.5.2.3 **Reusable or removable media such as CDs and USB drives:** Files that will no longer be used must be permanently deleted from reusable or removable media before transferring the media outside the researcher’s control. In addition, reusable media must be destroyed when discarded. Any of the following means may be used for destroying electronic media: shredding, burning, melting, or other approved methods.

2.5.2.4 **Other Media:** Permanently destroy video or audio recordings, files, or other media, including data contained in microform when discarded (e.g., microfilm, microfiche, or similar high-data-density material). These media may be destroyed by shredding, burning, or other approved methods.

2.5.2.5 **Disposal of equipment:** If equipment will be discarded, contact the information technology support person in your department or office to coordinate the proper destruction of the equipment. IUSM Policy SEC-02, Disposition of IUSM Electronic Media, and its associated procedures outline the requirements for properly disposing of equipment.

2.5.3 IU policy specifies certain time frames required for retaining data. For more details, see the IUPUI SOPs for Confidentiality and Privacy and Data Management.
2.5.4 For additional information on securely removing data from storage media, see the Securely Removing Data guide.

2.6. **Backup and Disaster Recovery**

Policy Reference:
- [IU Guidelines for Handling Electronic Institutional and Personal Information](#)

PIs are responsible for ensuring that research team members understand and follow proper backup procedures. All research data must be backed up and fully recoverable in the event the primary copy is damaged or unavailable.

2.6.1 **Electronic Data Backup**

2.6.1.1 All electronic research data should be placed on a network server maintained by the IU wherever possible. It is the PI’s responsibility to verify where data are stored and confirm that it is, in fact, a university-maintained network server. The details of the backup process should be included in the approved security plan.
- Data stored on such network servers will automatically be backed up on a routine basis. As a result, researchers should not have to maintain a separate backup copy of these data.
- Electronic research data, such as Protected Health Information, should **not** be permanently stored on computers, laptops, or personal devices if at all possible. Data collected on these devices should be transferred to university-maintained network servers as soon as possible for permanent storage to avoid potential loss of data.

2.6.1.2 If data are stored locally, such as on a computer’s hard drive, backup copies should be made at least on a monthly basis until the data can be transferred to a network server for permanent storage. It is highly recommended that more frequent backups be made.
- At a minimum, one fully recoverable version of electronic research data must be stored off-site. It is also recommended that weekly, monthly, and yearly backups also be stored off-site.

2.6.2 **Printed Data Backup**

2.6.2.1 Researchers should assess the likelihood that paper records could be destroyed or damaged and assess whether backup copies of printed data should be made.

2.6.2.2 Copies of printed research data, such as questionnaires, reports, and forms as well as source documents, should be made whenever possible and stored at a secure off-site location to avoid loss of critical research and supporting data.

2.6.3 **Disaster Recovery**: The PI should ensure that the research team understands the
process for retrieving a backup copy of data if the primary copy becomes unusable. The retrieval process should be tested at least annually to ensure that data can be recovered from the backup copy.

2.7. **Responding to Security Incidents**

Policy References:
- IU Policy on Security of Information Technology Resources (IT-12)
- UIPO Incident Response

2.7.1 Known or suspected breaches of security of computer or technology research resources must be reported to the appropriate security contact for that office or location as soon as the incident is discovered:

2.7.1.1 For IU-Indianapolis, IU Health, Eskenazi Health, VA Medical Center, and IU School of Medicine:
- University Information Security Office (UISO), it-incident@iu.edu
- Office of Research Administration Research Support Services, inforsch@iupui.edu or 317-278-7189.

2.7.1.2 For IU-Bloomington:
- University Information Security Office (UISO), uiso@iu.edu or 812-855-8476.

2.7.2 If the incident pertains to compromise of research data in non-computer forms (e.g., paper records, video, audio), notify the appropriate compliance office as follows:

2.7.2.1 Office of Research Compliance (IRB Office), irb@iu.edu; and/or

2.7.2.2 For IU School of Medicine (IUSM): Office of Research Administration Research Support Services, inforsch@iupui.edu or 317-278-7189.

2.7.3 The PI and the research team must assist the Incident Response Team as needed with security incident investigations.

2.7.4 UISO and/or IUSM may remove or disconnect any computer resource that presents a risk to the university or the IUSM security. UISO and/or IUSM will determine, in consultation with the PI, whether to restore and resume operation of a computer or to pursue additional measures following investigation of an incident. The PI’s department will be responsible for all costs needed to investigate, clean up and recover from a security incident.

2.7.5 Pursuant to Indiana Code 4-1-11-5, whenever a security breach of electronic data is experienced that is reasonably believed to have exposed unencrypted “personal information” to unauthorized third party access, individuals whose data was exposed must be notified. For additional information, see IC
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Section II – Security of Research Data


2.8. Sanctions for Misuse or Abuse of Research Resources

Policy Reference: IU Policy on Misuse or Abuse of IU Technology Resources (IT-02)

Abuse or misuse of resources that contain research data will be investigated by the Institutional Review Board (IRB), Institutional Animal Care and Use Committee (IACUC), Institutional Biosafety Committee (IBC), or other appropriate offices. These offices have the authority to take disciplinary action, up to and including confiscation of equipment, termination of network connectivity, and/or termination of a research study.

2.9. Remote Access to the IUSM Network

Policy References:
- IU Policy on Extending the University Data Network (IT-19)
- IU Policy on Wireless Networking (IT-20)

2.9.1 Researchers are not permitted to independently install remote access devices, Virtual Private Networks, wireless networks, or dial-in modem services.

2.9.2 If a new or wireless network is being considered for the study (e.g., installing a wireless router to connect several computers that have wireless cards), the PI must coordinate with the information technology support person in his/her department and obtain written approval from the UITS Network Operations Center. This does not include computers with wireless cards that utilize the institution’s existing wireless network.

2.9.3 IU, VA, and Eskenazi all have stringent requirements that must be met before any new networks or remote access devices may be installed.

2.10. Electronic Mail Security

Policy References:
- IU Best Practices for Handling Electronic Institutional and Personal Information
- IU Policy on Use of Electronic Mail (IT-21)
- IU Policy on Eligibility to Use Information Technology Resources (IT-03)

2.10.1 IU email users must comply with state and federal laws, institutional policies, and normal standards of professional and personal ethics, courtesy and conduct related to email use.

2.10.2 When an individual is provided an IUPUI email address solely for the purpose of a research study (i.e., a sponsored email account), the person who sponsored the account must notify actadmin@iupui.edu when a researcher no longer needs access for that study.

2.10.3 Email accounts and account passwords shall not be shared.
2.10.4 Sensitive research data should not be sent via email unless specific steps are taken to confirm the transmission is secure. (Routine email within Indiana University (Outlook) or purchased services are generally not secure and their use for transmitting sensitive data should be minimized.)

2.10.4.1 Consult with the information technology support person to determine whether the department or office can implement a secured e-mail transmission.

2.10.4.2 Indiana state law has very specific requirements regarding the use of email for provider-to-patient communications. For more details, contact the IUSM Compliance Office.

2.10.5 Use of subject email lists to communicate with subjects or potential subjects must respect subject confidentiality and comply with all appropriate IU Standard Operating Procedures. Note that IRB approval of email content may also be required.

2.10.6 PIs are responsible for determining when research communications sent via email should be retained for a particular study and for communicating these requirements to the research team.

2.10.7 Emails that are sent with confidential information should include the following disclaimer:

CONFIDENTIALITY NOTICE: This email message, including any attachments, is for the sole use of the intended recipient(s) and may contain confidential and privileged information. Any unauthorized review, use, disclosure, or distribution is prohibited. If you are not the intended recipient, you must not forward, copy, print, save, use, or disseminate this message or any attachments. Please contact the sender by reply email and delete and/or destroy all copies of the original message. Thank you.

2.11. Anti-Virus Software

Policy References:
IU Policy on [Appropriate Use of Information Technology Resources](#) (IT-01)
IU Policy on [Security of Information Technology Resources](#) (IT-12)

2.11.1 PIs are responsible for ensuring that a current version of an anti-virus software program (e.g., Symantec’s Endpoint) is installed and maintained on all computers used for research purposes, and for updating the virus detection program on a routine basis.

2.11.2 Users should be aware of computer viruses and other destructive programs and take steps to avoid them. For instance:

2.11.2.1 Avoid opening emails from an unrecognized sender;

2.11.2.2 Avoid installing programs or files from unknown sources; and
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2.11.2.3 Routinely update the anti-virus software program.

2.12. Access to Research Data

Policy Reference:
- Research data may be accessed only for approved research studies according to the information’s sensitivity and the level of risk should the data be disclosed.

2.12.1 PIs are responsible for ensuring that appropriate measures are employed so that only authorized research personnel have access to research data for that study. This includes access to databases, records, software, or other sources used for research purposes that are within the PI’s or research team’s control.

2.12.2 The PI should ensure that researchers understand appropriate procedures for requesting access to data maintained by other parties.

2.12.3 In order for a non-IU research collaborator to access and use IU computer, network, and email resources, the PI must provide written certification of need and submit this certification to UIPO by completing the form found at https://itaccounts.iu.edu/. Directions for filling out the form are found at https://kb.iu.edu/d/akll. UIPO requires periodic renewal.

Access to research data and University resources should be appropriately terminated for research team members who end their involvement with the study by notifying acadmn@iupui.edu when a researcher no longer needs access.

2.13. Managing User Computer Accounts

Policy References:
- IU Guidelines for Handling Electronic Institutional and Personal Information
- IU Policy on Computer and Network Accounts Administration (IT-18)
- IU Guidelines on Passphrases

2.13.1 Setting Up Access to Systems or Computers: If new computers, systems, software, or databases are created or obtained for a study and these resources are not accessed through a secure IU network connection, then additional security measures apply. For more details, see the IU Policy on Network and Computer Accounts Administration (IT-18).

2.13.1.1 Each approved user is assigned an individual user name and asked to create a unique Network ID passphrase.

- Passphrases should be designed to restrict access to limited and restricted information whenever possible. For help creating a secure passphrase, see the IU guidelines on Passphrases and/or https://kb.iu.edu/d/acpu.
• An active user list should be maintained for new resources developed for a research study.

2.13.2 Procedures for Providing Access to University Systems

2.13.2.1 Provide access only to those who legitimately require it.

2.13.2.2 Require users to be identified and authenticated before allowing access.

2.13.2.3 Limit access to needed services and authorized individuals only.

2.13.2.4 Assign accounts only to individuals (i.e., don’t use group accounts).

2.13.3 Using Systems or Computers

2.13.3.1 Researchers may not share their passphrases with others;

2.13.3.2 Passphrases should be changed periodically;

2.13.3.3 Researchers may not assume the identity of another computer user; and

2.13.3.4 Researchers should log out of computers when stepping away, even for a moment. To prevent unauthorized access, researchers should shut down laboratory or test computers when finished using them and remove any removable storage devices.

2.14. Data Encryption

Policy References:

• IU Guidelines for Handling Electronic Institutional and Personal Information

Unencrypted data, whether stored in a file or transmitted over a network, is vulnerable to disclosure. Data should be encrypted whenever possible, particularly for archived data stored off-site and when sending data electronically (through email or file transfer). There is technology available to protect sensitive data contained in standalone files and email communications and passed between a web browser and a web server. For assistance, consult Best Practices for Securing IT Resources or contact the Information Technology support person in your office or location.

2.15. Computer Security

Policy References:

• IU Guidelines for Handling Electronic Institutional and Personal Information

2.15.1 PIs should know whether there are adequate safeguards to protect computers, including laptops, PDAs, data, and files. Computers that are not sufficiently
protected should be enhanced with additional appropriate safeguards.

2.15.2 Guidelines for using computers include but are not limited to:

2.15.2.1 Password-protected screen savers should be used whenever possible;

2.15.2.2 Computers should not be left unattended if that could result in unauthorized access;

2.15.2.3 Systems should be logged off and closed when not in use; and

2.15.2.4 Users should prevent others from inadvertently viewing their computer screen when working with sensitive data.

2.15.3 Guidelines for protecting system vulnerabilities:

2.15.3.1 Regularly update vendor-supplied security fixes (patches) to protect against system compromise.

2.15.3.2 Regularly scan computers for security vulnerabilities.

2.15.3.3 Remove unneeded services and software.

2.15.3.4 Stay informed of security issues. One way to do this is to routinely check the University Information Security Office website for current security issues and security guides.

2.16. Faxing Research Data

2.16.1 Researchers should use the following guidelines when faxing research data:

2.16.1.1 Include a fax cover sheet with a confidentiality statement, particularly when faxing restricted data such as PHI;

2.16.1.2 Use reasonable measures to ensure the receipt of fax transmissions is protected from general viewing; and

2.16.1.3 Locate fax machines utilized to transmit or receive research data in areas with restricted access or limited to authorized personnel only whenever possible.

2.17. Research Security Audits

2.17.1 PIs will cooperate with any mandatory, scheduled, and/or requested security audits and will maintain appropriate documentation needed for security audit purposes, including but not limited to:

2.17.1.1 A list of all researchers working on a given research project that have access to data used for that project;
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2.17.1.2 A copy of the security plan for that project, lab, or location; and

2.17.1.3 A copy of a security audit log when required by regulation (e.g., FDA, HIPAA) For example, this could include a list of researchers who accessed a research database or system, including the date and time of the access.

3. ADDITIONAL POLICIES AND PROCEDURES

3.1. Research Subject to FDA Regulations

N/A

3.2. Research Subject to HIPAA Regulations

N/A

3.3. Research Subject to VA Regulations

Researchers should refer to VHA Handbook 1200.12.

3.4. Research Subject to Other Regulations

3.4.1 Research Subject to Department of Defense (DoD) Regulations

N/A

3.4.2 Research Subject to Department of Education (ED) Regulations

N/A

3.4.3 Research Subject to Department of Justice (DOJ) Regulations

N/A
1. INTRODUCTION

The Belmont Report established three basic ethical principles – autonomy/respect for persons, beneficence, and justice – that are the cornerstone for regulations involving human subjects. It is these three basic ethical principles that Indiana University follows to govern the conduct of human subjects research. To this end, the policies and Standard Operating Procedures (SOPs) were established for the Human Research Protection Program (HRPP). Through well thought-out policies, clear and concise definitions, and standard procedures that fit well into the actual work process, an operation can function with regularity, efficiency, and good quality. SOPs provide the basis for orienting and educating new staff. The SOPs are the first place regulatory agencies and study sponsors go when seeking to assure themselves that a research department or investigator and staff are operating appropriately in their field of expertise.

2. POLICIES AND PROCEDURES

2.1. It is the policy of IU that research involving human subjects will be conducted according to the highest ethical and professional standards and in line with current research practices in the field.

2.2. SOPs will be written by individuals with specific technical expertise regarding quality and compliance in human subjects research. The writing of SOPs will be overseen by the Assistant Vice President, Office of Research Compliance. New SOPs will be reviewed and approved by the IRB Executive Committee.

2.3. SOPs will be followed by those conducting or supporting research.

2.4. SOPs will be the basis for educating new people on the conduct of human subjects research.

2.5. SOPs will be used to guide regulatory agency inspectors, sponsor company monitors or auditors, and IU research compliance staff as they examine and evaluate the conduct of human subjects research.

2.6. SOPs will be reviewed periodically by IU Human Subjects Office staff to assure they accurately reflect research processes within IU. The IU Human Subjects Office will seek additional topic experts to assist in these reviews as necessary.

2.7. Revisions of the SOPs may be made only by the IU Human Subjects Office. If revisions appear to be needed, requests for change should be made to the IU Human Subjects Office.
2.8. A record (official) copy of the SOPs will be maintained by the IU Human Subjects Office.

2.9. SOPs will be available on the IU Human Subjects Office website.

2.10. For training purposes and day-to-day use, SOPs may be printed and stored. However, when notified by the IU Human subjects Office that new versions have been created, all investigators who have printed copies have the responsibility to collect and destroy old versions.

3. ADDITIONAL POLICIES AND PROCEDURES

3.1. Research Subject to FDA Regulations

N/A

3.2. Research Subject to HIPAA Regulations

N/A

3.3. Research Subject to VA Regulations

N/A

3.4. Research Subject to Other Regulations

3.4.1 Research Subject to Department of Defense (DoD) Regulations

N/A

3.4.2 Research Subject to Department of Education (ED) Regulations

N/A

3.4.3 Research Subject to Department of Justice (DOJ) Regulations

N/A
1. INTRODUCTION

All non-exempt research proposals that are conducted outside the United States and target non-military, non-U.S. research subjects for enrollment must meet certain criteria before study-related procedures can be initiated. Internet research that may incidentally enroll non-U.S. research subjects are not subject to this policy.

2. POLICIES AND PROCEDURES

2.1 Special Considerations for International Research

2.1.1 These policies and procedures apply to all HSO staff and IRB members and to research submitted to the IRB. Procedures normally followed outside the United States for research involving human subjects may differ from those set forth in federal and IU policies. These may result from differences in language, cultural and social history, and social norms.

2.1.2 IU investigators should take special consideration of relevant national policies such as the availability of national health insurance, philosophically different legal systems, and social policies that may make U.S. research forms and procedures inappropriate.

2.1.3 While the IU IRB cannot impose its standards for written informed consent documentation on other cultures, IU does not relax the standards for ethical conduct of research for a meaningful consent process.

2.1.4 The IU IRB and investigators will pay special attention to local customs and to local culture and religious norms in preparing written consent documents or proposing alternative consent processes. Requests to review and waive some standard elements of the consent process or document may be considered by the IRB. Research proposals for which a waiver of written consent may be reasonable should include an explanation of cultural norms or conditions requiring the waiver.

2.2. Local Review and Procedures

2.2.1 If a project meets the definition of human subjects research, investigators are required to submit a research application to the IU IRB and must receive approval prior to conducting the research. In addition to the initial review of these studies, the IU IRB must also conduct continuing review, review modifications, review complaints, and reportable events, and perform post-approval monitoring.
2.2.2 Before research is conducted at an international site, the investigator must determine whether the country has laws or guidance related to the protection of human subjects.

2.2.2.1 If required and/or available, IRB approval from a local ethical board or group must first be obtained.

2.2.2.2 Where there is no equivalent board or group available, investigators must rely on local experts or community leaders to provide approval and/or consultation, or provide adequate justification as to why local review is not available.

2.2.2.3 Examples of local reviews may include the following:
   - Ethics committees
   - Drug approval agencies
   - Local ministries
   - Local governances

2.2.3 Local IRB or ethical group approval (as applicable) shall be submitted to the IU IRB upon receipt. Research must not commence until all necessary approvals have been obtained.

2.2.3.1 Examples of local approval may include the following:
   2.2.3.1.1 Approval documents from a local ethical review board or group.
   2.2.3.1.2 Letters from the community leaders or stakeholders acknowledging the conduct of the research.
   2.2.3.1.3 Acknowledgement of notification regarding the research to be conducted from the local community leaders, stakeholders, or ethics review board.

2.3 The Office of Human Research Protections (OHRP) provides a listing of the laws, regulations, and guidelines that govern human subjects research in many countries around the world.

3. ADDITIONAL POLICIES AND PROCEDURES

3.1 Research Subject to FDA Regulations

N/A

3.2 Research Subject to HIPAA Regulations

See the IU SOP on Confidentiality and Privacy for details.

3.3 Research Subject to VA Regulations
3.3.1 All international research must 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 VHA Child Research and Development Officer (CRADO).

3.4. Research Subject to Other Regulations

3.4.1 Research Subject to Department of Defense (DoD) Regulations

3.4.1.1 For studies being conducted under a DoD Addendum, investigators must comply with the following additional safeguards for research conducted with international populations:

3.4.1.1.1 The organization or investigator must have permission to conduct research in that country by certification or by local ethics review.

3.4.1.1.2 The investigator must follow all local laws, regulations, customs, and practices.

3.4.2 Research Subject to Department of Education (ED) Regulations

N/A

3.4.3 Research Subject to Department of Justice (DOJ) Regulations

N/A
1. INTRODUCTION

Pursuant to 45 CFR 46.111, the IRB must determine that specific requirements are satisfied in order to approve research with human subjects. One such requirement is that the selection of subjects is equitable (§46.111(a)(3)). In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, students, individuals lacking consent capacity, economically or educationally disadvantaged persons, persons with limited treatment options, and persons with increased susceptibility to harm including economic, social, or legal consequences from the study. Because of the special vulnerability of these populations, the federal regulations, state and local laws, and institutional policies require additional protections for these individuals.

