IU Human Research Protection Program (HRPP) 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.

IU Institutional Review Board (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:

- 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.

**IU HRPP Policies**

Research conducted at IU and its affiliates must be conducted in accordance with IU HRPP Policies. IU HRPP Policies apply the Common Rule protections to all research, with some very minor differences, and apply other relevant requirements based on additional federal regulations, state law, and institutional policy. Each policy includes the following:

- A scope statement which clearly defines the research governed by the policy. All IU HRPP Policies govern research reviewed by the IU IRBs; however, some policies also govern exempt research or research conducted by IU and its affiliates which is reviewed by an external IRB.
- Policy statements which reflect requirements mandated by regulation, policy, or accreditation standards
- Mandatory procedures for implementation of the policy statements, where applicable
- Sanctions
- History, including a summary of the most recent revision
- Related information, including hyperlinks to relevant guidance, regulations, policies, accreditation standards, etc.
## IU HRPP Policies – Overview and application

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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:
  o 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.
  o 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, research personnel 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 study team completes the human subject 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 debarment from engaging in research with human subjects at Indiana University.

5.0 History

Minor corrections to formatting and wording throughout

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
Auditing Human Subjects Research

1.0 Scope
This policy applies to the conduct of human subjects research under the jurisdiction of the IU Human Research Protection Program (HRPP). This includes research under the oversight of the IU IRBs and research for which IU or its affiliates are relying on an external IRB for oversight.

2.0 Policy Statement
Research personnel are expected to fully cooperate with all audits, monitoring visits, and compliance inspections (audits) conducted by IU’s QIO (internal audits) or regulatory agencies, funding agencies, or study sponsors (external audits), including taking appropriate steps to make necessary improvements to align their conduct of research with applicable federal regulations, state laws, and institutional policies.

2.1. Internal audits
QIO staff conduct not-for-cause (scheduled) and for-cause (directed) internal audits of research studies. QIO develops a scheduled audit plan that describes the criteria for selecting and prioritizing research protocols and/or PIs for not-for-cause audits. The scheduled audit plan is reviewed and approved by the IU IRB Executive Committee on a semiannual basis. Scheduled audits may be requested by the IRB or appropriate institutional officials.

2.2. External audits
Research personnel must immediately notify QIO upon notification of an external audit. 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 audit and to coordinate key aspects of any written response to the inspecting agency. Research personnel shall immediately provide to QIO all audit-related correspondence and communications to and from the inspecting agency. Research personnel must respond to both FDA Form
483 and Warning Letter correspondence within 15 business days of receipt; for other FDA correspondence (e.g., Untitled Letters), research personnel must seek guidance from QIO regarding whether a response should be prepared. QIO must review responses prior to their submission to the FDA.

2.3. **IRB review of audit findings**
Findings from audits must be reported to and reviewed by the IRB in accordance with the IU HRPP Policy on Reportable Events.

For internal audits, QIO staff tracks audit findings and prepares periodic summary reports which are presented to the University Director, HRPP, and IRB Executive Committee. Reports describe general audit finding trends, any serious or continuing noncompliance, and any unanticipated problems involving risks to subjects or others determinations made in relation to the audit findings.

### 3.0 Procedures

#### 3.1. **Response to audits**
When an audit report is received, research personnel are expected to respond to all requests. 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.

If the study team fails to respond, the department chair may be contacted for assistance. QIO staff may involve an appropriate IRB or other applicable authority for additional assistance at any time.

For internal audits, research personnel must respond within fourteen (14) days unless an extension is granted by QIO staff. The final report is submitted to the IRB via KC IRB.

#### 3.2. **Research subject to VA regulations**
For-cause audits involving the VA are conducted in cooperation with the local VA research office. Audit findings are promptly shared with the local VA Research Office for audits that include VA subjects.

### 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 debarment from engaging in research with human subjects at Indiana University.

### 5.0 History
Replaces previous IU SOP for Research Involving Human Subjects – Auditing Human Subjects Research (v01/2018)

### 6.0 Related Information
- AAHRPP Standards
  - Element 1.5.A
  - Element 1.5.B
IU HRPP Documents

- Policies
  - Reportable Events
- Guidance
  - Quick Guide: Internal Audits of human subjects research

KC IRB Questionnaires (see KC Crosswalk)

- Reportable Events

Regulatory References

- FDA Information Sheet Guidance for IRBs, Clinical Inspectors, and Sponsors: FDA Inspections of Clinical Investigators (June 2010)
- FDA Compliance Program Guidance Manual, Program 7348.811 – Biomedical Research Monitoring, Clinical Investigators (December 8, 2008)
Children in Research

About This Policy

Effective Date:
07/19/2018

Last Updated:
07/19/2018

Policy Contact:
IU Human Subjects Office
(317) 274-8289
irb@iu.edu

1.0 Scope

This policy applies to the conduct of non-exempt human subjects research involving children under the oversight of the IU IRBs.

This policy does not apply to minors who, under applicable law, may consent on their own behalf.

Per Indiana law, the following minors have authority to consent for themselves:

- Legally emancipated minors;
- Minors at least 14 years old who are not dependent on a parent for support, who live apart from their parents or an individual in loco parentis, and who manage their own affairs;
- Minors who are married; and
- Minors in the military.

In addition, minors have authority to consent for themselves in the following special circumstances and may consent to research that involves only these procedures:

- Minors who are at least 17 years old may donate blood without parental permission.
- Minors who have, suspect they have, or have been exposed to a venereal disease may consent to research related to treatment.

2.0 Policy Statement

Since children cannot legally provide consent for themselves, additional mechanisms must be implemented to ensure conduct of compliant and ethical research. In addition, some children may be vulnerable to coercion or undue influence, requiring additional protections to protect the rights and welfare of these subjects.
2.1. **Categories of research involving children**

The IRB can approve research involving children as research subjects only when it determines the research satisfies the conditions of one or more of the categories outlined below.

**Category 404**: Research not involving greater than minimal risk

Research which the IRB finds to present no more than minimal risk to the children; and adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians.

**Category 405**: Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects

Research which the IRB finds presents more than minimal risk to 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, and:

- the risk is justified by the anticipated benefits to the subjects;
- 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
- adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians.

**Category 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

Research which the IRB finds 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, and:

- 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;
- the intervention or procedure is likely to yield generalizable knowledge about the subjects’ disorder or condition which is of vital importance for the understanding or amelioration of the subjects’ disorder or condition; and
- adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians.

**Category 407**: Research not otherwise approvable

The IRB may approve research which does not meet the requirements of the categories listed above if 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 children.

For federally-funded research which meets this criteria, the DHHS Secretary 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, must determine either:

- that the research in fact satisfies the conditions above; or
- 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; 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.

2.2. **Adequate provisions for soliciting the assent of children**

The IRB may find that all children, some children, or no children are capable of assenting. When the IRB finds children are capable of providing assent, the IRB must also find that adequate provisions are made for soliciting the assent of the children, and determine that the plan for soliciting the assent of the children is appropriate.

The assent of the children is not required if the IRB finds any of the following is true:

- The children are not capable of providing assent based on their age, maturity, or psychological state.
- The capability of the children is so limited that they cannot reasonably be consulted.
- The intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research.

The IRB may waive the assent requirement for some or all children when the IRB determines all of the following criteria are met:

- The research does not involve more than minimal risk to subjects.
- The research could not be practically carried out without the waiver.
- If the research involves using identifiable private information or identifiable biospecimens, the research could not practically be carried out without using such information or biospecimens in an identifiable manner.
- The waiver will not adversely affect the rights and welfare of the subjects.
- When appropriate, subjects will be provided with additional pertinent information after participation.

Research personnel may only approach a child-subject to obtain his/her assent to participate in the research after the parents/guardian have given written permission (unless waived).

When the IRB finds that assent is required, it shall also approve a plan for whether assent will be documented and, if so, the mechanism for documentation.

2.3. **Adequate provisions for soliciting the permission of each child’s parents or legal guardian(s)**

The IRB must find that adequate provisions are made for soliciting the permission of each child’s parents or guardian, when required, and determine that the plan for soliciting the permission of the parent/guardian is appropriate.