2. POLICIES AND PROCEDURES

2.1. Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research (Subpart B)

2.1.1. Research involving women who are or may become pregnant should receive special attention from the IRB because of women’s additional health concerns during pregnancy and because of the need to avoid unnecessary risk to the fetus. Further, in the case of a pregnant woman, the IRB must determine when informed consent of the father is required for the research. Special attention is justified because of the involvement of a third party (the fetus) who may be affected but cannot give consent and because of the need to prevent harm or injury to future members of society.

2.1.2. Research Involving Pregnant Women or Human Fetuses. Pursuant to 45 CFR 46.204, pregnant women or human fetuses may be involved in research if all of the following conditions are met:

2.1.2.1. Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on nonpregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;

2.1.2.2. The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important generalizable knowledge that cannot be obtained by any other means;
2.1.2.3. Any risk is the least possible for achieving the objectives of the research;

2.1.2.4. If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important generalizable knowledge that cannot be obtained by any other means, her consent is obtained in accord with the informed consent provisions of 45 CFR 46, Subpart A;

2.1.2.5. If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accord with the informed consent provisions of 45 CFR 46, Subpart A, except that the father’s consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity, or if the pregnancy resulted from rape or incest.

2.1.2.6. Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;

2.1.2.7. For children as defined in §46.402(a) who are pregnant, assent and permission are obtained in accord with the provisions of 45 CFR 46, Subpart D;

2.1.2.8. No inducements, monetary or otherwise, will be offered to terminate a pregnancy;

2.1.2.9. Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and

2.1.2.10. Individuals engaged in the research will have no part in determining the viability of a neonate.

2.1.3. **Research Involving Neonates.** Pursuant to 45 CFR 205(a), neonates of uncertain viability and nonviable neonates may be involved in research if all of the following conditions are met:

2.1.3.1. Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.

2.1.3.2. Each individual providing consent under §46.205(b)(2) or §46.205(c)(5) is fully informed regarding the reasonably foreseeable impact of the research on the neonate.

2.1.3.3. Individuals engaged in the research will have no part in determining the viability of a neonate.
2.1.3.4. The requirements of §46.205(b) or §46.205(c) have been met as applicable.

2.1.4. Pursuant to 45 CFR 46.205(b), until it has been ascertained whether a neonate is viable, a neonate may not be involved in research covered by Subpart A of 45 CFR 46 unless the following additional conditions have been met:

2.1.4.1. The IRB determines that: (a) the research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective, or (b) the purpose of the research is the development of important generalizable knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research; and

2.1.4.2. The legally effective informed consent of either parent of the neonate or, if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent’s legally authorized representative (LAR) is obtained in accord with subpart A of 45 CFR 46, except that the consent of the father or his LAR need not be obtained if the pregnancy resulted from rape or incest.

2.1.5. Research Involving Nonviable Neonates. Pursuant to 45 CFR 46.205(c), after delivery, a nonviable neonate may not be involved in research covered by Subpart A of 45 CFR 46 unless all of the following additional conditions are met:

2.1.5.1. Vital functions of the neonate will not be artificially maintained;

2.1.5.2. The research will not terminate the heartbeat or respiration of the neonate;

2.1.5.3. There will be no added risk to the neonate resulting from the research;

2.1.5.4. The purpose of the research is the development of important generalizable knowledge that cannot be obtained by other means; and

2.1.5.5. The legally effective informed consent of both parents of the neonate is obtained in accord with subpart A of 45 CFR 46, except that the waiver and alteration provisions of §46.116(c) and (d) do not apply. However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable neonate will suffice to meet the requirements of this paragraph (c)(5), except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest. The IRB cannot approve the consent of an LAR for a nonviable neonate.

2.1.6. Pursuant to 45 CFR 46.205(d), a neonate, after delivery, that has been determined to be viable may be included in research only to the extent permitted by and in accord with the requirements of 45 CFR 46, Subparts A and D.
2.1.7. Pursuant to 45 CFR 46.206, research involving, after delivery, the placenta; the dead fetus; macerated fetal material; or cells, tissue, or organs excised from a dead fetus shall be conducted only in accord with any applicable federal, state, or local laws and regulations regarding such activities. If information associated with the material is recorded for research purposes in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research subjects and all pertinent subparts of this part are applicable.

2.1.8. In evaluating the inclusion of pregnant women, human fetuses, and neonates in research, the IRB will consider the protocol-specific findings provided by the investigator in the Pregnant Women, Fetuses, Neonates Questionnaire in the KC Protocol and document its determination in the IRB minutes.

2.1.9. Pursuant to 45 CFR 46.207, the Secretary will conduct or fund research that the IRB does not believe meets the requirements of §46.204 or §46.205 only if:

2.1.9.1. The IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates; and

2.1.9.2. The Secretary, after consultation with a panel of experts in pertinent disciplines (e.g., science, medicine, ethics, law) and following opportunity for public review and comment, including a public meeting announced in the Federal Register, has determined either (a) That the research in fact satisfies the conditions of §46.204, as applicable; or (b) The following: (i) The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates; (ii) The research will be conducted in accord with sound ethical principles; and (iii) Informed consent will be obtained in accord with the informed consent provisions of subpart A and other applicable subparts of this part.

2.1.10. **Research in which Pregnancy Is Coincidental to Subject Population.** Any research in which women of childbearing potential are possible subjects may inadvertently include women already pregnant or women who may become pregnant. HHS regulations, specifically 45 CFR 46.116(b)(1), require that, when appropriate, the informed consent document include a statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) that are currently unforeseeable. The IRB must then judge whether the mother’s participation would pose any risk to the fetus or nursing infant. In some studies, the IRB may need to ensure that nonpregnant subjects are advised to avoid pregnancy or nursing for a time during or following the research. Furthermore, where appropriate, subjects should be advised to notify the investigator immediately should they become pregnant. In some instances there may be potential risk
sufficient to justify requiring that pregnant women either be specifically excluded from the research or studied separately.

2.1.11. Investigator Responsibilities When Involving Pregnant Women, Human Fetuses, and/or Neonates in Research

2.1.11.1. When research proposes to enroll pregnant women, human fetuses, or neonates, the investigator must obtain approval from the IRB before any such subjects may be enrolled in the research.

2.1.11.2. For a new study proposing to enroll such subjects, the investigator must complete and submit the Pregnant Women, Fetuses, Neonates Questionnaire in the KC IRB Protocol with the new study application.

2.1.11.3. For an existing study proposing to enroll such subjects, the investigator must submit an amendment along with the completed Pregnant Women, Fetuses, Neonates Questionnaire in the KC IRB Protocol.

2.2. Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects (Subpart C)

2.2.1. Pursuant to 45 CFR 46.306(a)(2), federally funded biomedical or behavioral research may involve prisoners as subjects only if the IRB determines that the proposed research involves one or more of the following:

2.2.1.1. Study of the possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;

2.2.1.2. Study of prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;

2.2.1.3. Research on conditions particularly affecting prisoners as a class (for example, vaccine trials and other research on hepatitis, which is much more prevalent in prisons than elsewhere; and research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults) provided that the study may proceed only after the Secretary has consulted with appropriate experts including experts in penology, medicine, and ethics, and published notice in the Federal Register of the intent to approve such research; or

2.2.1.4. Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subjects. In cases in which those studies require the assignment of prisoners in a manner consistent with studies approved by the IRB to control groups that may not benefit from the research, the study may proceed only after the Secretary has consulted with appropriate experts, including experts in penology, medicine, and ethics, and
2.2.2. Per notice in the federal register, the requirement that the research represent one of the categories of research permissible under 45 CFR 306(a)(2) may be waived when DHHS conducts or supports certain important and necessary epidemiologic research on prisoners that meet the following criteria:

2.2.2.1. In which the sole purposes are (i) to describe the prevalence or incidence of a disease by identifying all cases, or (ii) to study the potential risk factor associations for a disease; and

2.2.2.2. Where the institution responsible for the conduct of research certifies to the Office of Human Research Protections, DHHS, acting on behalf of the Secretary, that the IRB approved the research and fulfilled its duties under 45 CFR 46.305(a)(2)-(7) and determined and documented that:

2.2.2.2.1. The research presents no more than minimal risk and no more than inconvenience to the prisoner-subjects, and

2.2.2.2.2. Prisoners are not a particular focus of the research.

2.2.3. The exemptions outlined at 45 CFR 46.101(b) do not apply to prisoners.

2.2.4. Additional Duties of the Institutional Review Boards. In addition to all other responsibilities under 45 CFR 46, the IRB shall review and approve research involving prisoners only if it finds that:

2.2.4.1. For federally funded research, the research represents one of the categories of research permissible under §46.306(a)(2) or waiver of this requirement is appropriate per 2.2.2 above;

2.2.4.2. Any possible advantages accruing to the prisoner through his/her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities, and opportunity for earnings in the prison, are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired;

2.2.4.3. The risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers;

2.2.4.4. Procedures for the selection of subjects within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the Principal Investigator provides to the IRB justification in writing for following some other procedures, control subjects must be selected randomly from the group of available prisoners who meet the characteristics needed for that particular research project;
2.2.4.5. The information is presented in language understandable to the subject population;

2.2.4.6. Adequate assurance exists that parole boards will not take into account a prisoner’s participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have no effect on his/her parole;

Where the IRB finds there may be a need for follow-up examination or care of subjects after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoners’ sentences, and for informing subjects of this fact; and

2.2.4.7. The investigators and the study team are appropriately qualified to work and interact with prisoners, based on previous research experience, academic preparation, and/or relevant training and oversight by the PI.

2.2.4.8. In evaluating the inclusion of prisoners in research, the IRB will consider the protocol-specific findings provided by the investigator in the Prisoners Questionnaire of the KC Protocol and document its determination in the IRB minutes.

2.2.5. Additional Considerations When Research Proposes to Involve Prisoners.

2.2.5.1. When a prisoner is also a child (e.g., an adolescent detained in a juvenile detention facility), appropriate additional requirements must be satisfied for the inclusion of children in research as outlined below.

2.2.6. Composition of the IRB Where Prisoners Are Involved. Pursuant to 45 CFR 46.304, in addition to satisfying the requirements in 45 CFR 46.107, an IRB that regularly reviews research involving prisoners shall include one or more individuals who are knowledgeable about and experienced in working with this population to serve as a voting IRB member. The composition of the IRB must satisfy the following requirements found at 45 CFR 46.304(a) and (b):

2.2.6.1. A majority of the IRB (exclusive of prisoner members) shall have no association with the prison(s) involved, apart from their membership on the IRB; and

2.2.6.2. At least one member of the IRB must be a prisoner, or a prisoner representative with appropriate background and experience to serve in that capacity, except that where a particular research project is reviewed by more than one IRB only one IRB need satisfy this requirement.

2.2.6.3. In the absence of choosing someone who is a prisoner or has been a prisoner, the IRB will choose a prisoner representative who has a close working knowledge, understanding, and appreciation of prison
conditions from the perspective of a prisoner. Suitable individuals could include prison chaplains; prison psychologists, prison social workers, or other prison service providers; persons who have conducted advocacy for the rights of prisoners; or any individuals who are qualified to represent the rights and welfare of prisoners by virtue of appropriate background and experience.

2.2.7. When the convened IRB reviews research involving prisoners (including initial review, continuing review, amendments, and reportable events), the prisoner representative, who is a voting member, must receive all materials pertaining to the research (i.e., the same information as the primary reviewer) and be present at the meeting. If the prisoner representative is not present (either in person or via telephone or video conferencing), research involving prisoners cannot be reviewed or approved.

2.2.8. Expedited Review of Research Involving Prisoners

2.2.8.1. Expedited review of research involving interaction with prisoners is allowed only when a determination is made by the primary IRB reviewer and the prisoner representative that the research is minimal risk for the prison population being studied or included.

2.2.8.2. Expedited review of research with prisoners that does not involve interaction with prisoners (i.e., research involving existing data or record review) is allowed only when a determination is made by the primary reviewer that the research poses minimal risk for the prison population being studied or included.

2.2.9. Modifications to Previously Approved Research Involving Prisoners

2.2.9.1. Substantial modifications to research requiring review by the convened IRB and involving prisoners (i.e., Major Amendments) must be reviewed by the convened IRB using the same procedures for initial review, including the responsibility of the prisoner representative.

2.2.9.2. Minor modifications (i.e., Minor Amendments) may be reviewed using the expedited procedure referenced above in Sections 2.2.7.

2.2.10. Continuing Review of Research Involving Prisoners

2.2.10.1. Continuing review of research requiring review by the convened IRB and involving prisoners must be reviewed by the convened IRB using the same procedures for initial review, including the responsibility of the prisoner representative.

2.2.10.2. Continuing review of research involving prisoners may be reviewed using the expedited procedure referenced under Modifications to Previously Approved Research Involving Prisoners, above.
2.2.11. Additional Requirements for Conducting Research Within the Indiana Department of Corrections (DOC) Facility

2.2.11.1. Research with human subjects involving medical testing, chemical, experimental drugs, etc., is prohibited by the DOC’s Health Care Services Directives.

2.2.11.2. Pursuant to 210 IAC 1-6-7, all requests for access to offender or juvenile records for research purposes shall be made to the director of planning services in written form. Such requests shall include the name of the agency or organization performing the research and the names of the persons directly responsible for the following:

2.2.11.2.1. Conducting such research.

2.2.11.2.2. The purpose of such research.

2.2.11.2.3. How the research is to be performed.

2.2.11.2.4. What measures will be taken to assure the proper protection of classified information.

2.2.11.3. Approval of such requests will be granted or denied consistent with provisions of 210 IC 4-1-6-8.6 and department procedures.

2.2.11.4. Note that other states may have similar or additional requirements.

2.2.12. Investigator Responsibilities When Involving Prisoners in Research

2.2.12.1. Investigators may not screen for, recruit into, or enroll any individual involuntarily confined or detained in a penal institution to a research study without prior IRB approval.

2.2.12.2. Investigators are responsible for obtaining and providing documentation to the IRB of approval from detention or correctional facilities involved in the research.

2.2.12.3. For a new study proposing to enroll such subjects, the investigator must complete the Prisoners Questionnaire of the KC IRB Protocol.

2.2.12.4. For an existing study proposing to enroll such subjects, the investigator must submit an amendment along with completing the Prisoners Questionnaire of the KC IRB Protocol.

2.2.13. Procedures When a Current Subject Becomes a Prisoner During the Research

2.2.13.1. When a human subject involved in ongoing research becomes a prisoner during the course of the study, and the relevant research study was not previously approved by the IRB for the inclusion of prisoners,
the investigator must promptly notify the IRB. Additionally, all research interactions and interventions with, and obtaining identifiable private information about, the now-incarcerated prisoner-subject must be suspended immediately, except as noted below.

2.2.13.2. If the investigator wishes to have the prisoner-subject continue to participate in the research, the IRB must promptly re-review the proposal in accordance with the requirements of Subpart C (for federally funded research). The investigator must submit to the IRB:

2.2.13.2.1. Notification that a previously enrolled research subject has become a prisoner;

2.2.13.2.2. An amendment requesting the inclusion of prisoners; and

2.2.13.2.3. A completed Prisoners Questionnaire in the KC IRB Protocol.

2.2.13.3. The IRB review must occur at a convened IRB meeting.

2.2.13.4. **Exception:** The federal regulations allow for one important exception to the requirement that all research interactions or interventions with, and obtaining identifiable information about, the now-incarcerated prisoner-subject must cease until the regulatory requirements for research involving prisoners are met. In special circumstances in which the investigator asserts that it is in the best interest of the prisoner-subject to continue to receive interactions or interventions and/or for the investigator to obtain private identifiable information from the prisoner-subject in the research study while he/she is incarcerated, the IRB Chair may determine that the prisoner-subject may continue to participate in the research until the above requirements are met. The investigator must promptly notify the IRB of this occurrence, so that the IRB can re-review the study.

2.2.13.5. IRB review and approval are not required if research interactions and interventions or obtaining of identifiable private information will not occur during the incarceration period.

2.2.14. **Additional Requirements for Research Conducted or Supported by HHS that Involves Prisoners.** Pursuant to 45 CFR 46.306(a), biomedical or behavioral research conducted or support by HHS may involve prisoners as subjects only if:

2.2.14.1. The institution has certified to the Secretary that the IRB has approved the research under §46.305.

2.2.14.2. In the judgment of the Secretary the proposed research involves solely one of the permitted categories of research involving prisoners listed under 45 CFR 46.306(a)(2); or
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Standard Operating Procedures
for Research Involving Human Subjects

2.2.14.3. Research involves epidemiologic studies that meet the following criteria:

2.2.14.3.1. The sole purposes of the research are one of the following:
(a) to describe the prevalence or incidence of a disease by identifying all cases; or (b) to study potential risk factor associations for a disease.

2.2.14.3.2. The institution certifies to the Office for Human Research Protections (OHRP) that the IRB approved the research and fulfilled its duties under 45 CFR 46.305(a)(2)-(7) and determined and documented that: (a) the research presents no more than minimal risks and no more than inconvenience to the prisoner-subjects; and (b) prisoners are not a particular focus of the research.

2.2.14.4. Except as provided in §46.306, biomedical and behavioral research conducted or supported by HHS shall not involve prisoners as subjects.

2.3. Additional Protections for Children Involved as Subjects in Research (Subpart D)

2.3.1. Exemptions at §46.101(b)(1) and (b)(3) through (b)(6) are applicable to this subpart. The exemption at §46.101(b)(2) regarding educational tests is also applicable to this subpart. However, the exemption at §46.101(b)(2) for research involving survey or interview procedures or observations of public behavior does not apply to research covered by this subpart, except for research involving observation of public behavior when the investigator(s) does not participate in the activities being observed.

2.3.2. Pursuant to 45 CFR 46, Subpart D and 21 CFR 50, Subpart D, the IRB can approve federally funded research involving children as research subjects only when it satisfies the conditions outlined below.

2.3.2.1. 45 CFR 46.404. Research not involving greater than minimal risk.
To approve research in this category, the IRB must find and document the following determinations:

2.3.2.1.1. the research presents no more than minimal risk to the children; and

2.3.2.1.2. adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth at §46.408.

2.3.2.1.3.

2.3.2.2. 45 CFR 46.405. Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects.
To approve research in this category, the IRB must find and document the following determinations:
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2.3.2.2.1. the research presents more than minimal risk to the children by an intervention or procedure that holds out the prospect of direct benefit for the individual subject, or by a monitoring procedure that is likely to contribute to the subject’s well-being;

2.3.2.2.2. the risk is justified by the anticipated benefits to the subjects;

2.3.2.2.3. the relation of the anticipated benefit to the risk presented by the study is at least as favorable to the subjects as that provided by available alternative approaches; and

2.3.2.2.4. adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth at §46.408.

2.3.2.3. 45 CFR 46.406. Research involving greater than minimal risk and no prospect of direct benefit to the individual subjects, but likely to yield generalizable knowledge about the subject’s disorder or condition. To approve research in this category, the IRB must find and document the following determinations:

2.3.2.3.1. the research presents a minor increase over minimal risk by an intervention or procedure that does not hold out the prospect of direct benefit for the individual subject, or by a monitoring procedure that is not likely to contribute to the well-being of the subject;

2.3.2.3.2. the intervention or procedure presents experiences to the subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations;

2.3.2.3.3. the intervention or procedure is likely to yield generalizable knowledge about the subjects’ disorder or condition of vital importance for the understanding or amelioration of the subjects’ disorder or condition; and

2.3.2.3.4. adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth at §46.408.

2.3.2.4. A fourth category of research requires a special level of HHS review under 45 CFR 46.407 beyond that provided by the IRB: Research not otherwise approvable (i.e., the research does not meet the conditions of §46.404, §46.405, or §46.406) that presents an opportunity to further understand, prevent, or alleviate a serious problem affecting the health
or welfare of children. Research in this category may be conducted only if:

2.3.2.4.1. The IRB believes that the research does not meet the requirements of §46.404, §46.405, or §46.406 but finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; and

2.3.2.4.2. The Secretary, HHS or his/her designee, after consulting with a panel of experts in pertinent disciplines (e.g., science, medicine, education, ethics, law) and following an opportunity for public review and comment, determines either:

2.3.2.4.2. that the research in fact satisfies the conditions of §46.404, §46.405, or §46.406; or

2.3.2.4.2. the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; the research will be conducted in accordance with sound ethical principles; and adequate provisions are made for soliciting the assent of children and the permission of their parents or legal guardians as set forth in §46.408.

2.3.3. Adequate provisions for soliciting the assent of children. Pursuant to 45 CFR 46.408(a) and 21 CFR 50.55(a), the IRB shall determine and document that adequate provisions are made for soliciting the assent of the children, when in the judgment of the IRB the children are capable of providing assent.

2.3.3.1. In determining whether children are capable of assenting, the IRB shall take into account the ages, maturity, psychological status, and health condition of the children involved. Assents may apply to all or some of the children involved in the research. In general, the IRB will require assent from children ages seven (7) to seventeen (17); however, the IRB acknowledges there are situations in which it may be appropriate for younger children, depending on their aptitude/ability to provide assent. Alternatively, there may be situations in which older children with higher cognitive ability may be able to read, understand, and subsequently sign the adult consent document. In these instances, the investigator must prospectively justify this scenario in the IRB submission and make the necessary changes to the informed consent document (for example, the inclusion of "you/your child" language and a child signature line).
2.3.3.2. The assent of the children is not required if the IRB determines that either of the following is true:

2.3.3.2.1. the children are not capable of providing assent based on their age, maturity, or psychological state; or

2.3.3.2.2. the capability of the children is so limited that they cannot reasonably be consulted.

2.3.3.3. Even when children are capable of providing assent, there are circumstances in which it may be appropriate for the IRB to waive assent. The IRB can waive assent if either of the following criteria is satisfied:

2.3.3.3.1. The intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and available only in the context of the research (45 CFR 46.408); or

2.3.3.3.2. The study meets the criteria for waiver of informed consent under 45 CFR 46.116(d).

- Research does not involve more than minimal risk to subjects.
- The waiver will not adversely affect the rights and welfare of the subjects.
- The research could not be practicably carried out without the waiver.
- When appropriate, subjects will be provided with additional pertinent information after participation.
- The research is not FDA-regulated.

2.3.3.4. The investigator can prospectively request a waiver of assent for some or all children in the IRB submission.

2.3.3.5. When the IRB approves a waiver of assent for some or all children, it will determine which children are not required to assent.

2.3.3.6. Even where the IRB approves a waiver of child assent, an age-appropriate information sheet may still need to be given to the child-subjects.

2.3.3.7. When the IRB determines that assent is required, it shall determine whether and how assent must be documented.
2.3.4. **Adequate provisions for soliciting the permission of each child’s parents or guardian.** Pursuant to 45 CFR 46.408(b), the IRB shall determine and document, in accordance with and to the extent that consent is required by §46.116 of Subpart A, that adequate provisions are made for soliciting the permission of each child’s parents or guardian.

2.3.4.1. Where parental permission is to be obtained, the IRB may find that the permission of one parent is sufficient for research to be conducted under §46.404 or §46.405.

2.3.4.1.1. Although the regulations allow permission of only one parent or guardian for research conducted under §46.404 or §46.405, the IRB must determine that the permission of one parent or guardian is sufficient. For example, it may be inappropriate to allow permission of only one parent or guardian in a standard therapeutic trial for childhood cancer where the researcher has time to obtain permission from both parents, unless one is deceased, unknown, incompetent, or not reasonably available, or when only one parent or guardian has legal responsibility for the care and custody of the child, just because the research is conducted under §46.404 or §46.405.

2.3.4.2. Where research is covered by §46.406 and §46.407 and permission is to be obtained from parents, both parents must give their permission unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.

2.3.4.3. Permission by parents or guardians shall be documented in accordance with and to the extent required by §46.117, Documentation of informed consent.

2.3.5. **Waiver of parental or guardian permission.** The IRB may waive the requirement for obtaining parental or guardian permission if it determines and documents the findings under either §46.116(c) or §46.116(d) and that the research is not FDA-regulated. In addition and pursuant to 45 CFR 46.408(c), if the IRB determines that a research study is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children), it may waive the parental permission requirements provided an appropriate mechanism is in place to protect the children, and provided further that the waiver is not inconsistent with federal, state, or local law. The choice of an appropriate substitute mechanism (for example, appointing a child advocate or an assent monitor) for protecting children participating in research would depend upon the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research subjects, and their age, maturity, status, and condition. In addition, the IRB may waive the parental permission requirements in cases involving older adolescents who, under applicable law,
may consent on their own behalf for selected treatments (for example, for venereal disease, drug abuse, or emotional disorders).

2.3.6. The investigator can prospectively request a waiver of parental/guardian permission in the IRB submission.

2.3.7. **Disagreement between a child and his/her parents about research participation.** If a child is capable of assent and the IRB requires that assent be sought, it must be obtained before the child can participate in the research activity. Thus, if the child dissents from participating in research, even if his/her parents or guardian have granted permission, the child’s decision prevails, unless the IRB has waived the assent requirement under §46.408(a). Conversely, if a child assents to participate in research and parental permission has not been waived by the IRB, the permission of the parents or guardian is required before the child can be enrolled in the research.

2.3.8. **When a child reaches the legal age of consent while enrolled in a research study.** When a child who was enrolled in research with parental or guardian permission subsequently reaches the legal age of consent to the procedures involved in ongoing research, the subject’s participation in the research is no longer regulated by the requirements of §46.408 regarding parental or guardian permission and subject assent. As such, unless the IRB determines that the requirements for obtaining informed consent can be waived, the investigators should seek and obtain the legally effective informed consent, as described in §46.116, for the now-adult subject for any ongoing interactions or interventions with the subjects. This is because the prior parental permission and child assent are not equivalent to legally effective informed consent for the now-adult subject. The IRB could, however, approve a waiver of informed consent under §46.116(d), if it finds and documents that the required conditions are met. Similarly, if the research does not involve any ongoing interactions or interventions with the subjects, but continues to meet the regulatory definition of human subjects research (for example, it involves the continued analysis of specimens or data for which the subject’s identity is readily identifiable to the investigator(s)), then it would be necessary for the investigator(s) to seek and obtain the legally effective informed consent of the now-adult subject.

2.3.9. **Wards of the State or Other Agency.** Pursuant to 45 CFR 46.409(a), children who are wards of the state or any other agency, institution, or entity can be included in research approved under §46.406 or §46.407 only if the IRB finds and documents that such research is either:

2.3.9.1. Related to their status as wards; or

2.3.9.2. Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.

2.3.9.3. If the research is approved under §46.409(a), the IRB must require appointment of an advocate for each child who is a ward.
2.3.9.3.1. The advocate will serve in addition to any other individual acting on behalf of the child as guardian or *in loco parentis*.

2.3.9.3.2. One individual may serve as advocate for more than one child.

2.3.9.3.3. The advocate must be an individual who has the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child's participation in the research.

2.3.9.3.4. The advocate must not be associated in any way (except in the role as advocate or member of the IRB) with the research, the investigator(s), or the guardian organization.

2.3.10. Investigator Responsibilities When Involving Children in Research

2.3.10.1. Investigators may not screen for, recruit into, or enroll any child to a research study without prior IRB approval.

2.3.10.2. For studies proposing to enroll such subjects, the investigator must complete the IRB submission. The investigator will make the initial determination regarding the appropriate category in which the research falls, including justification as to why that category was selected. In addition, an explanation regarding how adequate provisions are made for soliciting the assent of the children and the permission (parental/guardian informed consent) of each parent or guardian must be provided.

2.3.10.3. If the IRB grants a waiver of child assent, the investigator must still obtain parental/guardian permission (consent), unless a waiver of parental/guardian permission has also been granted.

2.3.10.4. The investigator may only approach a child-subject to obtain his/her assent to participate in the research after the parents/guardian have given written permission (consent).

2.3.11. IRB Responsibilities When Reviewing Research Involving Children

2.3.11.1. In evaluating the inclusion of children in research, the IRB will consider the protocol-specific findings provided by the investigator in the Children and Child Assent & Parental Consent Process Questionnaires of the KC IRB Protocol and document its determination in the IRB minutes.

2.3.11.2. When the convened IRB reviews research involving children, an individual who is knowledgeable about and experienced in working with this population must be present at the meeting.
2.4. **Additional Protections for Individuals Lacking Consent Capacity.** See the IU HRPP Policy on Adult Individuals Lacking Consent Capacity.

2.5. **Additional Protections for Research Involving Students**

2.5.1. The relationship of teacher and student is inherently one that raises the issue of voluntariness. As such, researchers proposing to enroll their own students into a research project should refer to the specific IU IRB Guidance document.

3. **ADDITIONAL POLICIES AND PROCEDURES**

3.1. **Research Subject to FDA Regulations**

3.1.1. The IRB must follow the requirements specified in Subpart D for research involving children.

3.2. **Research Subject to VA Regulations**

3.2.1. **Additional VA Requirements for Research Involving Pregnant Women, Human Fetuses and Neonates.**

3.2.1.1. Research that involves provision of in vitro fertilization services cannot be conducted by VA investigators while on official duty, or at VA facilities, or at approved off-site facilities. NOTE: Prospective and retrospective studies that enroll or include pregnant subjects who conceived through in vitro fertilization or other artificial reproductive technologies are permitted.

3.2.1.2. Research in which the focus is either a fetus or human fetal tissue in-utero or ex-utero (or uses human fetal tissue) cannot be conducted by VA investigators while on official duty, at VA facilities, or at VA-approved off-site facilities. Use of stem cells shall be governed by the policy set by NIH for recipients of NIH research funding.

3.2.1.3. VA investigators cannot conduct interventions in research that enrolls neonates while on official duty, at VA facilities, or at VA-approved off-site facilities. Prospective observational and retrospective record review studies that involve neonates or neonatal outcomes are permitted.

3.2.1.4. Women who are known to be pregnant and/or their fetuses may be involved in research if all of the requirements of 45 CFR 46.204 are met, including informed consent requirements and the following ethical and scientific criteria:

3.2.1.4.1. Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;
3.2.1.4.2. The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or fetus. If there is no such prospect of benefit, then the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means;

3.2.1.4.3. Any risk is the least possible for achieving the objectives of the research; and

3.2.1.4.4. The VA medical facility Director certifies that the medical facility has sufficient expertise in women’s health to conduct the proposed research.

3.2.2 Additional VA Requirements for Research Involving Prisoners.
Research involving prisoners cannot be conducted by VA investigators while on official duty, at VA facilities, or at VA-approved off-site facilities unless a waiver has been granted by the Chief Research and Development Officer. If the waiver is granted, the research must be in accordance with 45 CFR 46, Subpart C.

3.2.3 Additional VA Requirements for Research Involving Children.

3.2.3.1 Research involving children must be reviewed carefully by the IRB for its relevance to VA and must not be greater than minimal risk. The VA medical facility Director must approve participation in the proposed research that includes children.

3.2.3.2 VA 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.

3.2.3.3 The IRB must have the appropriate expertise to evaluate any VA research involving children and must comply with the requirements of 45 CFR 46.401 – 46.404 and 46.408.

3.2.4 Additional VA Requirements for Research Involving Subjects Lacking Decision-Making Capacity.

3.2.4.1 Criteria for Enrollment. Individuals who lack decision-making capacity (i.e. lack consent capacity) may be enroll in VA research where:

3.2.4.1.1 The IRB determines that the proposed research entails:
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3.2.4.1.1 No greater than minimal risk to the subject; or

3.2.4.1.2 Presents a greater probability of direct benefit to the subject than harm to the subject; or

3.2.4.1.3 Greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject’s disorder or condition that is of vital importance for the understanding or amelioration of the subject’s disorder or condition.

3.2.4.1.2 In addition to satisfying the conditions above, the IRB determines that:

3.2.4.1.2.1 The research cannot be performed solely with persons who possess decision-making capacity and the focus of the research is the disorder leading to the subjects’ lack of decision-making capacity, whether or not the lack of decision-making itself is being evaluated (e.g., an individual who lacks decision-making capacity as the result of a stroke can participate in a study of cardiovascular effects of a stroke); or

3.2.4.1.2.2 The subject of the research is not directly related to the subjects’ lack of decision-making capacity but the investigator has presented a compelling argument for including such subjects (e.g., transmission of methicillin-resistant staphylococcus aureus infections in a nursing home where both individuals with and without decision-making capacity are affected).

3.2.4.2 Determination of Capacity. When planning to enter subjects with impaired decision-making capacity, investigators must address in the protocol how they will determine when surrogate consent (i.e., a LAR) will be required. 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. However, the IRB must review and approve the plan to ensure that it is appropriate given the population and setting of the research. Note: Individuals ruled incompetent by a court of law are considered to lack decision-making capacity.

3.2.4.3 Surrogate consent. 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.

3.2.4.4 Authorized Person. The following persons are authorized to consent on behalf of persons who lack decision-making capacity in the following order of priority in accordance with VA regulations at 38 CFR 17.32(e), (g)(3). Note: Consent for research is required in addition to the consent that is obtained for the patient’s non-research-related treatments and procedures.

3.2.4.4.1 Health care agent (i.e., an individual named by the subject in a Durable Power of Attorney for Health Care);

3.2.4.4.2 Legal guardian or special guardian;

3.2.4.4.3 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

3.2.4.4.4 Close friend.

Note: the persons authorized to consent on behalf of persons who lack decision-making capacity for participation in the research may not necessarily be the same as the persons authorized to provide permission for the use and disclosure of information on a HIPAA authorization on behalf of persons who lack decision-making capacity.

3.2.4.5 Dissent or Assent. If feasible, the investigator must explain the proposed research to the prospective research subject even when the surrogate 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.
3.2.4.6 **Responsibilities of LARs.** LARs are acting on behalf of the potential subjects, therefore:

3.2.4.6.1 LARs must be told that their obligation is to try to determine what the subjects would do if able to make an informed decision.

3.2.4.6.2 If the potential subjects’ wishes cannot be determined, the LARs must be told they are responsible for determining what is in the subjects’ best interest.

3.3 **Research Subject to HIPAA Regulations**

N/A

3.4 **Research Subject to Other Regulations**

3.4.3 **Research Subject to Department of Defense (DoD) Regulations**

3.4.3.1 Research involving prisoners of war (detained persons, as defined in Articles 4 and 5 of the Geneva Convention) is prohibited.

3.4.3.2 Research involving prisoners cannot be reviewed by the expedited procedure.

3.4.3.3 If consent is to be obtained from a subject’s LAR, the research must intend to benefit the individual subject. The determination that research is intended to be beneficial to the individual subject must be made by an IRB.

3.4.3.4 At least one prisoner representative must be present for a quorum when the IRB reviews research involving prisoners.

3.4.3.5 In addition to allowable categories of research on prisoners in Subpart C, epidemiological research is also allowable when:

3.4.3.5.1 The research describes the prevalence or incidence of a disease by identifying all cases or studies potential risk factor association for a disease;

3.4.3.5.2 The research presents no more than minimal risk;

3.4.3.5.3 The research presents no more than an inconvenience to the subject.

3.4.4 **Research Subject to Department of Education (ED) Regulations.**
Research involving access to educational records must comply with the Family Educational Rights and Privacy Act (FERPA). Please refer to the specific IU IRB Guidance document for additional information.

When the IRB reviews research funded by the National Institute on Disability and Rehabilitation Research (NIDRR) that purposefully requires inclusion of children with disabilities or individuals with mental disabilities, the IRB will include at least one person primarily concerned with the welfare of these research subjects.

In compliance with the Protection of Pupil Rights Amendment (PPRA), no student will be required, as part of any research project, to submit without prior consent to surveys; psychiatric examination, testing, or treatment; or psychological examination, testing, or treatment in which the primary purpose is to reveal information concerning one or more of the following:

- Political affiliations or beliefs of the student or the student’s parent.
- Mental or psychological problems of the student or the student’s family.
- Sex behavior or attitudes.
- Illegal, anti-social, self-incriminating, or demeaning behavior.
- Critical appraisals of other individuals with whom respondents have close family relationships.
- Legally recognized privileged or analogous relationships, such as those of lawyers, physicians, and ministers.
- Religious practices, affiliations, or beliefs of the student or student’s parent.
- Income (other than that required by law to determine eligibility for participation in a program or for receiving financial assistance under such program).

Note: The Department of Education defines parent as including natural parents, a guardian, or an individual acting as a parent in the absence of a parent or guardian (34 CFR 99.3). Prior consent refers to prior consent of the student, if the student is an adult or emancipated minor, or to prior written consent of the parent/guardian, if the student is not an emancipated minor (34 CFR 303.314).
3.4.4.4 For certain types of research projects not directly funded by ED and conducted in a school that receives funding from ED, policies and procedures include a process to verify compliance with ED regulations that schools are required to develop and adopt policies in conjunction with parents regarding:

3.4.4.4.1 The right of a parent of a student to inspect, upon the request of the parent, a survey created by a third party before the survey is administered or distributed by a school to a student.

3.4.4.4.1.1 Any applicable procedures for granting a request by a parent for reasonable access to such survey within a reasonable period of time after the request is received.

3.4.4.4.2 Arrangements to protect student privacy that are provided by the agency in the event of the administration or distribution of a survey to a student containing one or more of the following items (including the right of a parent of a student to inspect, upon the request of the parent, any survey containing one or more of such items):

3.4.4.4.2.1 Political affiliations or beliefs of the student or the student’s parent.

3.4.4.4.2.2 Mental or psychological problems of the student or the student’s family.

3.4.4.4.2.3 Sex behavior or attitudes.

3.4.4.4.2.4 Illegal, anti-social, self-incriminating, or demeaning behavior.

3.4.4.4.2.5 Critical appraisals of other individuals with whom respondents have close family relationships.

3.4.4.4.2.6 Legally recognized privileged or analogous relationships, such as those of lawyers, physicians, and ministers.

3.4.4.4.2.7 Religious practices, affiliations, or beliefs of the student or the student’s parent.

3.4.4.4.2.8 Income (other than that required by law to determine eligibility for
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3.4.4.3 The right of a parent of a student to inspect, upon the request of the parent, any instructional material used as part of the educational curriculum for the student.

3.4.4.4 The administration of physical examinations or screenings that the school or agency may administer to a student.

3.4.4.5 The collection, disclosure, or use of personal information collected from students for the purpose of marketing or for selling that information (or otherwise providing that information to others for that purpose), including arrangements to protect student privacy that are provided by the agency in the event of such collection, disclosure, or use.

3.4.5 Research Subject to Department of Justice (DOJ) Regulations

3.4.5.1 For research conducted with the Bureau of Prisons (BOP), the requirements of 28 CFR 512 must be followed, including:

3.4.5.1.1 The research must not involve medical experimentation, cosmetic research, or pharmaceutical testing.

3.4.5.1.2 The research design must be compatible with both the operation of prison facilities and protection of human participation in a program or for receiving financial assistance under such a program).
subjects. The researcher must observe the rules of the institution or office in which the research is conducted.

3.4.5.1.3 Any researcher who is a non-employee of the Bureau must sign a statement in which the researcher agrees to adhere to the provisions of 28 CFR 512.

3.4.5.1.4 All research proposals will be reviewed by the Bureau Research Review Board.

3.4.5.1.5 For additional information regarding research applications to the BOP, see Steps to Submit a Research Proposal.

3.4.5.1.6 Implementation of Bureau programmatic or operational initiatives made through pilot projects are not considered to be research.
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Pursuant to 45 CFR 46.111, the IRB must determine that specific requirements are satisfied in order to approve research with human subjects. One such requirement is that the selection of subjects is equitable (§46.111(a)(3)). In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, students, individuals lacking consent capacity, economically or educationally disadvantaged persons, persons with limited treatment options, and persons with increased susceptibility to harm including economic, social, or legal consequences from the study. Because of the special vulnerability of these populations, the federal regulations, state and local laws, and institutional policies require additional protections for these individuals.