- For Categories 404 or 405, the IRB may find that the permission of one parent or guardian is sufficient.
- For Categories 406 and 407, 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.
- Permission by parents or guardians shall be documented in accordance with the IU HRPP Policy on Informed Consent.
- Pursuant to Indiana law IC 16-36-1-5, the IRB may approve, on a case-by-case
basis, that one of the following may consent in lieu of a parent or guardian:
  o An adult sibling if there is no parent or guardian or the parent or guardian is not reasonably available
  o A grandparent of the child if there is no parent or guardian or the parent or guardian is not reasonably available

The IRB may waive the requirement for obtaining parental or guardian permission if:
  • The IRB determines all of the following criteria are met:
    o The research does not involve more than minimal risk to subjects.
    o The research could not be practicably carried out without the waiver.
    o The waiver will not adversely affect the rights and welfare of the subjects.
    o If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable manner.
    o When appropriate, subjects will be provided with additional pertinent information after participation.
  • 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, provided an appropriate mechanism is in place to protect the children, and 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.

2.4. Wards of the state or other agency
Children who are wards of the state or any other agency, institution, or entity can be included in research approved under Categories 406 or 407 only if the IRB finds the research is either:
  • Related to their status as wards; or
  • Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.

For research with wards approved under Categories 406 or 407, the IRB must require appointment of an advocate for each child who is a ward.
  • The advocate serves in addition to any other individual acting on behalf of the child as guardian or in loco parentis.
  • One individual may serve as advocate for more than one child.
  • 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.
  • The advocate must not be associated in any way (except in the role as advocate or member of the IRB) with the research, research personnel, or the guardian organization.

2.5. Research subject to VA regulations
Research involving children must be reviewed carefully by the IRB for its relevance to
the VA and must not be greater than minimal risk. The VA medical facility Director must approve participation in proposed research that includes children.

VA research involving biospecimens or data obtained from children is considered to be research involving children even if de-identified. If the biospecimens or data were previously collected, they must have been collected under applicable policies and ethical guidelines.

VA research personnel cannot conduct interventions in research that enrolls newborns within four weeks of birth while on official duty, at VA facilities, or at VA-approved offsite facilities. Prospective observational and retrospective record review studies that involve neonates or neonatal outcomes are permitted.

3.0 Procedures

3.1. IRB submission and review
For studies proposing to enroll children, the study team completes the IRB application and provides protocol-specific information related to research with children. The study team makes the initial determination regarding the appropriate categories of research involving children in which the research falls, including justification as to why the categories were selected. In addition, the study team provides 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. The IRB considers the information in the IRB application and documents its determinations, as appropriate.

3.2. Assent of children
In deciding whether children are capable of assenting, the IRB shall take into account the ages, maturity, psychological status, and health condition of the children involved. The IRB’s findings may apply to all or some of the children involved in the research.

When the IRB finds that assent is required and a child expresses a wish to decline participation in research, the child’s decision prevails, even if his/her parents or guardian have granted permission.

3.3. Permission from parents/guardians
If permission from both parents/guardians is required but an exception applies, the study team must document the exception. A study team can find that a parent/guardian is not reasonably available after the study team has made and documented repeated attempts to contact the parent/guardian 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 parents/guardians are not reasonably available.

If a parent or guardian is not reasonably available to provide consent for a potential subject, and the study team believes that allowing an adult sibling and/or grandparent would provide reasonable protections for that potential subject, the study team may submit a subject-specific request to the IRB that the sibling or grandparent provide consent for the particular subject and provide appropriate justification.

3.4. 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, the subject’s participation in the research is no longer covered by this policy, and the permission granted by the parent/guardian for the minor to participate is no longer valid for continued participation.

- All research procedures with the now-adult subject, including interactions and interventions and collection of identifiable private information, must immediately cease.
- Research personnel must seek and obtain informed consent for the now-adult subject’s continued participation in the research, or request a waiver of informed consent, as described in the IU HRPP Policy on Informed Consent.

3.5. Pregnant minors in Indiana

In Indiana, pregnant minors cannot, by virtue of their pregnant status alone, consent on their own behalf to participate in research. Please note that although pregnant minors cannot consent for their own participation in research, once the child is born, the mother, even if she is still a minor, is the appropriate person to consent for her child to participate in research.

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 debarment from engaging in research with human subjects at Indiana University.

5.0 History

Replaces portions of the IU SOP for Research Involving Human Subjects – Vulnerable Populations (v2/2017)

6.0 Related Information

AAHRPP Standards
- Element II.3.F
- Element II.3.G
- Element II.4.A
- Element II.4.B
- Element III.1.F

IU HRPP Documents
- Policies
  - Informed Consent
  - IRB Review Process
- Guidance
  - N/A

KC IRB Questionnaires (see KC Crosswalk)
- Questionnaire G1 – Children
- Questionnaire J – Child Assent & Parental Consent Process

Regulatory References
- 21 CFR 50 Subpart D, §§ 50.50-50.56
- 45 CFR 46 Subpart D, §§ 46.401-46.409
- Indiana Code 16-36-1-3
- OHRP Guidance:
  - Children as Research Subjects and the HHS “407” Process
  - Children: Information on Special Protections for Children as Research Subjects
  - Research with Children FAQs
- VHA Handbook 1200.05 – Requirements for the Protection of Human Subjects in Research, especially section 19
Conflict of Interest Reporting to the IRB

About This Policy

Effective Date: 07/19/2018

Last Updated: 07/19/2018

Policy Contact:
IU Human Subjects Office
(317) 274-8289
irb@iu.edu

1.0 Scope
This policy applies to the conduct of human subjects research under the jurisdiction of the IU Human Research Protection Program (HRPP). This includes research under the oversight of the IU IRBs and research for which IU and its affiliates are relying on an external IRB for oversight.

2.0 Policy Statement
The institution and all individuals conducting human subjects research must report financial relationships related to research and, where appropriate, cooperate in the management of any potential conflicts of interest.

2.1. Annual disclosure of individual financial interests in research disclosure
IU faculty, staff, and students responsible for the design, conduct, or reporting of IU research (i.e., key personnel) must disclose significant financial interests in accordance with the IU policy on Financial Conflicts of Interest in Research annually or when interests change or new interests occur.

2.2. Protocol-specific COI disclosure
For each protocol, the Principal Investigator (PI) is responsible for reporting any potential financial interest to the IU Human Subjects Office (HSO), regardless of financial value, held by research personnel or immediate family member which could affect or be affected by the research.

2.3. Institutional financial interests
All IU intellectual property and investment is held and managed by the IU Innovation and Commercialization Office (ICO). All major gifts to IU and investments of the Indiana University Foundation (IUF) are held and managed by the IUF. IUF and ICO are committed in principle and practice to respecting and maintaining the autonomy of IU’s
research integrity and operations in general and to its HRPP in particular, and are committed to non-interference with the IU HRPP.

For each protocol, the PI must report any institutional conflict of interest which could affect or be affected by the research. IURTC and IUF are committed to providing relevant information as requested by the IRB in support of its reviews and deliberations.

3.0 Procedures

3.1. Annual disclosure of individual financial interests in research disclosure
For IU faculty, staff, and students, the process for annual disclosure of individual financial interests in research is facilitated by the IU Conflicts of Interest Office. Any management plans established to manage a disclosed interest related to a human subjects protocol are made available to the IRB. See the Office of Research Compliance website for detailed procedures.

Disclosures from non-IU research personnel which include outside interests are forwarded to the HSO for review by the IRB.

3.2. Protocol-specific conflict of interest disclosure
Protocol-specific potential financial interests are reported in the IRB application. Conflict of interest reporting for non-affiliated individuals whose institutions have agreed to rely on the IU IRB for oversight of their participation in research is conducted in accordance with the associated reliance agreement for the protocol.

3.3. Institutional conflicts of interest
Institutional conflicts of interest are reported on a protocol-specific basis in the IRB application. If an institutional conflict of interest is reported, the IU HSO will notify appropriate institutional officials and IRB review will not proceed until the conflict has been mitigated and/or managed appropriately.

3.4. IRB review of conflicts of interest
HSO staff confirm all key personnel have appropriately submitted annual disclosures as described above at initial submission and renewal, if required.