POLICIES AND PROCEDURES

2.1. Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research (Subpart B)

2.1.1. Research involving women who are or may become pregnant should receive special attention from the IRB because of women’s additional health concerns during pregnancy and because of the need to avoid unnecessary risk to the fetus. Further, in the case of a pregnant woman, the IRB must determine when informed consent of the father is required for the research. Special attention is justified because of the involvement of a third party (the fetus) who may be affected but cannot give consent and because of the need to prevent harm or injury to future members of society.

2.1.2. Research Involving Pregnant Women or Human Fetuses. Pursuant to 45 CFR 46.204, pregnant women or human fetuses may be involved in research if all of the following conditions are met:

2.1.2.1. Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on nonpregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;

2.1.2.2. The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important generalizable knowledge that cannot be obtained by any other means;
2.1.2.3. Any risk is the least possible for achieving the objectives of the research;

2.1.2.4. If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important generalizable knowledge that cannot be obtained by any other means, her consent is obtained in accord with the informed consent provisions of 45 CFR 46, Subpart A;

2.1.2.5. If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accord with the informed consent provisions of 45 CFR 46, Subpart A, except that the father’s consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity, or if the pregnancy resulted from rape or incest.

2.1.2.6. Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;

2.1.2.7. For children as defined in §46.402(a) who are pregnant, assent and permission are obtained in accord with the provisions of 45 CFR 46, Subpart D;

2.1.2.8. No inducements, monetary or otherwise, will be offered to terminate a pregnancy;

2.1.2.9. Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and

2.1.2.10. Individuals engaged in the research will have no part in determining the viability of a neonate.

2.1.3. Research Involving Neonates. Pursuant to 45 CFR 205(a), neonates of uncertain viability and nonviable neonates may be involved in research if all of the following conditions are met:

2.1.3.1. Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.

2.1.3.2. Each individual providing consent under §46.205(b)(2) or §46.205(c)(5) is fully informed regarding the reasonably foreseeable impact of the research on the neonate.

2.1.3.3. Individuals engaged in the research will have no part in determining the viability of a neonate.
2.1.3.4. The requirements of §46.205(b) or §46.205(c) have been met as applicable.

2.1.4. Pursuant to 45 CFR 46.205(b), until it has been ascertained whether a neonate is viable, a neonate may not be involved in research covered by Subpart A of 45 CFR 46 unless the following additional conditions have been met:

2.1.4.1. The IRB determines that: (a) the research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective, or (b) the purpose of the research is the development of important generalizable knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research; and

2.1.4.2. The legally effective informed consent of either parent of the neonate or, if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent’s legally authorized representative (LAR) is obtained in accord with subpart A of 45 CFR 46, except that the consent of the father or his LAR need not be obtained if the pregnancy resulted from rape or incest.

2.1.5. **Research Involving Nonviable Neonates.** Pursuant to 45 CFR 46.205(c), after delivery, a nonviable neonate may not be involved in research covered by Subpart A of 45 CFR 46 unless all of the following additional conditions are met:

2.1.5.1. Vital functions of the neonate will not be artificially maintained;

2.1.5.2. The research will not terminate the heartbeat or respiration of the neonate;

2.1.5.3. There will be no added risk to the neonate resulting from the research;

2.1.5.4. The purpose of the research is the development of important generalizable knowledge that cannot be obtained by other means; and

2.1.5.5. The legally effective informed consent of both parents of the neonate is obtained in accord with subpart A of 45 CFR 46, except that the waiver and alteration provisions of §46.116(c) and (d) do not apply. However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable neonate will suffice to meet the requirements of this paragraph (c)(5), except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest. The IRB cannot approve the consent of an LAR for a nonviable neonate.

2.1.6. Pursuant to 45 CFR 46.205(d), a neonate, after delivery, that has been determined to be viable may be included in research only to the extent permitted by and in accord with the requirements of 45 CFR 46, Subparts A and D.
2.1.7. Pursuant to 45 CFR 46.206, research involving, after delivery, the placenta; the dead fetus; macerated fetal material; or cells, tissue, or organs excised from a dead fetus shall be conducted only in accord with any applicable federal, state, or local laws and regulations regarding such activities. If information associated with the material is recorded for research purposes in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research subjects and all pertinent subparts of this part are applicable.

2.1.8. In evaluating the inclusion of pregnant women, human fetuses, and neonates in research, the IRB will consider the protocol-specific findings provided by the investigator in the Pregnant Women, Fetuses, Neonates Questionnaire in the KC Protocol and document its determination in the IRB minutes.

2.1.9. Pursuant to 45 CFR 46.207, the Secretary will conduct or fund research that the IRB does not believe meets the requirements of §46.204 or §46.205 only if:

2.1.9.1. The IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates; and

2.1.9.2. The Secretary, after consultation with a panel of experts in pertinent disciplines (e.g., science, medicine, ethics, law) and following opportunity for public review and comment, including a public meeting announced in the Federal Register, has determined either (a) That the research in fact satisfies the conditions of §46.204, as applicable; or (b) The following: (i) The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates; (ii) The research will be conducted in accord with sound ethical principles; and (iii) Informed consent will be obtained in accord with the informed consent provisions of subpart A and other applicable subparts of this part.

2.1.10. **Research in which Pregnancy Is Coincidental to Subject Population.** Any research in which women of childbearing potential are possible subjects may inadvertently include women already pregnant or women who may become pregnant. HHS regulations, specifically 45 CFR 46.116(b)(1), require that, when appropriate, the informed consent document include a statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) that are currently unforeseeable. The IRB must then judge whether the mother’s participation would pose any risk to the fetus or nursing infant. In some studies, the IRB may need to ensure that nonpregnant subjects are advised to avoid pregnancy or nursing for a time during or following the research. Furthermore, where appropriate, subjects should be advised to notify the investigator immediately should they become pregnant. In some instances there may be potential risk...
sufficient to justify requiring that pregnant women either be specifically excluded from the research or studied separately.

2.1.11. Investigator Responsibilities When Involving Pregnant Women, Human Fetuses, and/or Neonates in Research

2.1.11.1. When research proposes to enroll pregnant women, human fetuses, or neonates, the investigator must obtain approval from the IRB before any such subjects may be enrolled in the research.

2.1.11.2. For a new study proposing to enroll such subjects, the investigator must complete and submit the Pregnant Women, Fetuses, Neonates Questionnaire in the KC IRB Protocol with the new study application.

2.1.11.3. For an existing study proposing to enroll such subjects, the investigator must submit an amendment along with the completed Pregnant Women, Fetuses, Neonates Questionnaire in the KC IRB Protocol.

2.2. Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects (Subpart C)

2.2.1. Pursuant to 45 CFR 46.306(a)(2), federally funded biomedical or behavioral research may involve prisoners as subjects only if the IRB determines that the proposed research involves one or more of the following:

2.2.1.1. Study of the possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;

2.2.1.2. Study of prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;

2.2.1.3. Research on conditions particularly affecting prisoners as a class (for example, vaccine trials and other research on hepatitis, which is much more prevalent in prisons than elsewhere; and research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults) provided that the study may proceed only after the Secretary has consulted with appropriate experts including experts in penology, medicine, and ethics, and published notice in the Federal Register of the intent to approve such research; or

2.2.1.4. Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subjects. In cases in which those studies require the assignment of prisoners in a manner consistent with studies approved by the IRB to control groups that may not benefit from the research, the study may proceed only after the Secretary has consulted with appropriate experts, including experts in penology, medicine, and ethics, and
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published notice in the Federal Register of the intent to approve such research.

2.2.2. Per notice in the federal register, the requirement that the research represent one of the categories of research permissible under 45 CFR 306(a)(2) may be waived when DHHS conducts or supports certain important and necessary epidemiologic research on prisoners that meet the following criteria:

2.2.2.1. In which the sole purposes are (i) to describe the prevalence or incidence of a disease by identifying all cases, or (ii) to study the potential risk factor associations for a disease; and

2.2.2.2. Where the institution responsible for the conduct of research certifies to the Office of Human Research Protections, DHHS, acting on behalf of the Secretary, that the IRB approved the research and fulfilled its duties under 45 CFR 46.305(a)(2)-(7) and determined and documented that:

2.2.2.2.1. The research presents no more than minimal risk and no more than inconvenience to the prisoner-subjects, and

2.2.2.2.2. Prisoners are not a particular focus of the research.

2.2.3. The exemptions outlined at 45 CFR 46.101(b) do not apply to prisoners.

2.2.4. Additional Duties of the Institutional Review Boards. In addition to all other responsibilities under 45 CFR 46, the IRB shall review and approve research involving prisoners only if it finds that:

2.2.4.1. For federally funded research, the research represents one of the categories of research permissible under §46.306(a)(2) or waiver of this requirement is appropriate per 2.2.2 above;

2.2.4.2. Any possible advantages accruing to the prisoner through his/her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities, and opportunity for earnings in the prison, are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired;

2.2.4.3. The risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers;

2.2.4.4. Procedures for the selection of subjects within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the Principal Investigator provides to the IRB justification in writing for following some other procedures, control subjects must be selected randomly from the group of available prisoners who meet the characteristics needed for that particular research project;
2.2.4.5. The information is presented in language understandable to the subject population;

2.2.4.6. Adequate assurance exists that parole boards will not take into account a prisoner’s participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have no effect on his/her parole;

Where the IRB finds there may be a need for follow-up examination or care of subjects after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoners’ sentences, and for informing subjects of this fact; and

2.2.4.7. The investigators and the study team are appropriately qualified to work and interact with prisoners, based on previous research experience, academic preparation, and/or relevant training and oversight by the PI.

2.2.4.8. In evaluating the inclusion of prisoners in research, the IRB will consider the protocol-specific findings provided by the investigator in the Prisoners Questionnaire of the KC Protocol and document its determination in the IRB minutes.

2.2.5. Additional Considerations When Research Proposes to Involve Prisoners.

2.2.5.1. When a prisoner is also a child (e.g., an adolescent detained in a juvenile detention facility), appropriate additional requirements must be satisfied for the inclusion of children in research as outlined below.

2.2.6. Composition of the IRB Where Prisoners Are Involved. Pursuant to 45 CFR 46.304, in addition to satisfying the requirements in 45 CFR 46.107, an IRB that regularly reviews research involving prisoners shall include one or more individuals who are knowledgeable about and experienced in working with this population to serve as a voting IRB member. The composition of the IRB must satisfy the following requirements found at 45 CFR 46.304(a) and (b):

2.2.6.1. A majority of the IRB (exclusive of prisoner members) shall have no association with the prison(s) involved, apart from their membership on the IRB; and

2.2.6.2. At least one member of the IRB must be a prisoner, or a prisoner representative with appropriate background and experience to serve in that capacity, except that where a particular research project is reviewed by more than one IRB only one IRB need satisfy this requirement.

2.2.6.3. In the absence of choosing someone who is a prisoner or has been a prisoner, the IRB will choose a prisoner representative who has a close working knowledge, understanding, and appreciation of prison...
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conditions from the perspective of a prisoner. Suitable individuals could include prison chaplains; prison psychologists, prison social workers, or other prison service providers; persons who have conducted advocacy for the rights of prisoners; or any individuals who are qualified to represent the rights and welfare of prisoners by virtue of appropriate background and experience.

2.2.7. When the convened IRB reviews research involving prisoners (including initial review, continuing review, amendments, and reportable events), the prisoner representative, who is a voting member, must receive all materials pertaining to the research (i.e., the same information as the primary reviewer) and be present at the meeting. If the prisoner representative is not present (either in person or via telephone or video conferencing), research involving prisoners cannot be reviewed or approved.

2.2.8. Expedited Review of Research Involving Prisoners

2.2.8.1. Expedited review of research involving interaction with prisoners is allowed only when a determination is made by the primary IRB reviewer and the prisoner representative that the research is minimal risk for the prison population being studied or included.

2.2.8.2. Expedited review of research with prisoners that does not involve interaction with prisoners (i.e., research involving existing data or record review) is allowed only when a determination is made by the primary reviewer that the research poses minimal risk for the prison population being studied or included.

2.2.9. Modifications to Previously Approved Research Involving Prisoners

2.2.9.1. Substantial modifications to research requiring review by the convened IRB and involving prisoners (i.e., Major Amendments) must be reviewed by the convened IRB using the same procedures for initial review, including the responsibility of the prisoner representative.

2.2.9.2. Minor modifications (i.e., Minor Amendments) may be reviewed using the expedited procedure referenced above in Sections 2.2.7.

2.2.10. Continuing Review of Research Involving Prisoners

2.2.10.1. Continuing review of research requiring review by the convened IRB and involving prisoners must be reviewed by the convened IRB using the same procedures for initial review, including the responsibility of the prisoner representative.

2.2.10.2. Continuing review of research involving prisoners may be reviewed using the expedited procedure referenced under Modifications to Previously Approved Research Involving Prisoners, above.
2.2.11. Additional Requirements for Conducting Research Within the Indiana Department of Corrections (DOC) Facility

2.2.11.1. Research with human subjects involving medical testing, chemical, experimental drugs, etc., is prohibited by the DOC’s Health Care Services Directives.

2.2.11.2. Pursuant to 210 IAC 1-6-7, all requests for access to offender or juvenile records for research purposes shall be made to the director of planning services in written form. Such requests shall include the name of the agency or organization performing the research and the names of the persons directly responsible for the following:

2.2.11.2.1. Conducting such research.

2.2.11.2.2. The purpose of such research.

2.2.11.2.3. How the research is to be performed.

2.2.11.2.4. What measures will be taken to assure the proper protection of classified information.

2.2.11.3. Approval of such requests will be granted or denied consistent with provisions of 210 IC 4-1-6-8.6 and department procedures.

2.2.11.4. Note that other states may have similar or additional requirements.

2.2.12. Investigator Responsibilities When Involving Prisoners in Research

2.2.12.1. Investigators may not screen for, recruit into, or enroll any individual involuntarily confined or detained in a penal institution to a research study without prior IRB approval.

2.2.12.2. Investigators are responsible for obtaining and providing documentation to the IRB of approval from detention or correctional facilities involved in the research.

2.2.12.3. For a new study proposing to enroll such subjects, the investigator must complete the Prisoners Questionnaire of the KC IRB Protocol.

2.2.12.4. For an existing study proposing to enroll such subjects, the investigator must submit an amendment along with completing the Prisoners Questionnaire of the KC IRB Protocol.

2.2.13. Procedures When a Current Subject Becomes a Prisoner During the Research

2.2.13.1. When a human subject involved in ongoing research becomes a prisoner during the course of the study, and the relevant research study was not previously approved by the IRB for the inclusion of prisoners,
the investigator must promptly notify the IRB. Additionally, all research interactions and interventions with, and obtaining identifiable private information about, the now-incarcerated prisoner-subject must be suspended immediately, except as noted below.

2.2.13.2. If the investigator wishes to have the prisoner-subject continue to participate in the research, the IRB must promptly re-review the proposal in accordance with the requirements of Subpart C (for federally funded research). The investigator must submit to the IRB:

2.2.13.2.1. Notification that a previously enrolled research subject has become a prisoner;

2.2.13.2.2. An amendment requesting the inclusion of prisoners; and

2.2.13.2.3. A completed Prisoners Questionnaire in the KC IRB Protocol.

2.2.13.3. The IRB review must occur at a convened IRB meeting.

2.2.13.4. **Exception**: The federal regulations allow for one important exception to the requirement that all research interactions or interventions with, and obtaining identifiable information about, the now-incarcerated prisoner-subject must cease until the regulatory requirements for research involving prisoners are met. In special circumstances in which the investigator asserts that it is in the best interest of the prisoner-subject to continue to receive interactions or interventions and/or for the investigator to obtain private identifiable information from the prisoner-subject in the research study while he/she is incarcerated, the IRB Chair may determine that the prisoner-subject may continue to participate in the research until the above requirements are met. The investigator must promptly notify the IRB of this occurrence, so that the IRB can re-review the study.

2.2.13.5. IRB review and approval are not required if research interactions and interventions or obtaining of identifiable private information will not occur during the incarceration period.

2.2.14. **Additional Requirements for Research Conducted or Supported by HHS that Involves Prisoners.** Pursuant to 45 CFR 46.306(a), biomedical or behavioral research conducted or support by HHS may involve prisoners as subjects only if:

2.2.14.1. The institution has certified to the Secretary that the IRB has approved the research under §46.305.

2.2.14.2. In the judgment of the Secretary the proposed research involves solely one of the permitted categories of research involving prisoners listed under 45 CFR 46.306(a)(2); or
2.2.14.3. Research involves epidemiologic studies that meet the following criteria:

2.2.14.3.1. The sole purposes of the research are one of the following: (a) to describe the prevalence or incidence of a disease by identifying all cases; or (b) to study potential risk factor associations for a disease.

2.2.14.3.2. The institution certifies to the Office for Human Research Protections (OHRP) that the IRB approved the research and fulfilled its duties under 45 CFR 46.305(a)(2)-(7) and determined and documented that: (a) the research presents no more than minimal risks and no more than inconvenience to the prisoner-subjects; and (b) prisoners are not a particular focus of the research.

2.2.14.4. Except as provided in §46.306, biomedical and behavioral research conducted or supported by HHS shall not involve prisoners as subjects.

2.3. Additional Protections for Children Involved as Subjects in Research (Subpart D)

2.3.1. Exemptions at §46.101(b)(1) and (b)(3) through (b)(6) are applicable to this subpart. The exemption at §46.101(b)(2) regarding educational tests is also applicable to this subpart. However, the exemption at §46.101(b)(2) for research involving survey or interview procedures or observations of public behavior does not apply to research covered by this subpart, except for research involving observation of public behavior when the investigator(s) does not participate in the activities being observed.

2.3.2. Pursuant to 45 CFR 46, Subpart D and 21 CFR 50, Subpart D, the IRB can approve federally funded research involving children as research subjects only when it satisfies the conditions outlined below.

2.3.2.1. 45 CFR 46.404. Research not involving greater than minimal risk.
To approve research in this category, the IRB must find and document the following determinations:

2.3.2.1.1. the research presents no more than minimal risk to the children; and

2.3.2.1.2. adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth at §46.408.

2.3.2.2. 45 CFR 46.405. Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects.
To approve research in this category, the IRB must find and document the following determinations:
2.3.2.2.1. the research presents more than minimal risk to the children by an intervention or procedure that holds out the prospect of direct benefit for the individual subject, or by a monitoring procedure that is likely to contribute to the subject’s well-being;

2.3.2.2.2. the risk is justified by the anticipated benefits to the subjects;

2.3.2.2.3. the relation of the anticipated benefit to the risk presented by the study is at least as favorable to the subjects as that provided by available alternative approaches; and

2.3.2.2.4. adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth at §46.408.

2.3.2.3. 45 CFR 46.406. Research involving greater than minimal risk and no prospect of direct benefit to the individual subjects, but likely to yield generalizable knowledge about the subject’s disorder or condition. To approve research in this category, the IRB must find and document the following determinations:

2.3.2.3.1. the research presents a minor increase over minimal risk by an intervention or procedure that does not hold out the prospect of direct benefit for the individual subject, or by a monitoring procedure that is not likely to contribute to the well-being of the subject;

2.3.2.3.2. the intervention or procedure presents experiences to the subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations;

2.3.2.3.3. the intervention or procedure is likely to yield generalizable knowledge about the subjects’ disorder or condition of vital importance for the understanding or amelioration of the subjects’ disorder or condition; and

2.3.2.3.4. adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth at §46.408.

2.3.2.4. A fourth category of research requires a special level of HHS review under 45 CFR 46.407 beyond that provided by the IRB: Research not otherwise approvable (i.e., the research does not meet the conditions of §46.404, §46.405, or §46.406) that presents an opportunity to further understand, prevent, or alleviate a serious problem affecting the health
or welfare of children. Research in this category may be conducted only if:

2.3.2.4.1. The IRB believes that the research does not meet the requirements of §46.404, §46.405, or §46.406 but finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; and

2.3.2.4.2. The Secretary, HHS or his/her designee, after consulting with a panel of experts in pertinent disciplines (e.g., science, medicine, education, ethics, law) and following an opportunity for public review and comment, determines either:

2.3.2.4.2. that the research in fact satisfies the conditions of §46.404, §46.405, or §46.406; or

2.3.2.4.2. the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; the research will be conducted in accordance with sound ethical principles; and adequate provisions are made for soliciting the assent of children and the permission of their parents or legal guardians as set forth in §46.408.

2.3.3. Adequate provisions for soliciting the assent of children. Pursuant to 45 CFR 46.408(a) and 21 CFR 50.55(a), the IRB shall determine and document that adequate provisions are made for soliciting the assent of the children, when in the judgment of the IRB the children are capable of providing assent.

2.3.3.1. In determining whether children are capable of assenting, the IRB shall take into account the ages, maturity, psychological status, and health condition of the children involved. Assents may apply to all or some of the children involved in the research. In general, the IRB will require assent from children ages seven (7) to seventeen (17); however, the IRB acknowledges there are situations in which it may be appropriate for younger children, depending on their aptitude/ability to provide assent. Alternatively, there may be situations in which older children with higher cognitive ability may be able to read, understand, and subsequently sign the adult consent document. In these instances, the investigator must prospectively justify this scenario in the IRB submission and make the necessary changes to the informed consent document (for example, the inclusion of "you/your child" language and a child signature line).


2.3.3.2. The assent of the children is not required if the IRB determines that either of the following is true:

2.3.3.2.1. the children are not capable of providing assent based on their age, maturity, or psychological state; or

2.3.3.2.2. the capability of the children is so limited that they cannot reasonably be consulted.

2.3.3.3. Even when children are capable of providing assent, there are circumstances in which it may be appropriate for the IRB to waive assent. The IRB can waive assent if either of the following criteria is satisfied:

2.3.3.3.1. The intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and available only in the context of the research (45 CFR 46.408); or

2.3.3.3.2. The study meets the criteria for waiver of informed consent under 45 CFR 46.116(d).

- Research does not involve more than minimal risk to subjects.
- The waiver will not adversely affect the rights and welfare of the subjects.
- The research could not be practicably carried out without the waiver.
- When appropriate, subjects will be provided with additional pertinent information after participation.
- The research is not FDA-regulated.

2.3.3.4. The investigator can prospectively request a waiver of assent for some or all children in the IRB submission.

2.3.3.5. When the IRB approves a waiver of assent for some or all children, it will determine which children are not required to assent.

2.3.3.6. Even where the IRB approves a waiver of child assent, an age-appropriate information sheet may still need to be given to the child-subjects.

2.3.3.7. When the IRB determines that assent is required, it shall determine whether and how assent must be documented.
2.3.4. **Adequate provisions for soliciting the permission of each child’s parents or guardian.** Pursuant to 45 CFR 46.408(b), the IRB shall determine and document, in accordance with and to the extent that consent is required by §46.116 of Subpart A, that adequate provisions are made for soliciting the permission of each child’s parents or guardian.

2.3.4.1. Where parental permission is to be obtained, the IRB may find that the permission of one parent is sufficient for research to be conducted under §46.404 or §46.405.

2.3.4.1.1. Although the regulations allow permission of only one parent or guardian for research conducted under §46.404 or §46.405, the IRB must determine that the permission of one parent or guardian is sufficient. For example, it may be inappropriate to allow permission of only one parent or guardian in a standard therapeutic trial for childhood cancer where the researcher has time to obtain permission from both parents, unless one is deceased, unknown, incompetent, or not reasonably available, or when only one parent or guardian has legal responsibility for the care and custody of the child, just because the research is conducted under §46.404 or §46.405.

2.3.4.2. Where research is covered by §46.406 and §46.407 and permission is to be obtained from parents, both parents must give their permission unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.

2.3.4.3. Permission by parents or guardians shall be documented in accordance with and to the extent required by §46.117, Documentation of informed consent.

2.3.5. **Waiver of parental or guardian permission.** The IRB may waive the requirement for obtaining parental or guardian permission if it determines and documents the findings under either §46.116(c) or §46.116(d) and that the research is not FDA-regulated. In addition and pursuant to 45 CFR 46.408(c), if the IRB determines that a research study is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children), it may waive the parental permission requirements provided an appropriate mechanism is in place to protect the children, and provided further that the waiver is not inconsistent with federal, state, or local law. The choice of an appropriate substitute mechanism (for example, appointing a child advocate or an assent monitor) for protecting children participating in research would depend upon the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research subjects, and their age, maturity, status, and condition. In addition, the IRB may waive the parental permission requirements in cases involving older adolescents who, under applicable law,
may consent on their own behalf for selected treatments (for example, for venereal disease, drug abuse, or emotional disorders).

2.3.6. The investigator can prospectively request a waiver of parental/guardian permission in the IRB submission.

2.3.7. **Disagreement between a child and his/her parents about research participation.** If a child is capable of assent and the IRB requires that assent be sought, it must be obtained before the child can participate in the research activity. Thus, if the child dissents from participating in research, even if his/her parents or guardian have granted permission, the child’s decision prevails, unless the IRB has waived the assent requirement under §46.408(a). Conversely, if a child assents to participate in research and parental permission has not been waived by the IRB, the permission of the parents or guardian is required before the child can be enrolled in the research.

2.3.8. **When a child reaches the legal age of consent while enrolled in a research study.** When a child who was enrolled in research with parental or guardian permission subsequently reaches the legal age of consent to the procedures involved in ongoing research, the subject’s participation in the research is no longer regulated by the requirements of §46.408 regarding parental or guardian permission and subject assent. As such, unless the IRB determines that the requirements for obtaining informed consent can be waived, the investigators should seek and obtain the legally effective informed consent, as described in §46.116, for the now-adult subject for any ongoing interactions or interventions with the subjects. This is because the prior parental permission and child assent are not equivalent to legally effective informed consent for the now-adult subject. The IRB could, however, approve a waiver of informed consent under §46.116(d), if it finds and documents that the required conditions are met. Similarly, if the research does not involve any ongoing interactions or interventions with the subjects, but continues to meet the regulatory definition of human subjects research (for example, it involves the continued analysis of specimens or data for which the subject’s identity is readily identifiable to the investigator(s)), then it would be necessary for the investigator(s) to seek and obtain the legally effective informed consent of the now-adult subject.

2.3.9. **Wards of the State or Other Agency.** Pursuant to 45 CFR 46.409(a), children who are wards of the state or any other agency, institution, or entity can be included in research approved under §46.406 or §46.407 only if the IRB finds and documents that such research is either:

2.3.9.1. Related to their status as wards; or

2.3.9.2. Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.

2.3.9.3. If the research is approved under §46.409(a), the IRB must require appointment of an advocate for each child who is a ward.
Section II: SOPs/Policies

Standard Operating Procedures for Research Involving Human Subjects

2.3.9.3.1. The advocate will serve in addition to any other individual acting on behalf of the child as guardian or in loco parentis.

2.3.9.3.2. One individual may serve as advocate for more than one child.

2.3.9.3.3. The advocate must be an individual who has the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child's participation in the research.

2.3.9.3.4. The advocate must not be associated in any way (except in the role as advocate or member of the IRB) with the research, the investigator(s), or the guardian organization.

2.3.10. Investigator Responsibilities When Involving Children in Research

2.3.10.1. Investigators may not screen for, recruit into, or enroll any child to a research study without prior IRB approval.

2.3.10.2. For studies proposing to enroll such subjects, the investigator must complete the IRB submission. The investigator will make the initial determination regarding the appropriate category in which the research falls, including justification as to why that category was selected. In addition, an explanation regarding how adequate provisions are made for soliciting the assent of the children and the permission (parental/guardian informed consent) of each parent or guardian must be provided.

2.3.10.3. If the IRB grants a waiver of child assent, the investigator must still obtain parental/guardian permission (consent), unless a waiver of parental/guardian permission has also been granted.

2.3.10.4. The investigator may only approach a child-subject to obtain his/her assent to participate in the research after the parents/guardian have given written permission (consent).

2.3.11. IRB Responsibilities When Reviewing Research Involving Children

2.3.11.1. In evaluating the inclusion of children in research, the IRB will consider the protocol-specific findings provided by the investigator in the Children and Child Assent & Parental Consent Process Questionnaires of the KC IRB Protocol and document its determination in the IRB minutes.

2.3.11.2. When the convened IRB reviews research involving children, an individual who is knowledgeable about and experienced in working with this population must be present at the meeting.
2.4. **Additional Protections for Individuals Lacking Consent Capacity.** In the absence of evidence to the contrary, it is assumed that adults have the capacity to provide informed consent to participate in research. However, certain groups of individuals may be suspected of lacking consent capacity such that they cannot provide informed consent for themselves and consent from a legally authorized representative is needed. These include persons under the influence of drugs or alcohol, sedated or unresponsive, suffering from a clinical illness or traumatic brain disorder or dementia, or who have evidence of history of psychiatric illness or disorder or a recent psychotic event, among others.

2.4.1. Consent capacity is demonstrated by the individual’s ability to:

2.4.1.1. understand the nature of the research and of his/her participation;

2.4.1.2. appreciate the consequences of the participation;

2.4.1.3. show the ability to consider alternatives, including the option not to participate; and

2.4.1.4. show the ability to make a reasoned choice.

2.4.2. When research proposes involving individuals who may lack consent capacity, potential subjects should be assessed prior to obtaining informed consent to ensure consent capacity exists. Investigators should propose an appropriate plan for assessing consent capacity of potential subjects, as well as a plan for obtaining consent from the individual’s legally authorized representative and assent from the potential subject, when appropriate.

2.4.3. **IRB Responsibilities When Reviewing Research Involving Individuals Lacking Consent Capacity.**

2.4.3.1. In addition to satisfying the requirements in 45 CFR 46.107, an IRB that regularly reviews research involving individuals lacking consent capacity shall consider the inclusion of one or more individuals who are knowledgeable about and experienced in working with this population to serve as a voting IRB member. However, to fulfill this requirement, the IRB may invite consultants (i.e., non-voting individuals) to assist in the review of issues related to this subject population.

2.4.3.2. When the convened IRB reviews research involving individuals lacking consent capacity (including initial review, continuing review, amendments, and reportable events), an individual who is knowledgeable about and experienced in working with this subject population must be present at the meeting.

2.4.3.3. When the convened IRB reviews research involving individuals lacking consent capacity, it must find and document:
2.4.3.3.1. That appropriate provisions are made for assessing the potential subject’s consent capacity, including the process for ongoing assessment of consent capacity and willingness to participate. The consent procedures should describe a plan for assessing and protecting individuals who may lose consent capacity while participating in research activities. The IRB may waive consent requirements pursuant to §46.116 of Subpart A, General requirements for informed consent.

2.4.3.3.2. When the potential subject lacks consent capacity, that appropriate provisions are made for obtaining informed consent from the individual’s LAR and obtaining assent from the subject, when appropriate.

2.4.3.4. Because of the obvious vulnerability of inpatient psychiatric subjects, additional safeguards must be considered and applied. The IRB must consider the rationale and justification for involvement of inpatient psychiatric subjects and ensure that additional safeguards will be implemented to protect subjects from potential coercion or undue influence.

2.4.3.5. In evaluating the inclusion of individuals lacking consent capacity, the IRB will consider the protocol-specific information provided by the investigator in the KC IRB Questionnaire and document its determinations in the IRB minutes or the Reviewer Checklist.

2.5. Additional Protections for Research Involving Students

2.5.1. The relationship of teacher and student is inherently one that raises the issue of voluntariness. As such, researchers proposing to enroll their own students into a research project should refer to the specific IU IRB Guidance document.

3. ADDITIONAL POLICIES AND PROCEDURES

3.1. Research Subject to FDA Regulations

3.1.1. The IRB must follow the requirements specified in Subpart D for research involving children.

3.2. Research Subject to VA Regulations

3.2.1. Additional VA Requirements for Research Involving Pregnant Women, Human Fetuses and Neonates.

3.2.1.1. Research that involves provision of in vitro fertilization services cannot be conducted by VA investigators while on official duty, or at VA facilities, or at approved off-site facilities. NOTE: Prospective and retrospective studies that enroll or include pregnant subjects who
conceived through in vitro fertilization or other artificial reproductive technologies are permitted.

3.2.1.2. Research in which the focus is either a fetus or human fetal tissue in-utero or ex-utero (or uses human fetal tissue) cannot be conducted by VA investigators while on official duty, at VA facilities, or at VA-approved off-site facilities. Use of stem cells shall be governed by the policy set by NIH for recipients of NIH research funding.

3.2.1.3. VA investigators cannot conduct interventions in research that enrolls neonates while on official duty, at VA facilities, or at VA-approved off-site facilities. Prospective observational and retrospective record review studies that involve neonates or neonatal outcomes are permitted.

3.2.1.4. Women who are known to be pregnant and/or their fetuses may be involved in research if all of the requirements of 45 CFR 46.204 are met, including informed consent requirements and the following ethical and scientific criteria:

3.2.1.4.1. Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;

3.2.1.4.2. The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or fetus. If there is no such prospect of benefit, then the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means;

3.2.1.4.3. Any risk is the least possible for achieving the objectives of the research; and

3.2.1.4.4. The VA medical facility Director certifies that the medical facility has sufficient expertise in women’s health to conduct the proposed research.

3.2.2 Additional VA Requirements for Research Involving Prisoners.
Research involving prisoners cannot be conducted by VA investigators while on official duty, at VA facilities, or at VA-approved off-site facilities unless a waiver has been granted by the Chief Research and Development Officer. If the waiver is granted, the research must be in accordance with 45 CFR 46, Subpart C.

3.2.3 Additional VA Requirements for Research Involving Children.

3.2.3.1 Research involving children must be reviewed carefully by the IRB for its relevance to VA and must not be greater than
minimal risk. The VA medical facility Director must approve participation in the proposed research that includes children.

3.2.3.2 VA 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.

3.2.3.3 The IRB must have the appropriate expertise to evaluate any VA research involving children and must comply with the requirements of 45 CFR 46.401 – 46.404 and 46.408.

3.2.4 Additional VA Requirements for Research Involving Subjects Lacking Decision-Making Capacity.

3.2.4.1 Criteria for Enrollment. Individuals who lack decision-making capacity (i.e. lack consent capacity) may be enroll in VA research where:

3.2.4.1.1 The IRB determines that the proposed research entails:

3.2.4.1.1.1 No greater than minimal risk to the subject; or

3.2.4.1.1.2 Presents a greater probability of direct benefit to the subject than harm to the subject; or

3.2.4.1.1.3 Greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject’s disorder or condition that is of vital importance for the understanding or amelioration of the subject’s disorder or condition.

3.2.4.1.2 In addition to satisfying the conditions above, the IRB determines that:

3.2.4.1.2.1 The research cannot be performed solely with persons who possess decision-making capacity and the focus of the research is the disorder leading to the subjects’ lack of decision-making capacity, whether or not the lack of decision-making itself is being evaluated (e.g., an individual
who lacks decision-making capacity as the result of a stroke can participate in a study of cardiovascular effects of a stroke); or

3.2.4.1.2.2 The subject of the research is not directly related to the subjects’ lack of decision-making capacity but the investigator has presented a compelling argument for including such subjects (e.g., transmission of methicillin-resistant staphylococcus aureus infections in a nursing home where both individuals with and without decision-making capacity are affected).

3.2.4.2 Determination of Capacity. When planning to enter subjects with impaired decision-making capacity, investigators must address in the protocol how they will determine when surrogate consent (i.e., a LAR) will be required. 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. However, the IRB must review and approve the plan to ensure that it is appropriate given the population and setting of the research. Note: Individuals ruled incompetent by a court of law are considered to lack decision-making capacity.

3.2.4.3 Surrogate consent. 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.

3.2.4.4 Authorized Person. The following persons are authorized to consent on behalf of persons who lack decision-making capacity in the following order of priority in accordance with VA regulations at 38 CFR 17.32(e), (g)(3). Note: Consent for research is required in addition to the consent that is obtained for the patient’s non-research-related treatments and procedures.

3.2.4.4.1 Health care agent (i.e., an individual named by the subject in a Durable Power of Attorney for Health Care);

3.2.4.4.2 Legal guardian or special guardian;
3.2.4.3 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

3.2.4.4 Close friend.

Note: the persons authorized to consent on behalf of persons who lack decision-making capacity for participation in the research may not necessarily be the same as the persons authorized to provide permission for the use and disclosure of information on a HIPAA authorization on behalf of persons who lack decision-making capacity.

3.2.4.5 Dissent or Assent. If feasible, the investigator must explain the proposed research to the prospective research subject even when the surrogate 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.

3.2.4.6 Responsibilities of LARs. LARs are acting on behalf of the potential subjects, therefore:

3.2.4.6.1 LARs must be told that their obligation is to try to determine what the subjects would do if able to make an informed decision.

3.2.4.6.2 If the potential subjects’ wishes cannot be determined, the LARs must be told they are responsible for determining what is in the subjects’ best interest.

3.3 Research Subject to HIPAA Regulations

N/A

3.4 Research Subject to Other Regulations

3.4.3 Research Subject to Department of Defense (DoD) Regulations

3.4.3.1 Research involving prisoners of war (detained persons, as defined in Articles 4 and 5 of the Geneva Convention) is prohibited.

3.4.3.2 Research involving prisoners cannot be reviewed by the expedited procedure.
3.4.3.3 If consent is to be obtained from a subject’s LAR, the research must intend to benefit the individual subject. The determination that research is intended to be beneficial to the individual subject must be made by an IRB.

3.4.3.4 At least one prisoner representative must be present for a quorum when the IRB reviews research involving prisoners.

3.4.3.5 In addition to allowable categories of research on prisoners in Subpart C, epidemiological research is also allowable when:

3.4.3.5.1 The research describes the prevalence or incidence of a disease by identifying all cases or studies potential risk factor association for a disease;

3.4.3.5.2 The research presents no more than minimal risk;

3.4.3.5.3 The research presents no more than an inconvenience to the subject.

3.4.4 Research Subject to Department of Education (ED) Regulations.

3.4.4.1 Research involving access to educational records must comply with the Family Educational Rights and Privacy Act (FERPA). Please refer to the specific IU IRB Guidance document for additional information.

3.4.4.2 When the IRB reviews research funded by the National Institute on Disability and Rehabilitation Research (NIDRR) that purposefully requires inclusion of children with disabilities or individuals with mental disabilities, the IRB will include at least one person primarily concerned with the welfare of these research subjects.

3.4.4.3 In compliance with the Protection of Pupil Rights Amendment (PPRA), no student will be required, as part of any research project, to submit without prior consent to surveys; psychiatric examination, testing, or treatment; or psychological examination, testing, or treatment in which the primary purpose is to reveal information concerning one or more of the following:

3.4.4.3.1 Political affiliations or beliefs of the student or the student’s parent.

3.4.4.3.2 Mental or psychological problems of the student or the student’s family.

3.4.4.3.3 Sex behavior or attitudes.
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Standard Operating Procedures for Research Involving Human Subjects

3.4.4.3.4 Illegal, anti-social, self-incriminating, or demeaning behavior.

3.4.4.3.5 Critical appraisals of other individuals with whom respondents have close family relationships.

3.4.4.3.6 Legally recognized privileged or analogous relationships, such as those of lawyers, physicians, and ministers.

3.4.4.3.7 Religious practices, affiliations, or beliefs of the student or student’s parent.

3.4.4.3.8 Income (other than that required by law to determine eligibility for participation in a program or for receiving financial assistance under such program).

Note: The Department of Education defines parent as including natural parents, a guardian, or an individual acting as a parent in the absence of a parent or guardian (34 CFR 99.3). Prior consent refers to prior consent of the student, if the student is an adult or emancipated minor, or to prior written consent of the parent/guardian, if the student is not an emancipated minor (34 CFR 303.314).

3.4.4.4 For certain types of research projects not directly funded by ED and conducted in a school that receives funding from ED, policies and procedures include a process to verify compliance with ED regulations that schools are required to develop and adopt policies in conjunction with parents regarding:

3.4.4.4.1 The right of a parent of a student to inspect, upon the request of the parent, a survey created by a third party before the survey is administered or distributed by a school to a student.

3.4.4.4.1.1 Any applicable procedures for granting a request by a parent for reasonable access to such survey within a reasonable period of time after the request is received.