If research personnel indicates in the IRB application that he or she has a financial interest which could affect or be affected by the research, the IRB evaluates the interest as it relates to the research, including reviewing any COI Office or COI Committee determinations, and determines whether the management plan is appropriate and whether additional action is required to protect human subjects. Additional action may include:

- Appropriate language regarding the interest in the informed consent statement
- An independent investigator to obtain consent
- An independent investigator to conduct the study
- Independent safety monitoring
- Renewal or review at an interval less than one year
- Any other restrictive action deemed appropriate based on the nature of the conflict.
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 debarment from engaging in research with human subjects at Indiana University.

5.0 **History**

Replaces the IU SOP for Research Involving Human Subjects – Conflict of Interest Reporting to the IRB (v07/2015).

6.0 **Related Information**

**AAHRPP Standards**
- Element 1.6.A
- Element 1.6.B
- Element III.1.B

**IU HRPP Documents**
- Policies
  - N/A
- Guidance
  - N/A

**KC IRB Questionnaires (see KC Crosswalk)**
- Conflicts of Interest Questionnaire

**Regulatory References**
- [IU Policy on Financial Conflicts of Interest in Research](#)
Emergency Research Requesting Exception from Informed Consent (EFIC)

1.0 Scope
This policy applies to the conduct of all non-exempt human subjects research under the oversight of the IU IRBs when research personnel request exception from informed consent (EFIC).

This policy is not applicable to research subject to VA regulations or research subject to Department of Defense (DoD) regulations unless a waiver is obtained from the U.S. Secretary of Defense.

2.0 Policy Statement
The IRB may approve research without requiring that informed consent of all research subjects be obtained, if the IRB finds the following:

- The research is subject to FDA regulations.
- 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.
- Obtaining informed consent is not feasible because:
  - The subjects will not be able to give their informed consent as a result of their medical condition;
  - The intervention under investigation must be administered before consent from the subjects’ legally authorized representative (LAR) is feasible; and
  - There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the research.
- Participation in the research holds out the prospect of direct benefit to the subjects because:
  - Subjects are facing a life-threatening situation that necessitates intervention;
• 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
• 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.

• The research could not practicably be carried out without the waiver.
• 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 must summarize efforts made to contact LARs and make this information available to the IRB at the time of renewal.
• Informed consent consistent with the IU HRPP Policy on Informed Consent will be obtained and documented from subjects or their LARs when feasible.
• Procedures and information exist which provide an opportunity for a family member to object to a subject’s participation in the research in accordance with this policy.
• Additional protections of the rights and welfare of the subjects are provided, including, at least all of the following:
  o Consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the research will be conducted and from which the subjects will be drawn;
  o Public disclosure to the communities in which the research will be conducted and from which the subjects will be drawn, prior to initiation, of plans for the research and its risks and expected benefits;
  o Public disclosure of sufficient information following completion of the research to apprise the community and researchers of the study, including the demographic characteristics of the research population, and its results;
  o Establishment of an independent data monitoring committee to oversee the research; and
  o If obtaining informed consent is not feasible and a LAR 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 research. The investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review. Please note that, for Indiana subjects, all family members may serve as LAR per Indiana law and IU HRPP Policy; as such, this provision is not applicable to Indiana subjects.

2.1. Informing subjects after enrollment
The IRB must ensure procedures are in place to inform, at the earliest feasible opportunity, each subject or, if the subject remains incapacitated, his/her LAR, of the following:
• That the subject was enrolled in the research
• The details of the research
• Other information contained in the informed consent document
• 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 a LAR or family member is told about the research and the subject’s condition improves, the subject is also to be informed as soon as feasible.

If the subject dies before an LAR or family member can be contacted, information about the research is to be provided to the subject’s LAR or family member, if feasible.

3.0 Procedures

3.1. IRB submission and review
For studies enrolling subjects without informed consent pursuant to this policy, the study team completes the IRB application and provides protocol-specific information related to the determinations required by 2.0 above. The IRB considers the information in the IRB application and documents its determinations as appropriate.

3.2. Federally-funded research
If the IRB determines the research is not also subject to FDA regulations, the IRB must report to OHRP that the conditions outlined in 2.0 above have been met. This policy is not applicable to federally-funded research which involves pregnant women, human in vitro fertilization, or prisoners.

3.3. Research subject to FDA regulations
The research 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.

If the IRB determines that the criteria required by 2.0 above are not met, or that the research cannot be approved due to other relevant ethical concerns, the IRB must document its findings and provide these findings promptly in writing to the PI and to the sponsor. 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.

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 debarment from engaging in research with human subjects at Indiana University.

5.0 History
Replaces IU SOP for Research Involving Human Subjects – Planned Emergency Research (v02/2017)

6.0 Related Information
AAHRPP Standards
- Element II.4.C.
IU HRPP Documents
  • Policies
    o Informed Consent
  • Guidance
    o N/A

KC IRB Questionnaires (see KC Crosswalk)
  • Questionnaire H – Informed Consent Process

Regulatory References
  • 21 CFR 50.24
  • FDA Guidance for Institutional Review Boards, Clinical Investigators, and Sponsors: Exception from Informed Consent Requirements for Emergency Research (April 2013)
  • Informed Consent Requirements in Emergency Research (OPRR Letter, 1996)
Emergency Use of Investigational Test Articles

1.0 Scope
This policy applies to clinicians under the jurisdiction of the IU Human Research Protection Program (HRPP) using a non-FDA approved or non-FDA cleared test article when all of the following are true:

- The potential patient is in a life-threatening situation.
- No standard acceptable treatment is available.
- There is not sufficient time to obtain IRB approval.

This policy does not apply to off-label use of an FDA-approved test article.

2.0 Policy Statement
A clinician may use a test article without prospective IRB review and approval if the following conditions apply:

- The potential patient is in a life-threatening situation.
- No standard acceptable treatment is available.
- There is not sufficient time to obtain IRB approval.

Any subsequent use of the test article at the institution is subject to IRB review.

2.1 Informed consent
The clinician must obtain prospective, written informed consent from the patient or the patient’s legally authorized representative (LAR) in accordance with IU HRPP Policy on Informed Consent.

An exception to the informed consent requirement may apply if both the treating clinician and a physician who is not otherwise associated with the use of the test article
certify in writing all of the following:

- The patient is confronted by a life-threatening situation necessitating the use of the test article.
- Informed consent cannot be obtained because of an inability to communicate with or obtain legally effective consent from the patient.
- Time is not sufficient to obtain consent from the patient’s LAR.
- No alternative method of approved or generally recognized therapy is available that provides equal or greater likelihood of saving the life of the patient.

If, in the clinician's opinion, immediate use of the test article is required to preserve the life of the patient and time is not sufficient to obtain the independent determination regarding exception to the informed consent requirement in advance, the determination shall be made by the clinician 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 use of the test article.

3.0 Procedures

3.1. Emergency use procedures
During regular business hours, the clinician must contact the IU Human Subjects Office (HSO) and consult with staff regarding whether an existing IRB-approved protocol would allow use of the test article, whether an Investigational New Drug application (IND) or Investigational Device Exemption application (IDE) from the FDA is needed, and whether the situation allows for sufficient time to obtain IRB approval.

Outside of regular business hours, or if IU HSO is not available, the clinician may use the test article under this policy, carefully documenting the following:

- The conditions for emergency use specified in 2.0 are met.
- Consent was obtained and documented in accordance with the IU HRPP Policy on Informed Consent, unless the exception from informed consent requirements described in 2.1 above applies.

3.2. Reporting to the IRB
Use of a test article under this policy must be reported to the IRB within five (5) business days. The clinician must submit notification via a KC IRB Emergency Use submission and provide the following information:

- A full description of the situation, including justification for the emergency use;
- 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;
- A full description of the procedure(s) employed; and
- A description of the consent process used, including an unsigned copy of the informed consent document.

When the HSO receives notification of an emergency use that has taken place, an IU HSO Associate Director or the University Director, HRPP, review the report to determine if the use complied with FDA and institutional requirements. If requirements were met, an acknowledgement letter is sent to the clinician. If it is determined that requirements were not met, the matter is handled according to the noncompliance procedures delineated in the IU HRPP Policy on Reportable Events.
Use of the exception from informed consent requirements described in 2.1 above must be reported to the IRB within five (5) business days. The clinician must submit notification via KC IRB and provide the documentation from both the clinician and the physician who is not participating in the clinical investigation.