3.4.4.4.2 Arrangements to protect student privacy that are provided by the agency in the event of the administration or distribution of a survey to a student containing one or more of the following items (including the right of a parent of a student to inspect, upon the request of the parent, any survey containing one or more of such items):
3.4.4.2.1 Political affiliations or beliefs of the student or the student’s parent.

3.4.4.2.2 Mental or psychological problems of the student or the student’s family.

3.4.4.2.3 Sex behavior or attitudes.

3.4.4.2.4 Illegal, anti-social, self-incriminating, or demeaning behavior.

3.4.4.2.5 Critical appraisals of other individuals with whom respondents have close family relationships.

3.4.4.2.6 Legally recognized privileged or analogous relationships, such as those of lawyers, physicians, and ministers.

3.4.4.2.7 Religious practices, affiliations, or beliefs of the student or the student’s parent.

3.4.4.2.8 Income (other than that required by law to determine eligibility for participation in a program or for receiving financial assistance under such a program).

3.4.4.3 The right of a parent of a student to inspect, upon the request of the parent, any instructional material used as part of the educational curriculum for the student.

3.4.4.3.1 Any applicable procedures for granting a request by a parent for reasonable access to instructional material received.

3.4.4.4 The administration of physical examinations or screenings that the school or agency may administer to a student.

3.4.4.5 The collection, disclosure, or use of personal information collected from students for the purpose of marketing or for selling that information (or otherwise providing that information to others for that purpose), including arrangements to protect student privacy that are
provided by the agency in the event of such collection, disclosure, or use.

3.4.4.4.5.1 The right of a parent of a student to inspect, upon the request of the parent, any instrument used in the collection of personal information before the instrument is administered or distributed to a student.

3.4.4.4.5.2 Any applicable procedures for granting a request by a parent for reasonable access to such instrument within a reasonable period of time after the request is received.

3.4.5 Research Subject to Department of Justice (DOJ) Regulations

3.4.5.1 For research conducted with the Bureau of Prisons (BOP), the requirements of 28 CFR 512 must be followed, including:

3.4.5.1.1 The research must not involve medical experimentation, cosmetic research, or pharmaceutical testing.

3.4.5.1.2 The research design must be compatible with both the operation of prison facilities and protection of human subjects. The researcher must observe the rules of the institution or office in which the research is conducted.

3.4.5.1.3 Any researcher who is a non-employee of the Bureau must sign a statement in which the researcher agrees to adhere to the provisions of 28 CFR 512.

3.4.5.1.4 All research proposals will be reviewed by the Bureau Research Review Board.

3.4.5.1.5 For additional information regarding research applications to the BOP, see Steps to Submit a Research Proposal.

3.4.5.1.6 Implementation of Bureau programmatic or operational initiatives made through pilot projects are not considered to be research.
Definitions

1.0 Abbreviations

**CFR:** Code of Federal Regulations, or “Common Rule.”

**DoD:** U.S. Department of Defense

**DOJ:** U.S. Department of Justice

**ED:** U.S. Department of Education

**FDA:** U.S. Food and Drug Administration

**FIPS:** Federal Information Processing Standards

**FRC:** Federal Records Center

**HRPP:** IU Human Research Protection Program

**HHS:** U.S. Department of Health & Human Services

**IU:** Indiana University

**KC:** Kuali Coeus (an electronic management system)

**NARA:** National Archives and Records Administration

**OHRP:** HSS Office of Human Research Protections

**ORC:** IU Office of Research Compliance

**ORO:** Office of Research Oversight, U.S. Department of Veterans Affairs

**QIO:** IU Quality Improvement Office

**VA:** U.S. Department of Veterans Affairs

**VHA:** U.S. Veterans Health Administration

**VHA ORD:** VHA Office of Research and Development
2.0 Glossary of Terms

**administrative hold:** A voluntary interruption of research enrollment and ongoing research activities by an appropriate facility official, research investigator, or sponsor. As this definition applies only to VA research, this would include the VHA ORD when ORD is the sponsor.

- The term “administrative hold” does not apply to interruptions of VA research related to concerns regarding the safety, rights, or welfare of human research participants, research investigators, research staff, or others.
- An administrative hold must not be used to avoid reporting deficiencies or circumstances otherwise covered by VHA Handbooks or other federal requirements governing research.

**adult:** Defined by Indiana state law as “of full age,” and “person in his majority,” meaning a person at least eighteen (18) years of age.

**adverse events:** Any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (e.g., abnormal physical exam or laboratory finding), symptom, or disease temporally associated with the subject’s participation in the research, whether or not considered related to the subject’s participation in the research. Adverse events encompass both physical and psychological harms.

**allegation of noncompliance:** An assertion of noncompliance made by a second party that must be proved, supported, or denied with evidence.

**anonymous:** When referring to data, any information about a living individual that was collected in a manner such that identifiers were never associated with the information and no one was ever able to identify from whom the information was collected. Biospecimens cannot be anonymous.

**assent:** An individual’s affirmative agreement to participate in research obtained in conjunction with permission of the individual’s parents, guardian, or legally authorized representative. Mere failure to object should not, absent affirmative agreement, be construed as assent.

**audit:** A systematic and independent examination of study-related activities and documents to determine whether the evaluated study-related activities were conducted, and the data were recorded, analyzed, and accurately reported, according to applicable federal regulations, state laws, and institutional policies. Audits conducted by the IU QIO Auditor(s) “sample” information and observe parts of a research study, generally at the research site. A **scheduled (not-for-cause) audit** is an examination of research activities and documents conducted as part of the human subjects audit plan and schedule. A **directed (for cause) audit** is an examination of activities and documents conducted in response to a directive by the Associate Vice President for Research Compliance; University Director, HRPP; IRBs; or IRB Chairs.

**auditee:** The department, investigator, or research team to be audited.

**auditor:** A person trained in human subjects research who has experience related to applicable federal regulations, state laws, institutional policies, and auditing techniques. The auditor is independent from the research area, employed by the Quality Improvement Office within ORC, and reports to the Institutional Review Board. The auditor performs audits on human subjects research conducted under the auspices of IU and their affiliated organizations. The auditor will consult with and educate IU researchers who conduct human subjects research in fulfilling their responsibilities to assure compliance.
audit plans: Documents that describe, in general terms and to the degree possible, the types of audit activities that will be undertaken in relation to research compliance and subject safety. Audit plans may be modified in response to changes in regulations or institutional policies, and are reviewed and approved by the IU IRB Executive Committee, generally on a semiannual basis.

audit report: A report, written by an auditor, in which the observations and findings of an audit are documented. The audit report provides key points to counsel, educate, and help an auditee (1) self-correct areas of noncompliance and (2) report to applicable authorities when necessary.

audit trail: Documentation and/or a secure, computer-generated, time-stamped electronic record that allows reconstruction of the course of events relating to creation, modification, and deletion of data and/or records.

authorization: Express written permission from an individual to permit the release and use of his or her individually identifiable health information for a particular purpose. Authorizations are not required to use an individual’s health information to provide treatment or obtain payment, or for a provider’s health care operations. However, under HIPAA, research is not considered health care operations, and therefore requires an authorization or waiver of authorization with limited exception. The provider (or investigator) is responsible for obtaining an authorization from an individual.

benefit: A valued or desired outcome; an advantage.

biologics: A substance manufactured via biological process and otherwise meets the definition of a drug; includes a wide range of products such as vaccines, blood and blood components, allergens, somatic cells, gene therapy, tissues, and recombinant therapeutic proteins. Biologics, in contrast to drugs that are chemically synthesized, are derived from living sources (such as humans, animals, and microorganisms). Most biologics are complex mixtures that are not easily identified or characterized, and many biologics are manufactured using biotechnology. Biological products often represent the cutting edge of biomedical research and, in time, may offer the most effective means to treat a variety of medical illnesses and conditions that presently have no other treatments available. They are regulated by the FDA under the jurisdiction of the Center for Biologics Evaluation and Research (CBER) under Section 351 of the Public Health Service Act.

biospecimen: A quantity of tissue, blood, urine, or other human-derived material. A single biopsy may generate several biospecimens, including multiple paraffin blocks or frozen biological material. The molecular makeup of such specimens reflects the physiologic or pathologic condition of the person from whom they derive; therefore, they provide sensitive and specific insight into the biologic state of the donor. Examples of biospecimens include: subcellular structures (e.g., DNA), cells, tissue (e.g., bone, muscle, connective tissue, and skin), organs (e.g., liver, bladder, heart, and kidney), blood, buccal swabs, gametes, embryos, fetal tissue, saliva or other body fluids, and waste (e.g., urine and stool). Portions or aliquots of a biospecimen are referred to as samples.

blinding/masking: A procedure in which one or more parties to the trial are kept unaware of the treatment assignment(s). Single blinding usually refers to the subject(s) being unaware, and double blinding usually refers to the subject(s), investigator(s), monitor, and, in some cases, data analyst(s) being unaware of the treatment assignment(s).

Certificate of Confidentiality: Privacy protection from the U.S. Department of Health and Human Services for research subjects’ identifiable, sensitive information. The Certificate disallows investigators from disclosing (with certain exceptions) information, documents, or biospecimens that contain identifiable, sensitive information about research subjects that were created or compiled for purposes of the research (1) in federal, state, or local civil, criminal,
administrative, legislative or other proceeding, or (2) to persons not connected with the research.

**Certification:** The official notification by the institution to the supporting department or agency, in accordance with the requirements of 45 CFR 46, that a research project or activity involving human subjects has been reviewed and approved by an IRB in accordance with an approved assurance.

**Certified Copy:** A copy of original information that has been verified, as indicated by dated signature, as an exact copy having all of the same attributes and information as the original. A paper copy of electronic information is not automatically considered a “certified” copy, but instead must be verified as such.

**Children:** As defined by the federal regulations, children are “persons who have not attained the legal age for consent to treatments or procedures involved in the research or clinical investigation, under the applicable law of the jurisdiction in which the research or clinical investigation will be conducted.” Per Indiana state law, “minors” are defined as “persons less than 18 years of age”; therefore, they are considered “children” for purposes of the regulations. EXCEPTION: According to Indiana state law, a minor may consent for himself/herself if any of the following are true: 1) By law the minor is considered emancipated; 2) the minor is at least fourteen (14) years of age, not dependent on a parent for support, is living apart from parents or from a legally responsible individual or organization and managing his/her own affairs; 3) the minor is or has been married; 4) the minor is in the military service of the United States; OR 5) the minor is authorized to consent to the health care by any other statute. For studies that involve prospective and/or current subject(s) that reside in states other than Indiana, the applicable law(s) of each applicable state will be reviewed to ensure that the applicable requirements for children to consent are met.

**Clinical Investigation:** Any experiment that involves a test article (drugs, including botanicals, biologicals, gene therapy, and genetically derived products that meet the definition of “drug,” and medical devices for human use) and one or more human subjects, and that either must meet the requirements for prior submission to the FDA under §505(i), §507(d), or §520(g) of the Food, Drug & Cosmetic Act, or need not meet the requirements for prior submission to the FDA under these sections of the act, but the results of which are intended to be later submitted to, or held for inspection by, the FDA as part of an application for a research or marketing permit. The term does not include experiments that must meet the provisions of part 58 regarding nonclinical laboratory studies (21 CFR 50.3(c)). The terms “research,” “clinical research,” “clinical study,” “study,” and “clinical investigation” are deemed to be synonymous for purposes of this part.

**Clinical Investigator:** As defined in 21 CFR 54, a listed or identified investigator or sub-investigator (co-investigator) who is directly involved in the treatment or evaluation of research subjects. The term also includes the spouse and each dependent child of the investigator.

**Clinical Trial:** As defined by the National Institutes of Health (NIH), a prospective biomedical or behavioral research study of human subjects that is designed to answer specific questions about biomedical or behavioral interventions (drugs, treatments, devices, or new ways of using known drugs, treatments, or devices).

**Coded Samples:** Coded samples are those from which the source of the specimen can be identified by reference to a code rather than a name or other personal identifier. When such samples are obtained from a tissue repository, the repository retains information linking the code to a particular human specimen. Information is sufficient such that the investigator, repository, or third party could link the biological sample or information derived from the research using the sample with a particular person or small group of identifiable individuals.
colleague: Another provider or clinician with a covered entity or practice plan, or a co-investigator in a research protocol.

collector-investigators: Persons charged with the responsibility of obtaining specimens from subjects for the purposes of adding to a repository.

commercial value: Potential economic value of biospecimen materials, including but not limited to cell lines, cultures, plasmids, vectors, nucleotides, proteins, bacteria, and other physical materials (including remnant samples) if sold to a third party.

custom device: A device that 1) necessarily deviates from devices generally available or from an applicable performance standard or premarket approval requirement in order to comply with the order of an individual physician or dentist; 2) is not generally available to, or generally used by, other physicians or dentists; 3) is not generally available in finished form for purchase or for dispensing upon prescription; 4) is not offered for commercial distribution through labeling or advertising; and 5) is intended for use by an individual patient named in the order of a physician or dentist, and is to be made in a specific form for that patient, or is intended to meet the special needs of the physician or dentist in the course of professional practice.

data integrity: The accuracy or correctness of the data in a database. Data integrity can be compromised in a number of ways, such as human errors when data is entered; errors that occur when data is transmitted from one computer to another; software bugs or viruses;
hardware malfunctions such as disk crashes or memory leaks; or natural disasters such as fires and floods.

**data safety/security:** The protection of personally identifiable, sensitive, or confidential information resulting from research or belonging to the federal government. Only authorized people or systems are allowed access to the data. Access to the data is limited by roles, which are granted permissions to view, update, or delete data within the database.

**data use agreement:** To use or disclose a *limited data set* for the purpose of research, public health, or healthcare operations, a covered entity must enter into a data use agreement with the recipient of the information. The agreement may take the form of a formal contract if the relationship is with a third party, or could be a simple confidentiality agreement that workforce members sign when a provider wants to create and use a limited data set for its own research purposes. The principal investigator can determine if co-investigators within the covered entity will be required to sign a data use agreement. The agreement must meet detailed requirements as follows: specify permitted uses and disclosures of the limited data set; identify who may use or receive the limited data set; and restrict further use and disclosure.

**data validation/audit:** A method or process where data in its former, current, and future states are accounted for. This includes but is not limited to tracking the original data entered, tracking who and when an individual or system viewed or changed any data, and tracking why data was changed.

**dead fetus:** A fetus that does not exhibit heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, or pulsation of the umbilical cord.

**deception:** An investigator providing false information to subjects or intentionally misleading them about some aspect of the research.

**de-identified:** Health information is de-identified if there is no reasonable basis to believe that the data can be used to identify an individual, or if the provider has no reasonable basis to believe it can be used to identify the individual. The Privacy Rule requires one of the two following approaches to de-identify data:

1) If a person with appropriate knowledge and experience applying generally accepted statistical and scientific principles and methods for rendering information not individually identifiable makes a determination that the risk is very small that the information could be used, either by itself or in combination with other available information, by anticipated recipients to identify a subject of the information.

or

2) If all 18 identifiers have been removed, including name; all geographic subdivisions smaller than a state, including street address, city, county, precinct, ZIP code and equivalent geocodes (except for the initial three digits of a ZIP code if more than 20,000 people reside in the area); all elements of dates (except year), including birthdays, and ages over 89 (including year); phone numbers; fax numbers; email addresses; Social Security numbers; medical record numbers; health plan beneficiary numbers; account numbers; certificate/license numbers; vehicle identifiers and serial numbers (including license plate numbers); device identifiers and serial numbers; web universal resource locators (URLs); Internet Protocol (IP) address numbers; biometric identifiers; full-face photographic images and any comparable images; and any other unique identifier, characteristic, or code. Note: Other demographic information, such as gender, race, ethnicity, and marital status, is not included in the list of identifiers that must be removed.

**delivery:** Complete separation of the fetus from the woman by expulsion or extraction or any other means.
**department or agency head:** The head of any federal department or agency and any other officer or employee of any department or agency to whom authority has been delegated.

**designated record set:** For purposes of this SOP, this term means any item, collection, or grouping of information that includes Protected Health Information and is maintained, collected, used, or disseminated by or for a covered entity. Each covered entity must define its designated record set. Patients have a right to access and propose amendments to their designated record set and to know when their designated record set is disclosed for certain purposes, such as disclosures made under an IRB-approved waiver of authorization.

**device (medical device):** As regulated by the FDA, an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, OR intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes.

**direct advertising:** Advertising that is intended to be seen or heard by prospective participants to solicit their participation in a study.

**disclosure:** The release, transfer, provision of, access to, or divulging in any other manner, of information outside the entity holding the information.

**dissent:** An individual’s negative expressions, verbal and/or nonverbal, that they object to participation in the research or research activities.

**Data Safety Monitoring Board (DSMB):** A formally appointed independent group of experts assigned to conduct interim monitoring of accumulating data from research activities to assure the continuing safety of research subjects, relevance of the study question, appropriateness of the study, and integrity of the accumulating data. A Data Safety Monitoring Committee (DSMC) is synonymous with a DSMB.

**Data Safety Monitoring Plan (DSMP):** A plan established to assure that each research study has a system for appropriate oversight and monitoring of the conduct of the study to ensure the safety of subjects and the validity and integrity of the data.

**drug:** A substance manufactured via chemical process and intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease OR (other than food) intended to affect the structure or any function of the body of man. Regulated by the FDA. See also *legend drug*.

**electronic data:** Any combination of text, graphics, data, audio, pictorial, or any other information representation in digital form that is created, modified, maintained, archived, retrieved, or distributed by a computer system. This includes any information that has been collected and entered into a software application to move or process. This includes but is not limited to information on a handheld device or in an email system.

**electronic database:** A collection of any data organized so that its contents can easily be accessed, managed, updated, and stored electronically. This includes but is not limited to the storing of information in Microsoft’s Word, Excel, or Access and other proprietary software programs.

**electronic signature:** A method to authenticate the identity of the sender of a message or the signer of an electronic document.

**eligible domestic partner:** This person is the same sex as the employee; at least 18 years of age and competent to enter into a contract; not legally married or the domestic partner of another individual; has lived with the employee as a couple for at least six consecutive months; and has
submitted documentation to verify an interdependent relationship with the employee that is
the functional equivalent of a marriage.

emancipated minor: A legal status conferred by court order upon persons who have not yet
attained the age of legal competency but who are entitled to treatment as legal adults. For
additional information, please see Indiana Code 31-34-20-6.

emergency use: The use of a test article on a human subject in a life-threatening situation in
which no standard acceptable treatment is available, and in which there is not sufficient time to
obtain IRB approval.

encryption: The process of converting information, particularly identifiable information such as
Social Security number and name that identifies individuals, into a code to secure that
information from unauthorized access.

enrollment: If a subject requires screening tests to determine eligibility, enrollment begins when
the informed consent for screening is obtained. If there is no screening, then enrollment begins
at the time of consent for the study. In situations where waiver of consent is applicable,
enrollment begins when data is collected.

essential documents: Documents that individually and collectively permit evaluation of the
conduct of research and the quality of the data produced. These include but are not limited to
regulatory and patient specific records. A complete list of these documents can be found in the
ICH Guidelines, Section 8.0.

exclusion criteria: A list of requirements, any one of which excludes a potential subject from
selection and participation in a study.

exempt from IDE requirements: There are several categories of device studies that are exempt
from IDE requirements if certain criteria are met: (A) certain studies of custom devices; (B)
studies involving certain device modifications, combinations, or consumer preference testing of
already-approved or cleared devices; (C) studies involving non-invasive diagnostic devices; and
(D) studies involving already cleared or approved devices.

exempt review procedure: A review procedure consisting of a review of research involving
human subjects by an ORC staff person or a member of the IRB designated by the Chairperson.

expedited review procedure: A review procedure consisting of a review of research involving
human subjects by the IRB Chairperson or by one or more experienced reviewers designated by
the Chairperson from among members of the IRB.

experimental subject: According to the Department of Defense, a living individual involved in
research where there is an intervention or interaction for the primary purpose of obtaining data
regarding the effect of the intervention or interaction.

external: From the perspective of a multicenter clinical trial, other institutions engaged in the
clinical trial. An external entity is any person, trust, organization, enterprise, or other entity
(including government agencies) that is not an entity under the control of or under common
control with IU.

faculty sponsors: Full- or part-time faculty employed by IU who engage in classroom instruction;
supervise on- or off-campus internships, clinical experiences or practica; or mentor students
who are conducting independent projects.

federally funded: Supported, either directly or indirectly, by funds provided by the federal
government. This includes federal pass-through funding (i.e., subcontracts), no-cost extensions,
and support that is not specifically intended to support research activities, such as scholarships,
fellowships, training grants, etc.
Federalwide Assurance (FWA): A formal document between an institution and the federal government that commits the institution to comply with applicable regulations governing the conduct of all research involving human subjects.

fetus: The product of conception from implantation until delivery.

flexibility option: The election by IU to not apply the Common Rule (45 CFR 46) to all human subjects research. When no part of the research is federally supported or funded and the study is not subject to VA or FDA research regulations, the IU IRB and/or HSO may apply equivalent protections that differ from the federal requirements.

generalizable knowledge: Information that expands the knowledge base of a scientific discipline or other scholarly field of study.

genetic information: Information about an individual’s genetic tests; the genetic tests of an individual’s family members (including dependents and up to and including 4th-degree relatives); the genetic tests of any fetus of an individual or family member who is a pregnant woman; and genetic tests of any embryo legally held by an individual or family member utilizing assisted reproductive technology; the manifestation of a disease or disorder in an individual’s family members; and any request for, or receipt of, genetic services or participation in clinical research that includes genetic services (genetic testing, counseling, or education) of an individual or an individual’s family members.

genetic research: Research (not diagnostic testing) that involves either 1) the analysis of human chromosomes or DNA from an individual and/or family members for the purpose of deriving information concerning the individual or family about the presence, absence, or mutation of genes, DNA markers, or inherited characteristics; or 2) other studies with the intent of collecting and evaluating information about heritable diseases and/or characteristics within a family.

genetic test: An analysis of human DNA, RNA, chromosomes, proteins, or metabolites that detect genotypes, mutations, or chromosomal changes. Routine tests that do not detect genotypes, mutations, or chromosomal changes, such as complete blood counts, cholesterol tests, and liver enzyme tests, are not considered genetic tests. Genetic tests also do not include analyses of proteins or metabolites that are directly related to a manifested disease, disorder, or pathological condition that could reasonably be detected by a health care professional with appropriate training and expertise in the field of medicine involved.

good clinical practice (GCP): A standard by which clinical trials are designed, performed, monitored, audited, recorded, analyzed, and reported so that there is public assurance that the data are credible and that the rights, integrity, and confidentiality of subjects are protected.

greater than minimal risk: The probability and magnitude of harm or discomfort anticipated in the research are greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

guardian: An individual who is authorized under applicable state or local law to consent on behalf of a child to general medical care. The FDA includes in its definition that this individual can also consent on behalf of a child to participate in research, even when general medical care includes participation in research.

harm: A hurtful or adverse outcome of an action or event. Harms incurred by research can occur close in time to the research, or can follow long after it has concluded.

health care: Defined by Indiana state law as any care, treatment, service, or procedure to maintain, diagnose, or treat an individual’s physical or mental condition, including admission to a health care facility.

health care operations: Activities that are “compatible with and directly related to” treating an individual and obtaining payment for those services. Protected Health Information may be used
or disclosed for health care operations without an individual’s authorization. These activities include conducting quality assessment and improvement activities, including outcomes evaluation and development of clinical guidelines, provided that the obtaining of generalizable knowledge is not the primary purpose of any studies resulting from such activities. Research is not health care operations. As a result, if the purpose of the activity is to obtain generalizable knowledge, then the Privacy Rule’s research requirements apply. In addition, health care operations includes reviewing the competence or qualifications and accrediting/licensing of health care professionals and plans, evaluating health care professionals and health plan performance, training future health care professionals, insurance activities relating to the renewal of a contract for insurance, conducting or arranging for medical review and auditing services, and compiling and analyzing information in anticipation of or for use in a civil or criminal legal proceeding.

**HIPAA:** The Health Insurance Portability and Accountability Act of 1996. See also **Privacy Rule.**

**human fetal material:** Tissue or cells obtained from a dead human embryo or fetus after a spontaneous or induced abortion, or after a stillbirth.

**human subject:** A living individual about whom an investigator (whether professional or student) conducting research obtains 1) data through intervention or interaction with the individual, or 2) identifiable private information (as defined by 45 CFR 46.102(f)). FDA includes in its definition of “human subject” an individual who is or becomes a participant in research, either as a recipient of an investigational drug, as an individual on whom or on whose specimen an investigational device is used, or as a control. A “human subject” may either be a healthy human or a patient and is synonymous with “subject,” “participant,” and “volunteer.”

**humanitarian device exemption (HDE):** An FDA-approved authorization to market a HUD. The application is similar to a premarket approval (PMA) application but exempt from the effectiveness requirements of a PMA.

**humanitarian use device (HUD):** According to the FDA, “a medical device intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in fewer than 4,000 individuals in the United States per year.”

**Human Subjects Office:** A department within the Office of Research Compliance (ORC) responsible for providing administrative support to the IU Institutional Review Boards (IRBs).

**identified biospecimens:** Biospecimens for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen (45 CFR § 46.102(f)).

**identifiers:** Information that can be used to link a sample or scientific result with a specific person or group of people. HIPAA recognizes eighteen (18) identifiers that may make health information identifiable to an individual, including name; all geographic subdivisions smaller than a state, including street address, city, county, precinct, ZIP code and equivalent geocodes (except for the initial three digits of a ZIP code if more than 20,000 people reside in the area); all elements of dates (except year), including birthdays, and ages over 89 (including year); phone numbers; fax numbers; email addresses; Social Security numbers; medical record numbers; health plan beneficiary numbers; account numbers; certificate/license numbers; vehicle identifiers and serial numbers (including license plate numbers); device identifiers and serial numbers; web universal resource locators (URLs); Internet Protocol (IP) address numbers; biometric identifiers; full-face photographic images and any comparable images; and any other unique identifier, characteristic, or code.

**immortalized cell line:** A culture that is apparently capable of an unlimited number of population doublings.
implant: A device that is placed into a surgically or naturally formed cavity of the human body if it is intended to remain there for a period of 30 days or more. FDA may, in order to protect public health, determine that devices placed in subjects for shorter periods are also “implants.”

independent IRB: An Institutional Review Board not associated with a single institution or entity and which provides commercial IRB services for a fee (e.g., Western Institutional Review Board (WIRB)).

inclusion criteria: The requirements that prospective subjects must meet to be eligible for selection and participation in a study.

individually identifiable health information (IIHI): Information that is a subset of Protected Health Information (PHI), including demographic information collected from an individual, and that a) is created or received by a health care provider, health plan, employer, or health care clearinghouse; and b) relates to the past, present, or future physical or mental health or condition of an individual; the provision of health care to an individual; or the past, present, or future payment for the provision of health care to an individual; and that identifies the individual or with respect to which there is a reasonable basis to believe the information can be used to identify the individual.

individuals lacking consent capacity: Individuals who, for various reasons, lack the ability to understand the research, appreciate the consequences of their participation, consider alternatives, and/or make reasoned choices, such that they cannot provide informed consent for themselves

industry sponsor: A for-profit entity or company that has contracted with IU personnel to conduct a research study involving human subjects.

informed consent: An ongoing process by which a subject (or his/her legal representative) voluntarily confirms his or her willingness to participate in a particular research project, after having been informed of all aspects of the research that are relevant to the subject’s decision to participate. Informed consent is often but not always documented by means of a written, signed, and dated informed consent form with documentation, which is retained in the subject’s record.

in loco parentis: The legal doctrine under which someone acts in the place of a parent.

institution: A public or private entity, other than an individual, that engages in the conduct of research on subjects or in the delivery of medical services to individuals as a primary activity or as an adjunct to providing residential or custodial care to humans. The term includes, for example, a hospital, a retirement home, a confinement facility, an academic establishment, and a device manufacturer.

institutional facility: Any public or private health care entity with the primary purpose of providing a physical environment for subjects to obtain health care services, such as a convalescent home or a nursing home extended care facility

institutional official (IO): The individual legally authorized as signatory official to commit an institution to an assurance. The IO serves as the official representative of the institution to external agencies and oversight bodies, and provides all written communication with external departments, agencies, and oversight bodies. The VA facility director is the IO for the local VA facility.

Institutional Review Board (IRB): Any board, committee, or other group formally designated by an institution to review, to approve the initiation of, and to conduct periodic review of biomedical and/or behavioral (general) research involving human subjects. The primary purpose of such review is to assure the protection of the rights and welfare of the human subjects. This
independent body is constituted of members with varying backgrounds (e.g., medical, scientific, nonscientific, and unaffiliated).

**institutional work:** Works created at the instigation of the University, under the specific direction of the University, for the University’s use, by a person acting within the scope of his or her employment or subject to a written contract.

**interaction:** Includes communication or interpersonal contact between the investigator (or a member of the research team) and the subject.

**internal:** In reference to a multicenter clinical trial, IU (or its affiliates’) investigators engaged in the clinical trial.

**international research:** See *transnational research*.

**intervention:** Includes both physical procedures by which data are gathered (e.g., venipuncture) and manipulations of the subject or the subject’s environment that are performed for research purposes.

**investigational device:** A medical device that is the object of a clinical investigation or research involving one or more human subjects to determine its safety and effectiveness. This definition also includes “transitional devices” that had been previously regulated by the FDA as drugs prior to the passage of the Medical Device Amendments. Generally these are not approved by the FDA, or are being tested or studied for indications not previously approved by the FDA.

**investigational device exemption (IDE):** FDA authorization for research involving a device not yet approved by the FDA or research on a product for non-approved indication. In most cases, the sponsor holds the IDE, but in some studies, the investigator holds the IDE.

**investigational drug:** A new drug or biologic drug that is authorized for use in a clinical investigation. The terms “investigational drug” and “investigational new drug” are synonymous for this SOP.

**Investigational Drug Services (IDS):** A pharmacy specializing in the handling, storage, labeling, and distribution of investigational agents.

**Investigational New Drug Application (IND):** The application to the FDA for research involving a product not yet approved by the FDA or research on a product for a non-approved indication. In most cases, the sponsor holds the IND, but in some studies the investigator holds the IND.

**investigational product:** A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorization when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved indication, or when used to gain further information about an approved use. Under Indiana Code 25-26-13-2, “Investigational or new drug” means any drug that is limited by state or federal law to use under professional supervision of a practitioner authorized by law to prescribe or administer such drug.

**investigator:** Any individual involved in conducting human research studies; specifically, an individual who interacts with human subjects or accesses identifiable information for research purposes. Investigators may be categorized as key personnel or research (non-key) personnel. Persons without access to identifiable information, or persons whose activities are solely related to safety monitoring, are not considered investigators. See also *key personnel* and *non-key personnel*.

**IRB-approved protocol:** refers to all study information, including that contained in the KC IRB Questionnaires, formal protocol document, consents, etc.

**IRB Executive Committee:** A committee made up of the chairs and vice chairs of each of the IU Institutional Review Boards, along with other members as needed to achieve diversity. The
committee is responsible for developing and coordinating IU’s IRB policy and procedural matters involving the use of human subjects in research. Its operations are administered through the IU Human Subjects Office.

**IU:** Refers to anyone employed by or using the facilities of Indiana University or any affiliated institution as listed under the Federalwide Assurances found on the IU Human Subjects Office website, which must have human subjects research reviewed, approved, and monitored by an IU IRB.

**IU affiliates:** Organizations that maintain a FWA with HHS in which one or more of the IU IRBs is listed as the reviewing IRB, or organizations that have entered into a formal agreement with IU for the review and approval of human subjects research at their institutions. A list of these affiliates can be found on the IU Human Subjects Office website.

**IU-affiliated investigator:** Indiana University faculty, staff, and students engaged in human subjects research, and employees and staff of IU-affiliate institutions which have contracted with the IU IRBs for review and oversight of human subjects research. IU-affiliate institutions include Eskenazi Health, Indiana State Department of Health, IU Health, Purdue Pharmacy Practice, Regenstrief Institute, and Roudebush VAMC.

**key personnel:** a co-investigator responsible for the conduct and/or reporting of research. Such individuals may include, among others: investigators making critical decisions regarding eligibility of subjects, investigators obtaining consent for greater than minimal risk research, investigators listed on the FDA 1572 form or investigator agreement, and students who have designed and are conducting research in order to complete an education requirement under the mentorship of a principal investigator.

**legally authorized representative (LAR):** Defined in the federal regulations as an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective participant to the participant’s participation in the procedure(s) involved in the research. In Indiana, a representative (defined by Indiana Code 16-36-1-2; see “representative”) or a person authorized consent for incapable parties (Indiana Code 16-36-1-5) serves as the federally defined LAR. Pursuant to Indiana Code 16-36-1-5, this individual may be 1) a judicially appointed guardian of the person or a representative appointed; or 2) by a spouse, a parent, an adult child, an adult grandchild, an adult sibling, or a grandparent; or 3) the individual's religious superior, if the individual is a member of a religious order. As a result of this clarification, for studies conducted at the VA, the Indiana state law definition of LAR supersedes the VA definition of LAR. For studies that involve prospective and/or current subject(s) that reside in states other than Indiana, the applicable law(s) of each applicable state will be reviewed to ensure that the applicable requirements for an LAR to consent on behalf of a prospective subject are met.

**legend drug:** Any drug approved by the FDA that is required by federal or state law to carry a label that cautions against dispensing without prescription.

**life-threatening:** For purposes of “emergency use,” this includes the scope of both life-threatening and severely debilitating diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted, and diseases or conditions with potentially fatal outcomes, where the end point of clinical trial analysis is survival. The criteria for life-threatening do not require the condition to be immediately life-threatening or to immediately result in death. Rather, the subjects must be in a life-threatening situation requiring intervention before review at a convened meeting of the IRB is feasible. “Severely debilitating” means diseases or conditions that cause irreversible morbidity. Examples of severely debilitating conditions include blindness; loss of arm, leg, hand or foot; loss of hearing; and paralysis or stroke.
**limited data set**: A set of data that excludes facially identifiable information but still includes some identifiable information. As a result, the data are still “identifiable” and may be used for limited purposes, including research, public health, or healthcare operations as long as there is a data use agreement with the recipient of the limited data set. A limited data set must exclude 16 specified identifiers that are listed in the Privacy Rule, including name, street address, telephone and fax numbers, email address, Social Security number, certificate/license number, vehicle identifiers and serial numbers, URLs and IP addresses, and full face photos and any other comparable images. The limited data set may include the following identifiable information: admission, discharge, and service dates; birth date, date of death, and age (including age 90 and older); and the five-digit ZIP code.

**login**: A unique, specific, confidential credential that identifies the person as a legitimate and authorized user of the computer and/or electronic network.

**management plan**: An agreement with a researcher confirming that the researcher understands the policies that govern his/her activities at IU and specifying any requirements tailored to his/her specific activities. Management plans may address one or more of the following: disclosure, oversight, proprietary interest in the tested product, restriction on equity, divestiture, or severance of relationships that heighten or create actual or potential conflicts. For more information, see http://researchcompliance.iu.edu/coi/coi_manage_res.html.

**manufacturer**: Any legal person or entity engaged in the manufacture of a product subject to license under the Public Health Service Act, including an applicant for a license where the applicant assumes responsibility for compliance with the applicable product and establishment standards.

**master inventory list**: The original itemized catalog of the location of all data and documents being retained and/or stored.

**minimal risk**: The probability and magnitude of physical or psychological harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests (as defined by 45 CFR 46.102(i)) of healthy persons (who are not prisoners). Note: This definition differs from the definition in 45 CFR 46 Subpart A, used for reviews by an expedited procedure and the waiver and alteration of consent and consent document, and 45 CFR 46 Subpart D, for approval of research involving children as participants.

**minimum necessary standard**: A covered entity must make reasonable efforts to use, disclose, or request the least amount of information needed for the intended purpose. For example, if the entire medical record is desired, it must be justified as the minimum necessary. Although the Minimum Necessary Standard does not apply to use or disclosure of Protected Health Information under an authorization, the investigator is bound by the purposes described in the authorization. In addition, the Minimum Necessary Standard does not apply to a patient’s treatment.

**minor**: Defined by Indiana state law as a person less than eighteen (18) years of age unless the child meets the Indiana state law definition of an emancipated minor.

**National Cancer Institute Central Institutional Review Board Initiative**: The NCI CIRB Initiative is sponsored by the NCI in consultation with the Department of Health and Human Services Office of Human Research Protection (OHRP). The CIRB is an IRB designated by the institution as the IRB of record for certain adult and pediatric multi-center national cancer treatment trials.

**neonate**: A newborn child less than four weeks old. A nonviable neonate is an expelled or delivered fetus who, although living, cannot sustain life independently, even with medical intervention.
**non-affiliated:** For the purposes of IRB membership, this refers to a member not otherwise affiliated with Indiana University or its affiliates and who is not part of the immediate family of a person who is affiliated with Indiana University or its affiliates.

**non-affiliated investigator:** Investigators who are not faculty, staff, or students of IU, or employees or staff of IU-affiliate institutions.

**noncompliance:** Any action or activity associated with the conduct or oversight of research involving human subjects that fails to comply with federal or state regulations, requirements of VHA Handbook 1200.05, or institutional policies governing human subjects research or the requirements or determinations of the IRB.

- **continuing noncompliance:** A pattern of noncompliance that, in the judgment of the convened IRB, IRB Chair, or IRB Chair’s designee, indicates a lack of understanding of the regulations or institutional requirements that may affect the rights and welfare of participants; would have been foreseen as compromising the scientific integrity of a study such that important conclusions could no longer be reached; suggests the likelihood that noncompliance will continue without intervention; or frequent instances of minor noncompliance. Continuing noncompliance also includes failure to respond to a request to resolve an episode of noncompliance with human subject protection regulations, or a general persistent failure to adhere to the laws, regulations, or policies governing human subjects.

- **minor noncompliance:** Noncompliance that is neither serious nor continuing and which does not affect the scientific soundness of the research plan or the rights, safety, or welfare of human subjects. Examples might include: obtaining consent using an invalid/outdated consent document that contains all of the information required by the IRB, or failure to submit continuing review documentation prior to expiration of IRB approval.

- **observed or apparent noncompliance:** Noncompliance that does not require further information to confirm its occurrence.

- **serious noncompliance:** Any action or activity associated with the conduct or oversight of research involving human subjects that fails to comply with federal or state regulations, requirements of VHA Handbook 1200.5, or institutional policies governing human subjects research or the requirements or determinations of the IRB that increases the risks to subjects, decreases potential benefits to subjects, adversely affects the rights and welfare of subjects, or compromises the integrity or validity of the research. Examples of serious noncompliance include but are not limited to conducting human subjects research without appropriate IRB approval or enrollment of research subjects while study approval has lapsed.

**noninvasive:** When applied to a diagnostic device or procedure, means one that does not by design or intention: 1) penetrate or pierce the skin or mucous membranes of the body, the ocular cavity, or the urethra, or 2) enter the ear beyond the external auditory canal, the nose beyond the nares, the mouth beyond the pharynx, the anal canal beyond the rectum, or the vagina beyond the cervical os. For purposes of this part, blood sampling that involves simple venipuncture is considered noninvasive, and the use of surplus samples of body fluids or tissues that are left over from samples taken for noninvestigational purposes is also considered noninvasive.

**non-key personnel:** A co-investigator who conducts research procedures under the direction of the principal investigator or key personnel but who is not considered responsible for the conduct and/or reporting of research.
**non-scientist:** For the purposes of IRB membership, this refers to a member whose primary concerns are in nonscientific areas; specifically, little to no scientific or medical training or experience such that the individual would be considered unambiguously nonscientific. Examples of appropriate nonscientist representation may include patients, former research subjects, clergy, lawyers, and ethicists.

**nonsignificant risk (NSR) device research:** Research that does not meet the definition for a significant risk study. Research involving an NSR device should not be confused with the concept of “minimal risk” as defined in 45 CFR 46.102(i) and 21 CFR 56.102(i) to identify certain research that may be approved through an expedited review procedure.