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 debarment from engaging in research with human subjects at Indiana University.

5.0 **History**
Replaces the IU SOP for Research Involving Human Subjects – Emergency Use of Investigational Test Articles (v02/2017).

6.0 **Related Information**

**AAHRPP Standards**
- Element I.7.A
- Element I.7.C

**IU HRPP Documents**
- Policies
  - Informed Consent
  - Reportable Events
- Guidance
  - N/A

**KC IRB Questionnaires (see [KC Crosswalk](#))**
- Emergency Use

**Regulatory References**
- 21 CFR 50.23(a)
- 21 CFR 56, especially 56.102(d), 56.104(c)
- 45 CFR 46.116(f)
- FDA Guidance: [Emergency Use of an Investigational Drug or Biologic – Information Sheet](#)
Exempt Research

About This Policy

Effective Date:
03/29/2018

Last Updated:
07/19/2018

Policy Contact:
IU Human Subjects Office
(317) 274-8289
irb@iu.edu

1.0 Scope
This policy applies to the conduct of human subjects research granted exemption under 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 personnel 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 described by federal regulations
Research activities in which the only involvement of human subjects will be in one or more of the following categories, described at 45 CFR 46.101(b), are exempt from IRB review unless noted below.

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 research personnel participate 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 research personnel do 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 research personnel 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, research personnel 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 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 research personnel 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
research personnel do 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 research personnel 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 research personnel 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
research personnel have 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 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 Procedures

#### 3.1. Human subject submission and review

For proposed exempt research, the study team provides protocol-specific information via the human subjects application and submits the following additional materials, as applicable:

- Data collection instruments, including surveys, questionnaires, interview questions, etc.
- Recruitment methods and materials
- Other documents as applicable, e.g., letters of cooperation from research sites
- Grant proposal, if the research is subject to VA regulations and the IU investigator is the direct recipient of the funds

#### 3.2. 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.

If the research is subject to HIPAA and research personnel request a waiver of authorization, 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.

3.3. **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.

Research personnel request review of substantive changes by submitting an
amendment via KC IRB. 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,
research personnel will be notified. If the changes result in the research no longer
qualifying for exemption, research personnel will be notified accordingly and
instructed to submit an appropriate expedited or full board IRB submission.

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

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
debarment from engaging in research with human subjects at Indiana University.

5.0 **History**
Minor corrections to formatting and wording throughout; revision regarding submission of
grant application

6.0 **Related Information**
AAHRPP Standards
- Element I.1.D
- Elements II.2.A
- Element II.2.B

IU HRPP Documents
- Policies
  - N/A
- Guidance
  - Exempt Studies
KC IRB Questionnaires (see KC Crosswalk)

- Exempt Research

Regulatory References

- 45 CFR 46, especially 46.101(b)
- OHRP Guidance:
  - Exempt Research and Research that May Undergo Expedited Review
  - Exemptions for Public Benefit and Service Programs
- VHA Handbook 1200.05 – Requirements for the Protection of Human Subjects in Research, especially Appendix A
Humanitarian Use Devices

About This Policy

Effective Date:
07/19/2018

Last Updated:
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Policy Contact:
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1.0 Scope

This policy applies to clinicians under the oversight of the IU IRBs wishing to use a Humanitarian Use Device (HUD) for treatment or diagnosis, and the IU IRBs approving the use of the HUD.

This policy does not apply to clinical investigational use of a HUD (see Figure 1). Use of a HUD is considered to be part of a clinical investigation if safety and effectiveness data will be collected on the HUD for the purpose of supporting a premarket approval (PMA) application. If use of a HUD is considered part of a clinical investigation, the use is considered research and research personnel must follow all policies and procedures applicable to human subjects research.

This policy does not apply to situations in which use of a HUD is necessary to save the life or protect the well-being of a patient and there is not sufficient time to request IRB approval (see Figure 1). In these situations, clinicians must follow the procedures outlined in the IU HRPP Policy on Emergency Use of Investigational Test Articles.

2.0 Policy Statement

A HUD may only be administered in facilities under the oversight of an IRB acting in accordance with 21 CFR 56, including continuing review of the device, and only when use of the HUD has been approved by the IRB. In order to utilize a HUD for treatment or diagnosis, IRB approval must be obtained prior to use. Once approved, the HUD may be used only for the indications approved by the IRB.

In reviewing a request for HUD use, the IRB must consider the risks to patients as described in the product labeling, ensure the risks are minimized, and evaluate whether the risks are reasonable in relation to the proposed use of the device. The IRB has the discretion to approve use of the HUD for off-label indications given sufficient justification from the clinician(s).
3.0 Procedures

3.1 IRB submission and review
The use of a HUD must be initially reviewed at a convened IRB meeting and approved before the device can be used. To facilitate initial review, the HUD application must be submitted via KC IRB, with the following documentation attached:
- The HUD manufacturer’s product labeling, clinical brochure, and/or other pertinent manufacturer informational materials
- HUD manufacturer’s patient information packet, if available, which should be provided to patients
- The FDA HDE approval letter

Research informed consent and authorization documents are not applicable and should not be submitted, as use of a HUD under this policy is not considered research.

All facilities which will utilize the HUD must be listed on the Protocol tab in KC IRB, and any clinician wishing to access the device must be listed on the Personnel Tab in KC IRB.
3.2. **Continuing review**
The IRB must conduct continuing review/renewal of the use of the HUD within the appropriate time frame as specified by the IRB at time of initial review, or use of the HUD must cease until such time that it can be reviewed. Renewal information must be submitted via KC IRB and review may be conducted via the expedited procedure.

Clinicians should track and report the following at the time of renewal:
- The number of patients who received the HUD for all clinicians listed on the protocol since the last review
- Summary of 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 HUD manufacturer’s product labeling, clinical brochure, and/or other pertinent manufacturer informational materials
- Summary of actual benefits experienced by enrolled HDE patients
- Any relevant information, published or unpublished, since the last IRB review, that may impact patient safety or continued use of the HUD, especially information about the risks associated with the HUD. Relevant information may include literature publications, audits, patient complaints, or interim findings.

3.3. **Modifications to the HUD or device labeling**
If modifications to the initial IRB approval are needed to allow for additional indications, either FDA-approved or justified by the clinicians, the clinician(s) should submit an amendment to the existing protocol via KC IRB describing the modifications and the rationale.

3.4. **Reportable events**
Reportable Events must be reported to and reviewed by the IRB in accordance with the IU HRPP Policy on Reportable Events.

4.0 **Sanctions**
Individuals found to be in violation of this policy may be subject to sanctions related to the clinical use of the HUD at Indiana University’s affiliates, including withdrawal of IRB approval.

5.0 **History**
Replaces IU SOP for Research Involving Human Subjects - Humanitarian Use Devices (v02/2017)

6.0 **Related Information**

**AAHRPP Standards**
- N/A

**IU HRPP Documents**
- Policies:
  - Reportable Events
  - Emergency Use of Investigational Test Articles
- Guidance
  - N/A
KC IRB Questionnaires (see KC Crosswalk)
- Humanitarian Use Device

Regulatory References
- 21 CFR 814.124
- FDA Guidance: Humanitarian Device Exemption (HDE) Regulation: Questions and Answers; Guidance for HDE Holders, Institutional Review Boards (IRBs), Clinical Investigators, and Food and Drug Administration Staff (July 8, 2010)
Informed Consent

1.0 Scope
This policy applies to the conduct of non-exempt human subjects research under the oversight of the IU IRBs.

2.0 Policy Statement
Research personnel may not involve human subjects in research unless the legally effective informed consent has been obtained from the subject or the subject’s legally authorized representative (LAR). Exception to this policy requires that the IRB grant a waiver or modification of the informed consent requirement.

- Research personnel shall seek informed consent from the prospective subject or LAR only under circumstances that provide sufficient opportunity to discuss and consider whether to participate and that minimize the possibility of coercion or undue influence.
- The information that is given to the prospective subject or LAR (whether orally or in writing) shall be in language understandable to the subject or LAR.
- The prospective subject or the LAR must be provided with the information that a reasonable person would want to have in order to make an informed decision about whether to participate, and an opportunity to discuss that information.
- The informed consent form, as a whole, must present information in sufficient detail relating to the research, and must be organized and presented in a way that does not merely provide lists of isolated facts, but rather facilitates the prospective subject’s or LAR’s understanding of the reasons why one might or might not want to participate.
- The informed consent form cannot include any exculpatory language through which the subject or LAR is made to waive or appear to waive any of the subject’s legal rights, or that releases or appears to release research personnel, the sponsor, the institution, or its agents from liability for negligence.
Screening
Prospective subjects’ informed consent is not required for screening, recruiting, or determining eligibility of potential subjects when research personnel obtain information from the subjects through oral or written communication (i.e., interaction with potential subjects) or access identifiable records or stored biospecimens. HIPAA authorization may be required for these activities. Screening interventions (e.g., physical procedures such blood draws, imaging, etc.) that are being conducted solely for the purposes of the research project must be completed only after subjects have provided informed consent.

2.1. Elements of informed consent
Unless altered or waived by the IRB, the following information shall be provided to each prospective subject or LAR. The IRB may require that additional information 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.

- A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject’s participation, a description of the procedures to be followed, and identification of any procedures that are experimental
- 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
- A description of any benefits to the subject or to others that may reasonably be expected from the research
- A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject
- A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained, including a statement that notes the possibility that specific regulatory authorities (e.g., HHS, FDA, ED, DoD, DOJ), as applicable, may inspect the records
- For research involving more than minimal risk, an explanation as to whether any compensation and any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained
- An explanation of whom to contact for answers to pertinent questions about the research and research subjects’ rights, and whom to contact in the event of a research-related injury to the subject
- 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.
- One of the following statements about any research that involves the collection of identifiable private information or identifiable biospecimens:
  - A statement that identifiers might be removed from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the subject or LAR, if this might be a possibility; or
  - A statement that the subject’s information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies.
Unless altered or waived by the IRB, one or more of the following additional elements shall also be provided to each subject or the LAR, when appropriate:

- 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
- Anticipated circumstances under which the subject’s participation may be terminated by the investigator without regard to the subject’s or LAR’s consent
- For studies involving payment for subject participation, a payment statement explaining details and any conditions of payment
- Any additional costs to the subject that may result from participation in the research
- The consequences of a subject’s decision to withdraw from the research and procedures for orderly termination of participation by the subject
- A statement that significant new findings developed during the course of the research that may relate to the subject’s willingness to continue participation will be provided to the subject
- For greater than minimal risk research, the approximate number of subjects involved in the study
- A statement that the subject’s biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit
- For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (i.e. sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen)

The following information must be provided when applicable:

- When seeking informed consent for applicable clinical trials, as defined in 42 U.S.C. 282(j)(1)(A), the following statement notifying the subject that clinical trial information has been or will be submitted for inclusion in the clinical trial registry databank under paragraph (j) of section 402 of the Public Health Service Act: “A description of this clinical trial will be available on 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.”
- If research personnel have a financial interest related to a research study, a statement regarding the financial interest
- For studies where a Certificate of Confidentiality has been granted, including any study funded by the NIH, a statement regarding Certificate of Confidentiality protections (see IU HRPP Policy on Research Data Management)
- If the research involves genetic information, statement describing the protections provided by Genetic Information Nondiscrimination Act (GINA) of 2008
- If the radiation/radioactive materials in addition to what is used for standard clinical treatment are used for research purposes, radiation risk language.
- 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 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.
Research which is federally-funded
For federally-funded research, the informed consent document must also:
- Begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject or LAR in understanding the reasons why one might or might not want to participate in the research, or the IRB must find that the informed consent document is concise as written
- Include a statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects and, if so, under what conditions

Research subject to VA regulations
The VA consent document must also include the following:
- A statement that, in the event of a research-related injury, the VA will provide necessary medical treatment
- 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.
- 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 the VA. The IRB cannot waive informed consent to take a photograph, video, and/or audio recording.

Research subject to Department of Justice (DOJ) regulations
For research funded by the National Institute of Justice, the consent document must also include the following:
- The name(s) of the funding agency(ies)
- Statement 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 kept confidential, 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.
- Statement indicating that confidentiality can be broken only if the subject reports immediate harm to subjects or others

For research conducted within the Bureau of Prisons, the consent document must also include the following:
- Identification of the investigators
- Anticipated uses of the results of the research
- 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 (e.g., the inmate will be returned to regular assignment or activity by staff as soon as practicable)
- Statement regarding the confidentiality of the research information and exceptions to any guarantees of confidentiality required by federal or state law
(e.g., 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)

- Statement that participation in the research project will have no effect on the inmate subject’s release date or parole eligibility

### 2.2. Waiver or alteration of informed consent

The IRB may waive the requirement to obtain informed consent, or approve a consent procedure that omits some, or alters some or all, of the elements of informed consent if the IRB determines all of the following criteria are met:

- The research involves no more than minimal risk to the subjects
- The research could not practically be carried out without the requested waiver or alteration
- If the research involves using identifiable private information or identifiable biospecimens, the research could not practically be carried out without using such information or biospecimens in an identifiable manner
- The waiver or alteration will not adversely affect the rights and welfare of the subjects
- Whenever appropriate, the subjects or LARs will be provided with additional pertinent information after participation.

**Research or demonstration projects:**

The IRB may also waive the requirement to obtain informed consent, or approve a consent procedure that omits some, or alters some or all, of the elements of informed consent if the IRB determines all of the following criteria are met:

- 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: (i) public benefit or service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs
- The research could not practically be carried out without the waiver or alteration

**Emergency research requesting exception from informed consent (EFIC)**

The IRB may approve research 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 and for whom informed consent cannot be sought due to their medical condition and unavailability of legally authorized representative. See the IU HRPP Policy on Emergency Research Requesting Exception from Informed Consent for additional information.

**Waiver or alteration for research subject to FDA-regulations**

Pursuant to FDA Guidance “IRB Waiver or Alteration of Informed Consent for Clinical Investigations Involving No More than Minimal Risk to Human Subjects: Guidance for Sponsors, Investigators, and Institutional Review Boards” (July 2017), the IRB may waive the requirement to obtain informed consent, or approve a consent procedure that omits some, or alters some or all, of the elements of informed consent if the IRB determines all of the following criteria are met:

- The research involves no more than minimal risk to the subjects
• The research could not practicably be carried out without the requested waiver or alteration
• The waiver or alteration will not adversely affect the rights and welfare of the subjects
• If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable manner
• Whenever appropriate, the subjects or LARs will be provided with additional pertinent information after participation

**Exception for research subject to FDA-regulations**

An exception to the informed consent requirement may be made if both the investigator and a physician who is not otherwise participating in the clinical investigation certify in writing all of the following:

• The subject is confronted by a life-threatening situation necessitating the use of the test article
• Informed consent or authorization cannot be obtained because of an inability to communicate with or obtain legally effective consent or authorization from the subject
• Time is not sufficient to obtain consent or authorization from the subject’s legally authorized representative
• No alternative method of approved or generally recognized therapy is available that provides equal or greater likelihood of saving the life of the subject

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, 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.

Use of this exception must be reported to the IRB within five (5) business days. The investigator must submit notification via KC IRB and provide the documentation from both the investigator and the physician who is not participating in the clinical investigation.

**Research subject to Department of Defense (DoD) regulations**

When the research meets the DoD definition of “research involving a human being as an experimental subject,” (see IU HRPP Definitions), the IRB may not waive the informed consent process 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.

**2.3. Documentation of informed consent**

Unless waived by the IRB, informed consent is documented by the use of an approved, written consent document, signed and dated by the prospective subject or prospective subject’s LAR at the time of consent. A copy is given to the person signing the form.

The informed consent document may be either of the following:

• A written informed consent document approved by the IRB that meets the
requirements of this policy. Research personnel shall give either the subject or the subject’s LAR adequate opportunity to read the informed consent document before it is signed; alternatively, this form may be read to the subject or the subject’s LAR.