**Notice of Privacy Practices:** An individual has a right to adequate notice of the uses and disclosures of Protected Health Information that may be made by the covered entity and of the individual’s rights and the covered entity’s legal duties with respect to Protected Health Information. The covered entity must provide a notice that is written in plain language.

**off-site:** For purposes of securing research data, this refers to a location not in the immediate vicinity. This could be in a different office or building. While this could mean an “off-campus” location, “off-site” does not always mean “off-campus.”

**one-time:** A single use (or a single course of treatment, e.g., multiple doses of an antibiotic) of a test article with one subject at one institution (hospital-specific). Note: “Hospital-specific” shall in no case allow the same physician to move a patient from one hospital or physician to another for purposes of meeting the one-time emergency use provision.

**oversight:** The process by which a qualified person or group periodically reviews the results and conduct of a study to date, as it relates to subject safety.

**parent:** A child’s biological or adoptive parent.

**pass-through funding:** Federal grant funds received by a legal entity as a subrecipient rather than as the direct recipient, such as U.S. Public Health Service funding made available via the Centers for Disease Control and Prevention.

**permission:** The agreement of parent(s) or guardian(s) to the participation of their child or ward in research.

**personally identifiable information (PII):** Information that can be used alone or in conjunction with any other information to identify a specific individual. PII includes any information that can be used to search for or identify individuals or to access their files, such as name, Social Security number, date of birth, and license or other identification number. PII may be electronic or paper.

**practitioner:** A physician licensed under IC 25-22.5, a veterinarian licensed under IC 15-5-1.1, a dentist licensed under IC 25-14, a podiatrist licensed under IC 25-29, or any other person licensed by law to prescribe and administer legend drugs in Indiana.

**pregnancy:** Encompasses the period of time from implantation until delivery. A woman shall be assumed to be pregnant if she exhibits any of the pertinent presumptive signs of pregnancy, such as missed menses, until the results of a pregnancy test are negative or until delivery.

**premarket approval (PMA):** Any premarket approval application for a class III medical device, including all information submitted with or incorporated by reference therein. PMA includes a new drug application for a device under section 520(1) of the Federal Food, Drug, and Cosmetic Act.

**pre-screening:** The evaluation of generalized characteristics prior to screening to initially determine eligibility (e.g., review of charts).

**preventive action:** A process implemented to prevent occurrence of an event in the future.
**Principal Investigator (PI):** The responsible leader of a team of investigators (and research team), who has the ultimate responsibility for the conduct of the research. Eligibility requirements can be found in the IRB Instruction Packet.

**prisoner:** Any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute; individuals detained in other facilities by virtue of statutes or commitment procedures that provide alternatives to criminal prosecution or incarceration in a penal institution; and individuals detained pending arraignment, trial, or sentencing. Individuals are prisoners if they are in any kind of penal institution, such as a prison, jail, or juvenile offender facility, and their ability to leave the institution is restricted. Prisoners may be convicted felons, or may be untried persons who are detained pending judicial action, such as arraignment or trial. Examples of the application of the regulatory definition of “prisoner” include:

- Individuals who are detained in a residential facility for court-ordered substance abuse treatment as a form of sentencing or alternative to incarceration are prisoners; however, individuals who are receiving non-residential court-ordered substance abuse treatment and are residing in the community are not prisoners.
- Individuals with psychiatric illnesses who have been committed involuntarily to an institution as an alternative to a criminal prosecution or incarceration are prisoners; however, individuals who have been voluntarily admitted to an institution for treatment of a psychiatric illness, or who have been civilly committed to nonpenal institutions for treatment because their illness makes them a danger to themselves or others, are not prisoners.
- Parolees who are detained in a treatment center as a condition of parole are prisoners; however, persons living in the community and sentenced to community-supervised monitoring, including parolees, are not prisoners.
- Probationers and individuals wearing monitoring devices are generally not considered to be prisoners; however, situations of this kind frequently require an analysis of the particular circumstances of the planned subject population. Please consult the Research Compliance Administration office when questions arise about research involving these populations. See also the Prisoner Research FAQs at [http://www.hhs.gov/ohrp/policy/faq](http://www.hhs.gov/ohrp/policy/faq).

**privacy:** An individual’s freedom from unauthorized intrusion into or observation of his or her person. Privacy restricts access to the person, whereas confidentiality restricts access to the individual’s personal data.

**Privacy Board:** The group of individuals charged with the review and approval of activities related to privacy and confidentiality. The Privacy Board must have members with varying backgrounds and appropriate professional competency as necessary to review the effect of the research protocol on the individual’s privacy rights and related interests. The IU IRBs have been designated as the Privacy Board for research conducted at IU facilities or those of its affiliates.

**Privacy Rule:** Found at Title 45 Code of Federal Regulations part 160 and subparts A and E of part 164, the Rule requires appropriate safeguards to protect the privacy of personal health information, and sets limits and conditions on the uses and disclosures that may be made of such information without patient authorization. The Rule also gives patients rights over their health information, including rights to examine and obtain a copy of their health records, and to request corrections.

**private information:** Includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the
individual can reasonably expect will not be made public (e.g., medical records). To be considered private, the information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information).

**promptly reportable event**: An event which may represent noncompliance or an unanticipated problem involving risks to subjects or others, and which must be reported to the IRB within five (5) business days. See SOP on Reportable Events for a full list of promptly reportable events.

**proposed research protocol**: A new protocol submitted to an IRB for review and approval as required by HHS.

**proprietary interest in the tested product**: Property or other financial interest in the product including but not limited to a patent, trademark, copyright, or licensing agreement.

**prospective study**: A study that asks a question and looks forward. Prospective studies are designed before any information is collected. Study subjects are identified (e.g., workers with low-back injury claims) and followed forward to see if the outcome of interest (e.g., return to work) happens over time. This outcome is assessed relative to the intervention factor (e.g., physiotherapy).

**protected health information (PHI)**: Health information, including demographic information collected from an individual, that is created or received by a health care provider, health plan, employer, or health care clearinghouse; and relates to the past, present, or future physical or mental health or condition of an individual, or to the provision of health care to an individual.

**protocol**: As defined by federal regulations, a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge.

**protocol deviation**: An alteration/modification to the IRB-approved protocol that is not approved by the IRB prior to its initiation or implementation. The IRB-approved protocol includes the detailed protocol, summary safeguard statement, informed consent document(s), recruitment materials, questionnaires, and any other information relating to the research study. **A minor protocol deviation** does not impact subject safety, compromise the integrity of study data, and/or affect a subject’s willingness to participate in the study. Examples: Failure of the subject to return study medication; failure to follow the approved study procedure that, in the opinion of the investigator, does not affect subject safety or data integrity (e.g., study procedure conducted out of sequence; omitting an approved portion of the protocol; missing lab results). **A major protocol deviation** is a deviation to the IRB-approved protocol that may affect subject safety, the integrity of study data, and/or the subject’s willingness to participate in the study. Examples: Enrollment of a subject who did not meet all inclusion/exclusion criteria; performing a study procedure not approved by the IRB; drug/study medication dispensing or dosing error; failure to perform a required lab test or conducting a study visit outside the required time frame, if, in the opinion of the investigator, that may affect subject safety and/or data integrity.

**radiologic device**: Any manufactured or assembled article that emits radiation. This may be an implantable device, or a machine (such as a bone densitometer) that is used as part of an investigation. For the purposes of this SOP, “radiologic” implies that the article is being used for investigational purposes. The Center for Devices and Radiological Health (CDRH) includes the following definitions:

- **electronic product**: Any manufactured or assembled product which, when in operation, contains or acts as part of an electronic circuit; and emits (or in the absence of effective shielding or other controls would emit) electronic product radiation, or any manufactured or assembled article which is intended for use as a component, part, or accessory of a product described above and which when in operation emits (or in the absence of effective shielding or other controls would emit) such radiation.
• **electronic product radiation**: Any ionizing or non-ionizing electromagnetic or particulate radiation; or any sonic, infrasonic, or ultrasonic wave, which is emitted from an electronic product as the result of the operation of an electronic circuit in such product.

**randomization or random assignment**: The process of assigning research subjects to a specific study group (e.g., treatment or control) using an element of chance to determine the assignments in order to reduce bias.

**recipient-investigator**: A person approved to receive specimens from a repository to use for research purposes.

**recruitment**: The process by which individuals are identified, screened, and contacted or identified, screened, and determined to be not eligible for a specific study.

**regulatory agencies**: Government organizations, anywhere in the world, that set standards, establish policies, advocate laws, and provide oversight of specified activities within a country, such as the United States Food and Drug Administration (FDA).

**related or possibly related to participation in research**: There is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research.

**reliance**: An instance of IRB review when one or more relying institutions choose to accept IRB review and oversight for a research project from another institution’s reviewing IRB. In these situations, the reviewing IRB provides IRB review and oversight for conduct of the research at the relying institution(s).

**relying institution**: An institution engaged in human subjects research which relies on an external reviewing IRB for review and oversight of human subjects research.

**remnant**: Biospecimen material collected during a clinical or diagnostic procedure in quantities above and beyond what was needed for the procedure.

**renewal**: Continuing review of non-exempt human subjects research required by FDA and HHS throughout the life of a study. The review interval may not exceed one year for federally funded or regulated studies and/or those requiring review by the full convened IRB, or two years for studies qualifying for expedited review.

**reportable event**: An event which may represent noncompliance or an unanticipated problem involving risks to subjects or others. Reportable events are reported to the IRB in accordance with the SOP on Reportable Events.

**repository**: A site for common storage of biospecimens or data for research purposes. This may be one geographic location or may be a virtual aggregation of biospecimens or data from many locations. Repositories are also referred to as tissue banks, collections, resources, inventories, or by other terms. Repository activities involve three components: (1) the **collectors** of data and biospecimens; (2) the **repository** storage and data management center; and (3) the **recipient** investigators. Repositories may or may not have identifiable information.

**representative**: As defined by Indiana Code 16-36-1, an individual delegated to consent to health care of another who for a time will not be reasonably available to exercise the authority. The delegation: (1) must be in writing; (2) must be signed by the delegate; (3) must be witnessed by an adult; and (4) may specify conditions on the authority delegated. Unless the writing expressly provides otherwise, the delegate may not delegate the authority to another individual.

**research**: A systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge (as defined in 45 CFR 46.102(d)). 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. For example, some demonstration and service programs may include research activities (45 CFR 46.102(d)).

- The DOJ includes in its definition of research all basic, applied, and demonstration research and validation methodologies involving all fields of science, mathematics, engineering, and computer technology. For research conducted within the Bureau of Prison, implementation of Bureau programmatic or operational initiatives made through pilot projects is not considered to be research.

- The FDA includes in its definition of a research activity any experiment that involves a test article and one or more human subjects and that either meets requirements for prior submission to the FDA or the results of which are intended for a research or marketing permit.

- The VA defines research as a systematic investigation (including research development, testing, and evaluation) designed to develop or contribute to generalizable knowledge. VA research is conducted by VA investigators employed by the VA. The research may be funded by the VA or by other sponsors, or may be unfunded.

**research documents:** All records, in any form (including but not limited to written, electronic, magnetic, audio-visual, and optical records and scans, X-rays, and electrocardiograms) that describe or record the methods, conduct, and/or results of a study and the actions taken.

**research involving a human being as an experimental subject:** Per DoD Directive 3216.02, an activity, for research purposes, where there is an intervention or interaction with a human being for the primary purpose of obtaining data regarding the effect of the intervention or interaction (32 CFR 219.102(f), reference (c)). Examples of interventions or interactions include but are not limited to a physical procedure, a drug, a manipulation of the subject or subject’s environment, and the withholding of an intervention that would have been undertaken if not for the research purpose.

**research oversight plan:** The detailed map for oversight for a research study, such as what will be examined to assure subject well-being; the rationale of the plan; who will provide oversight; when oversight will be done; who will be informed of oversight results; what will be done with the findings; overall risk assessment and rationale; data to be reviewed by and acted upon by the research area; composition of the oversight committee and method of reporting; and criteria for stopping the study, unbinding, removing subjects, etc. If the oversight plan is contained within the protocol, this can be referenced.

**research team:** Any faculty, student, resident, lab staff, study coordinator, or other member who helps design and conduct the research project or clinical investigation.

**retrospective study:** A study that allows the investigator to look back at existing data (often collected for reasons other than research, such as administrative databases and medical records) to consider possible correlations where the outcomes are already known, such as for the purpose of estimating an effect or making predictions about a rare outcome.

**reviewing IRB:** The IRB responsible for review and oversight of a research project. Also known as the “IRB of record.”

**reviews preparatory to research:** Reviews of PHI conducted by and within a covered entity to allow analysis of the feasibility of conducting a study or to determine the potential number of patients with a specific disease for inclusion in a grant proposal. These do not usually require IRB approval, as they are not intended to provide generalizable knowledge and do not identify individuals for the purpose of recruitment.

**risk:** The probability of harm or injury (physical, psychological, social, or economic) occurring as a result of participation in a research study.
risk assessment: The careful and thorough cataloging and consideration of factors that could contribute to an unwanted or negative effect in a research study.

royalties: Revenue from intellectual property. In general, the Indiana University Intellectual Property Policy UA-05 requires all right, title, and interest in intellectual property developed while a faculty member is at Indiana University to be assigned to the IU Research and Technology Corporation (IURTC), which manages revenue distribution.

sample: See biospecimen.

scientist: For the purposes of IRB membership, this refers to a member whose primary concerns are in scientific areas; specifically, having had scientific or medical training or experience. Examples of appropriate representation include physicians, nurses, clinicians, and Ph.D.-level physical or biological scientists.

screen failure: Ineligibility of a consented subject for a research study based on the results of a screening process.

screening: Process by which a consented subject undergoes procedures or testing to determine eligibility for a research project.

Secretary: The Secretary of the Department of Health & Human Services (HHS) and any other officer or employee of the department to whom authority has been delegated.

security plan: A document that describes the security measures and processes within the local environment that are used to safeguard the confidentiality, integrity, and availability of research data. A plan typically identifies data inputs and explains the locations of collections of data and the type of data collected. This is typically accompanied by a data flow diagram. In addition, a plan explains the security controls used to protect the data.

serious adverse event (SAE): Any adverse event that results in death; is life-threatening (places the subject at immediate risk of death from the event as it occurred); results in inpatient hospitalization or prolongation of existing hospitalization; results in a persistent or significant disability/incapacity; results in a congenital anomaly/birth defect; or, based upon appropriate medical judgment, may jeopardize the subject’s health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition.

serious problem: For VA research, a serious problem is one that may reasonably be regarded as (1) involving substantive harm, or a genuine risk of substantive harm, to the safety, rights, or welfare of human research subjects, research staff, or others; or (2) substantively compromising the effectiveness of a facility’s human research protection or human research oversight programs.

significant financial interest: Any monetary value based on equity in publicly or nonpublicly traded entities, intellectual property rights, salary, remuneration, or similar payments, and any reimbursed or sponsored travel that accrues to the investigator or the investigator’s family members. For limits and other details, see the IU Policy on Financial Conflicts of Interest in Research (ACA-74).

significant payments of other sorts: For purposes of 21 CFR 54, payments made by the sponsor of a covered study to the investigator or the institution to support activities of the investigator that have a monetary value of more than $25,000, exclusive of the costs of conducting the clinical study or other clinical studies (e.g., a grant to fund ongoing research; compensation in the form of equipment or retainers for ongoing consultation or honoraria), during the time the clinical investigator is carrying out the study and for 1 year following the completion of the study.

significant risk (SR) device research: Per 21 CFR 812.3(m), investigational device that (1) is intended as an implant and presents a potential for serious risk to the health, safety, or welfare
of a subject; (2) is purported or represented to be for a use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject; (3) is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or (4) otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

**source documents**: Original records pertaining to a clinical trial, including hospital records, clinical and office charts, laboratory notes, memoranda, subjects’ diaries, questionnaires, or evaluation checklists, audio and/or video tapes, interview transcripts, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate and complete, microfiches, photographic negatives, microfilm or magnetic media, X-rays, and subject files and records kept at the pharmacy, at the laboratories, and at medico-technical departments.

**sponsor**: An individual, company, institution, or organization that takes responsibility for the initiation, management, and/or financing of a clinical trial. The sponsor does not conduct the investigation

**sponsored email**: An email account established for a non-IU employee for a specific purpose, with limited duration, and with the supervision (sponsorship) of an authorized University employee.

**sponsor-investigator**: An individual who both initiates and actually conducts, alone or with others, a clinical investigation (i.e., under whose immediate direction the test article is administered or dispensed/used).

**standard operating procedures (SOPs)**: At IU, documents that define in detail the underlying policies and the procedures for activities involved in the conduct of research involving human subjects.

**student**: Any individual enrolled for educational credit, including both formal lecture and seminar classes, clinical role courses, independent study courses, and thesis or dissertation projects.

**study site**: The location where any study-related interactions or interventions occur, including the consent process.

**subsequent use**: A second use of a test article with the same or another subject. Subsequent use of a test article at an institution is subject to IRB review and approval.

**suspension**: Temporary cessation of some or all activities in a currently approved research study.

**systematic investigation**: Research development, testing, and evaluation designed to develop or contribute to generalizable knowledge.

**termination**: For purposes of this SOP, this refers to a determination made by the IRB to permanently withdraw approval for some or all activities of a currently approved research study.

**test article**: Any drug for human use, biological product for human use, medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the Food, Drug, and Cosmetic Act or under §351 or §§354-360F of the Public Health Service Act.

**transitional device**: A device that the FDA considered to be a new drug or antibiotic before May 28, 1976.
transnational research: Any human subject research conducted at international sites (not within the United States, its territories, or commonwealths) or research using either human biological specimens or human data originating from an international site.

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.

unanticipated problem involving risks to subjects or others (UPIRTSO): In general, this includes any incident, experience, or outcome that meets all of the following criteria:

1. is unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;

2. is related or possibly related to participation in the research (“possibly related” means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and

3. suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

unapproved medical device: A device that is used for a purpose or condition for which the device requires but does not have an approved application. An unapproved device may be used in human subjects only if it is approved for clinical testing under an application for an investigational device exemption (IDE).

unexpected adverse event (UAE): Any adverse event occurring in one or more subjects participating in a research protocol, the nature, severity, or frequency of which is not consistent with either:

1. the known or foreseeable risk of adverse events associated with the procedures involved in the research that are described in (a) the protocol-related documents, such as the IRB-approved research protocol, summary safeguard statement, any applicable investigator brochure, and the current IRB-approved informed consent document, and (b) other relevant sources of information, such as product labeling and package inserts; or

2. the expected natural progression of any underlying disease, disorder, or condition of the subject(s) experiencing the adverse event and the subject’s predisposing risk factor profile for the adverse event.

use: With respect to individually identifiable health information, the sharing, employment, application, utilization, examination, or analysis of such information within an entity that maintains such information.

viable: As it pertains to the neonate, being able to survive post-delivery (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration.

vulnerable subjects: Persons not capable of appropriately judging the risks/benefits of their participation in a research study due to mental, emotional, or physical impairment. This includes individuals with incurable diseases, persons in nursing homes, unemployed or impoverished persons, patients in emergency situations, ethnic minority groups, homeless persons, refugees, children, persons with developmental disabilities or mental retardation or mental illness,
pregnant women, and those incapable of giving consent or whose capacity for giving informed consent is limited. Other vulnerable persons may include individuals whose willingness to volunteer in a research project may be unduly influenced by the expectation, whether justified or not, of benefits associated with participation, or of a retaliatory response in case of refusal to participate. Examples include students, subordinate hospital personnel, employees of a company, members of the U.S. Armed Forces, and persons in detention (prisoners).

**waiver of authorization:** HIPAA permits waivers of authorization when an Institutional Review Board reviews the request according to the required criteria. This review and approval of waiver of authorization request must be documented. For details, see the SOP on Confidentiality and Privacy.

**ward:** A child who is placed in the legal custody of the State or other agency, institution, or entity, consistent with applicable federal, state, or local law.

**waste:** Biospecimen material originally collected for clinical or diagnostic purposes but that is no longer needed for that purpose.