- When enrolling subjects who do not read English, a short form written informed consent document stating that the elements of informed consent required by 45 CFR 46.116 were presented orally to the subject or the subject’s LAR.
  - The IRB approves a written summary of what is to be said to the subject or LAR.
  - A witness who is conversant in both languages observes the oral presentation.
  - The short form is signed by the subject or the subject’s LAR.
  - The impartial witness signs both the short form and a copy of the summary.
  - The person actually obtaining consent signs a copy of the summary.
  - A copy of the summary is given to the subject or the subject’s LAR, in addition to a copy of the short form.

The IRB may waive the requirement for research personnel to obtain a signed informed consent document for some or all subjects if the IRB determines either of the following criteria are met:

- That the only record linking the subject and the research would be the informed consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject (or LAR) is asked whether the subject wants documentation linking the subject with the research, and the subject's wishes govern.
- 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.

In cases in which the documentation requirement is waived, the consent process must include all elements listed in Section 2.1. The IRB may require research personnel to provide subjects or LARs with a written statement regarding the research.

**Research subject to FDA regulations**

The IRB may waive the requirement that the subject or the subject’s LAR sign a written consent document only if the IRB determines 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.

### 3.0 Procedures

#### 3.1. IRB submission and review

The study team describes the informed consent process in the IRB application and provides an informed consent document for the IRB’s review and approval, when appropriate. The IRB reviews the information and ensures that all requirements consistent with this policy are met.

Upon approval, the informed consent document is electronically stamped. For research regulated by the VA, the informed consent document must indicate the date of approval.
3.2. Informed consent process
Informed consent is more than just a signature on a form. It is an ongoing process of information exchange that provides the prospective subject or subject’s LAR with adequate information pertaining to the research study; sufficient opportunity to consider aspects of the research, including the risks and benefits, and whether to participate; and the opportunity for the subject to ask questions and receive answers to those questions, thus minimizing the possibility of coercion or undue influence.

The informed consent process is often conducted via a conversation between the study team and the prospective subject or subject’s LAR, unless the IRB approves a consent process which does not include a conversation. The informed consent document provides a guide for the informed consent conversation and provides the subject/LAR with information which can be referenced later. If the informed consent conversation cannot be conducted face-to-face, the informed consent process may be conducted over the telephone or via other electronic means. The subject must be provided with a copy of the informed consent document prior to the conversation so they can review during the discussion.

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, 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.

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

3.3. Documentation of informed consent
Unless the IRB grants a waiver of documentation of informed consent as described above, informed consent must be documented as follows:

- Subjects who are willing to participate in research must sign a copy of the IRB-approved and electronically stamped informed consent document prior to participating in research procedures.
  - Signature may be provided via physical, “wet” signature, a physical or digital copy of a wet signature, or verified electronic signature via encrypted digital signature, electronic signature pad, voice print, digital fingerprint, or signature made with a fingerprint on a touchscreen.
  - For VA research, consent may be documented electronically so long as the informed consent process provides reasonable assurance that such consent is rendered by the proper individual and the subject dates the consent as is typical, or the software provides the current date when signed.
  - If the consent conversation is not conducted face-to-face, the subject may fax or email a signed copy of the informed consent document to the research site (preferably to the interviewer and/or research personnel). Unless the IRB approves otherwise, the study team must receive a copy of the signed informed consent document prior to beginning research procedures.
If the subject is physically unable to provide a signature, he/she makes a mark on the informed consent document and the study team must document the circumstances. If the subject is unable to make a mark, an impartial witness must witness the documentation process and sign the consent document.

- The subject (or LAR) must enter the date of signature on the consent document. The subject’s research record and/or medical record should document that the consent process occurred prior to participation in the research.
- The person conducting the consent discussion must also sign and date the informed consent document as the “person obtaining consent”. The signature of the PI is not required on the informed consent document, unless he/she is the person conducting the consent discussion.

3.4. Informed consent procedures for subjects who cannot read English

- The consent conversation and informed consent document must be in a language understandable to the subject (e.g., in the subject’s first language or a language in which the subject is fluent).
- If research personnel plan to enroll non-English-reading individuals, plans for language-appropriate consent procedures are considered and described in the IRB submission. If a non-English informed consent document is provided for IRB review and approval, the IRB requires certification that the translated documents are complete and accurate translations.
- If a non-English-reading subject is unexpectedly encountered and a translated informed consent document cannot be provided, the subject may be enrolled through oral presentation of the informed consent information in conjunction with a short form written consent document.
  - The oral presentation and the short form must be in a language understandable to the subject. A translator may be used to help conduct the oral presentation.
  - 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 45 CFR 46.116 have been presented orally to the subject or the subject’s LAR, and that key information was presented to the subject first, before other information, if any, was provided.
  - A witness, other than the person obtaining consent, must observe the oral presentation. The witness must be conversant in both English and the language of the subject. The translator may serve as the witness.
  - An IRB-approved written summary of information to be presented orally must be available for use during the oral presentation. The IRB-approved English informed consent document serves as the summary.
  - The subject or the subject’s LAR signs the short form consent document.
  - The witness signs both the short form consent document and a copy of the summary.
  - The person actually obtaining consent signs a copy of the summary.
  - A copy of the signed short form consent document and summary are given to the subject or the subject’s LAR.
  - The informed consent process is documented in the subject’s records. The translator or other appropriate individual should be part of the ongoing communication throughout the research study and must be conversant in both English and the language of the subject.
3.5. **Informed consent procedures with special populations**
Certain populations of subjects (including children, prisoners, pregnant women, and individuals lacking consent capacity) require additional protections regarding their consent to participate in a research study. Please see applicable IU HRPP Policies for additional consent requirements when involving these populations in research.

For further information about Informed Consent procedures in transnational research, please see the IU HRPP Guidance on transnational research.

3.6. **Revisions to the informed consent document**
Revisions to the informed consent document must be reviewed and approved by the IRB prior to implementation.

- Newly enrolled subjects must sign the most recently approved version of the informed consent document.
- When submitting a revised informed consent document for IRB review and approval, the study team must notify the IRB whether previously-enrolled subjects will be notified of the new information and, if so, the timing and mechanism of the notification. The IRB will consider the study team’s plan for notification and ensure its appropriateness.
- If the study team is aware of new or increased risks that are not reflected in the IRB-approved informed consent document, study teams must not enroll new subjects until the revised informed consent document incorporating these risks is reviewed and approved by the IRB.
- If the IRB agrees that previously-enrolled subjects must be re-consented using the new informed consent document, the re-consent process should be documented and a note made in the subject’s record when the re-consent process is completed. Any previously signed consent documents must be retained and not discarded.

3.7. **Subject withdraw from research**
If a subject wishes to discontinue participation in the research, data collected on the subject to the point of the subject’s withdrawal from a study remains part of the study records and may not be deleted. The subject may request that the data collected previously may not be used, but the informed consent document cannot give the subject the option of having data deleted.

If research personnel would like to seek the subject’s permission to follow the subject’s health and collect clinical data from his/her medical records after withdrawal from research interventions, the subject must consent to such collection. 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. If the subject declines to consent to the follow-up, the researcher must not access the subject’s medical record or other confidential records for purposes related to the research, but may consult public records, such as those establishing survival status.

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 debarment from engaging in research with human subjects at Indiana University.
5.0  History
Replaces IU SOP for Research Involving Human Subjects – Informed Consent (v02/2017)

6.0  Related Information

**AAHRPP Standards**
- Element 1.4.A
- Element 1.7.C
- Element II.3.F
- Element II.3.G
- Element II.4.B
- Element III.1.F
- Element III.1.G

**IU HRPP Documents**
- Policies
  - Adult Individuals Lacking Consent Capacity in Research
  - Children in Research
  - Research Personnel Responsibilities
  - Pregnant Women, Fetuses, Neonates in Research
  - Prisoners in Research
  - Research Data Management
- Guidance
  - [Biospecimens](#)
  - [FERPA and Research with Student Records](#)
  - [HIPAA](#)
  - [Research with Individuals Lacking Consent Capacity](#)
  - [Transnational Research](#)
- **Templates/Forms**
  - Informed Consent Document Checklist
  - Informed Consent Document Template – Biomedical
  - Informed Consent Document Template – Future Research
  - Informed Consent Document Template – Informational Risks Only
  - Informed Consent Document Template – Social/Behavioral/Educational (SBE)
  - Informed Consent Statement Short Forms: Arabic, Burmese, Chinese, English, French, Italian, Russian, Spanish, Vietnamese, Italian
  - Study Information Sheet – Expedited Template

**KC IRB Questionnaires (see [KC Crosswalk](#))**
- Questionnaire H – Informed Consent Process
- Questionnaire J – Child Assent and Parental Consent Process

**Regulatory References**
- [21 CFR 50, Subpart B](#)
- [21 CFR 56.109(c)](#)
- 45 CFR 46, especially 46.116, 46.117
- [DoD Instruction 3216.02 – Protection of Human Subjects and Adherence to Ethical Standards in DoD-Supported Research](#)
- [The Family Education Rights and Privacy Act (FERPA)](#), 20 U.S.C. § 1232g; [34 CFR 99](#)
- FDA Guidance
Review Boards and Clinical Investigators


- Genetic Information Nondiscrimination Act of 2008 (GINA), 29 CFR 1635

- Indiana Code
  - IC 16-36-1-2
  - IC 16-36-1-5

- OHRP Guidance
  - Informed Consent FAQs
  - IRB Review of Protocol and Informed Consent Changes for NCI/CTEP-Sponsored Clinical Trials
  - IRB Review of Protocol and Informed Consent Changes in Cooperative Group Protocols (OHRP Memo to the National Cancer Institute, 2008)
  - Use of Electronic Informed Consent: Questions and Answers (December 2016)

- National Institute of Justice Guidance: Informed Consent Requirements

- NIH Policy on Certificates of Confidentiality, specifically “Suggested Consent Language Describing the CoC Protections”

- NIH Genomic Data Sharing, especially:
  - Guidance on Consent for Future Research Use and Broad Sharing of Human Genomic and Phenotypic Data Subject to the NIH Genomic Data Sharing Policy
  - NIH Points to Consider for IRBs and Institutions

- VHA Handbook 1200.05 – Requirements for the Protection of Human Subjects in Research, especially sections 15-16
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 Procedures

3.1. Non-members at the IRB Executive Committee Meetings
The Chair may invite or allow a non-member to attend a meeting, as needed.

3.2. 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.

4.0 Sanctions
Individuals found to be in violation of this policy may be subject to sanctions relating to their participation in review of research with human subjects.

5.0 History
Minor corrections to formatting and wording throughout

6.0 Related Information
AAHRPP Standards
- N/A

IU HRPP Documents
- Policies
  - N/A
- Guidance
  - N/A

KC IRB Questionnaires (see KC Crosswalk)
- N/A

Regulatory References
- N/A
IRB Meetings and Minutes

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

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.

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.

**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

**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
- Description of the submission/event/circumstance
- 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 special populations, including children, prisoners, pregnant women, fetuses, neonates of uncertain viability or nonviable neonates, and individuals lacking consent capacity
- For determinations of unanticipated problem involving risks to subjects or others, or serious and/or continuing noncompliance, or if the IRB suspends or terminates approval of research:
  - Reasons for the IRB's actions
  - Plans for continued investigation and/or action
- For VA research:
  - Determination and documentation of the level of risk and the rationale for the IRB's determination
  - A summary of the justification for including nonveterans as participants
  - 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
  - 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
  - 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 Procedures

#### 3.1. 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 studies which are greater than minimal risk 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 nonaffiliated member may be assigned as a tertiary reviewer.

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.

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.

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;

Except for life-threatening emergencies that meet very specific requirements as outlined in the IU HRPP Policy on Emergency Use of Investigational Test Articles, review of all research that qualifies for full IRB review is performed at a convened IRB meeting.

4.0 Sanctions
Individuals found to be in violation of this policy may be subject to sanctions relating to their participation in review of research with human subjects.

5.0 History
Minor corrections to formatting and wording throughout; Section 2.2 - addition of information moved from previous IU SOPs for Research Involving Human Subjects

6.0 Related Information
AAHRPP Standards
- Element II.1.D
- Element II.1.E
- Element II.2.C
- Element II.2.D
- Element II.5.B

IU HRPP Documents
- Policies
  - Emergency Use of Investigational Test Articles
  - IRB Membership
- Guidance
  - N/A
- Templates/Forms
  - IRB Agenda Template
  - IRB Minutes Template

KC IRB Questionnaires
- N/A

Regulatory References
• 21 CFR 56
• 45 CFR 46
• OHRP/FDA Guidance:
  o Minutes of Institutional Review Board (IRB) Meetings; Guidance for Institutions and IRBs (September 2017)
• VHA Handbook 1200.05 – Requirements for the Protection of Human Subjects in Research, especially section 14
IRB Membership

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.
• Each IRB that regularly reviews research involving prisoners:
  o includes a majority of members that have no association with the prison(s) involved, apart from their membership on the IRB
  o has at least one voting member who is a prisoner or prisoner representative with a close working knowledge, understanding, and appreciation of prison conditions from the perspective of a prisoner

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.

Changes in IRB membership are reported to the Office for Human Research Protections (OHRP) quarterly and to Roudebush VAMC within 30 days.

3.0 Procedures

3.1. 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.

3.2. 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:
  - Call meetings to order
  - Facilitate discussions
  - Provide counsel to IRB Members
  - Call for motions and votes
  - 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

3.3. 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.

4.0 Sanctions
Individuals found to be in violation of this policy may be subject to sanctions relating to their participation in review of research with human subjects.

5.0 History
Section 2.1 - addition of information moved from previous IU SOPs for Research Involving Human Subjects; minor corrections to formatting and wording throughout

6.0 Related Information
AAHRPP Standards
- Element I.1.E
- Element II.1.A
- Element II.1.B
- Element II.1.C
• Policies
  ○ N/A
• Guidance
  ○ N/A
• Templates/Forms
  ○ IRB Member Information Sheet
  ○ IRB Member Evaluation Form

KC IRB Questionnaires (see KC Crosswalk)
• N/A

Regulatory References
• 21 CFR 56, especially 56.107
• 45 CFR 46, especially 46.107 and Subpart E
• International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH): Guideline for Good Clinical Practice E6(R2), especially section 3.2
• VHA Handbook 1200.05 – Requirements for the Protection of Human Subjects in Research, especially section 6
IRB Records and Retention

About This Policy

Effective Date:
07/19/2018

Last Updated:
07/19/2018

Policy Contact:
IU Human Subjects Office
(317) 274-8289
irb@iu.edu

1.0 Scope

This policy applies to all human subjects research under the oversight of the IU Human Research Protection Program (HRPP).

2.0 Policy Statement

HRPP Policies and IRB membership rosters, agendas, and minutes are retained indefinitely or until the Associate Vice President, Research Compliance, gives the authority to dispose of such records.

The IRB study file includes all documents reviewed by the IRB in connection with the research, including where applicable:

- IRB application
- Protocol or research plan
- Investigator brochures, package inserts, or instructions-for-use documents for medical devices
- Data collection instruments, including surveys, questionnaires, interview questions, etc.
- Recruitment materials
- Informed consent documents
- HIPAA authorization forms
- Documentation of scientific review, when provided by an external committee
- Modifications to previously approved research
- Records of renewal activities, including progress reports and data safety monitoring reports
- Reports of reportable events, including unanticipated problems involving risks to subjects or others and noncompliance
- Reports of injuries to subjects
• All correspondence between the IRB and researchers
• Documentation of the permissible category of exemption or expedited review category
• Description of the action taken by the reviewer
• IRB determinations findings required by federal laws and regulations, state and local laws and regulations, and institutional or agency policy or procedure

The IRB study file is retained while the study is active and for a period of three (3) years following closure, termination, or expiration of IRB approval, and may be destroyed after that time. The file is retained electronically for research not subject to 21 CFR Part 11 requirements or VA regulations.

Until destruction of IRB records has occurred, they are accessible for inspection and copying by interested parties, including but not limited to representatives of federal agencies and departments, sponsors, and institutional officials, at reasonable times and in a reasonable manner.

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.

3.0 Procedures
N/A

4.0 Sanctions
Individuals found to be in violation of this policy may be subject to sanctions relating to their participation in review of research with human subjects.

5.0 History
Replaces portions of the IU SOP for Research Involving Human Subjects – Data Management (v02/2017)

6.0 Related Information
AAHRPP Standards
• Element II.5.A
• Element II.5.B

IU HRPP Documents
• Policies
  o IRB Meetings and Minutes
  o IRB Membership
• Guidance
  o N/A

KC IRB Questionnaires (see KC Crosswalk)
• N/A

Regulatory References
• 21 CFR 56.115
• 45 CFR 46.115
• International Council for Harmonisation of Technical Requirements for Pharmaceuticals
for Human Use (ICH): Guideline for Good Clinical Practice E6(R2), especially section 3.4

- OHRP Guidance:
  - Expedited Review Procedures

- VHA Handbook 1200.05 – Requirements for the Protection of Human Subjects in Research, especially section 14
IRB Reporting

1.0 Scope
This policy applies to all Indiana University (IU) institutional review boards (IRBs). This policy does not apply to IRB review of administrative holds, events occurring at a site not under the jurisdiction of the IU IRBs, or suspensions not initiated by the IU IRB.

2.0 Policy Statement
When the IRB determines that reviewed information represents an unanticipated problem involving risks to subjects or others (UPIRTSO), or serious and/or continuing noncompliance, or if the IRB suspends or terminates approval of research, appropriate institutional officials and the federal department or agency head are notified of the determination, surrounding circumstances, reason for the determination, as well as relevant subsequent actions and information.

3.0 Procedures

3.1 IRB submission and review
When the convened IRB makes any of the determinations in 2.0 above, the determination is promptly reported to the appropriate entity as follows:
- If the research is conducted at the VA, the VA facility Director and the ACOS/R&D within 5 business days
- If the study is subject to HHS regulations, Office for Human Research Protections (OHRP)
- If the study is subject to FDA regulations, Food and Drug Administration (FDA)
- If the research is federally-funded and all study activities were suspended or terminated, Director of Grant Services
• IU Office for the Vice President General Counsel or counsel for engaged institutions, if applicable
• Institutional official or designee, Indiana University
• If the IU IRBs are serving as the IRB of record for external sites or investigators, the Relying Institution(s)
• If the study is under the oversight of an external IRB, the Reviewing IRB

The following individuals are provided with a copy of the report, as appropriate:
• The Principal Investigator (PI)
• For IU faculty, the PI’s department chair or division chief

3.2. Research subject to VA regulations
IRB determinations related to local research deaths, SAEs and serious problems, and apparent serious and/or continuing noncompliance must be reported in accordance with the IU HRPP Policy on Reportable Events, section 3.2.

The IRB must notify the VA facility Director and the ACOS/R&D within 5 business days of suspending or terminating VA research.

4.0 Sanctions
Individuals found to be in violation of this policy may be subject to sanctions relating to their participation in review of research with human subjects.

5.0 History
Replaces IU SOP for Research Involving Human Subjects – Reporting (v02/2017)

6.0 Related Information
AAHRPP Standards
• Element 1.5.D
• Element II.2.F
• Element II.2.G
• Element II.2.H

IU HRPP Documents
• Policies
  o Reportable Events
• Guidance
  o Reportable Events

KC IRB Questionnaires (see KC Crosswalk)
• Reportable Events

Regulatory References
• 46 CFR 46, especially 46.103(a) and 46.103(b)(5)
• 21 CFR 56, especially 56.108(b) and 56.113
• OHRP Guidance
  o Guidance on Reporting Incidents to OHRP
  o Unanticipated Problems Involving Risks to & Adverse Events Guidance (2007)
• VHA Handbook 1058.01 – Research Compliance Reporting Requirements
IRB Review Process

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 under the oversight 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 are 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 research personnel 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 approval
Based on the IRB’s review of information provided by the study team, 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 additional safeguards required for research involving special 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.

Research involving prisoners may be reviewed via expedited procedures, unless subject to Department of Defense requirements, if:
• For research involving interaction with prisoners, the primary IRB reviewer and the prisoner representative determine the research is minimal risk for the prison population being studied or included.
• For research that does not involve interaction with prisoners, the primary IRB reviewer determines the research poses minimal risk for the prison population being studied or included.

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 550ml 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 50ml or 3ml per kg in an 8 week period and
collection may not occur more frequently than 2 times per week.

**Category 3**

Prospective collection of biospecimens 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, electoretinography, 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 subject to FDA and/or VA regulations
- Research requiring review by the convened IRB, except as described below

The IRB is not required to conduct renewal for the following:
- Research granted exemption, including exempt research requiring a limited IRB review per the IU HRPP Policy on Exempt Research
- Research that is not subject to FDA or VA regulations and is eligible for expedited review per this policy
- Research that is not subject to FDA or VA regulations and requires 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 HRPP Policy 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, research personnel 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**

*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 Investigational New Drug application (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**


The IRB will consider relevance of the research to the mission of VA and the veteran population. 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.

**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 research personnel is notified of the suspension by the local VA research office, research personnel 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 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.

2.12. 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.

2.13. Transnational research
The IRB is not expected to have expertise in regulations or cultures outside of the U.S. The IRB reviews issues with transnational research based on the information provided by the study team via the human subjects application, including as applicable:
- Whether there is additional risk to subjects due to their location or inclusion in a culture
- Whether modifications to the informed Consent document are appropriate
- Whether the study team has sufficient knowledge and understanding of the target country to conduct research

3.0 Procedures

3.1. IRB administration and support
The day-to-day operations of the IRB are administered and supported by the IU 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 research personnel as to whether an activity requires IRB review; however, HSO staff may consult with members of the IRB with any questions.

HSO staff notify the PI and Student, Fellow, Resident PI in writing of IRB actions taken on research.
3.2. **IRB submission**

The study team provides protocol-specific information via the human subjects application and submits the following additional materials, as applicable:

- Data collection instruments
- Recruitment materials
- Informed consent or assent documents, unless a waiver of consent or assent is being requested
- Grant proposal, if the research is subject to VA regulations, and the IU investigator is the direct recipient of the funds

3.3. **IRB actions**

The IRB may take appropriate action to protect human subjects when reviewing a research study or submission, including new studies, amendments, renewals, and FYI items. All actions and determinations made by the IRB are conveyed to the PI and Student, Fellow, Resident PI in writing. Appropriate actions may include:

- **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.
- Accept the item with no further action required (i.e., protocol continues as previously approved and/or investigator’s proposed corrective and preventative action plans are adequate)
- Refer to or consult with other institutional entities (e.g., department head; University General Counsel, Chief Compliance Officer, or Privacy Officer; IRB Executive Committee)
- Restrict use of research data collected
- Audit the research study(ies)
- Modify the research protocol and/or informed consent process/form
- Request notification to or re-consent of past and/or current subjects if the report may relate to their willingness to continue to take part in the study
- Withdraw currently enrolled subjects if it is determined to be in their best interest
- Require additional training of the investigator and/or research team
- Modify the renewal schedule
- Require increased reporting by the investigator and/or increased monitoring of
the research and/or informed consent process

- Restrict privileges of the investigator to conduct human subjects research

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).

3.4. 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. If the IRB finds that research appearing in the categories in section 2.5 above is more than minimal risk, the IRB must document the rationale.

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 of 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.

3.5. 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.

3.6. 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 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 study team’s behalf)
• Any proposed modifications to the informed consent document or protocol
• For VA studies, the study team’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 special 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 study team 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 study team’s responsibility to ensure that the research is reapproved prior to the study’s expiration date.

• If the study team 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 study team 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.

3.7. Amendments to previously approved research
Submissions for amendment are made through the online KC IRB system. The study team provides information about the proposed changes and submits revised IRB-approved documents or new materials, as applicable.
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, study teams 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.

3.8. Reopening research
Research personnel 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 study team may need to submit a new research application to restart/continue the previously closed/expired research study at the discretion of the HSO.

3.9. Suspensions and terminations
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. Any suspension or termination includes a statement of the reasons for the IRB’s action and is reported promptly to the PI, appropriate institutional officials, and/or the department or agency head.

Suspensions can be lifted only by the convened IRB. If an IRB Chair or designee suspends research, it is reported to the full IRB for consideration and possible action. Termination of research can be made only by the convened IRB. Suspensions and terminations cannot be overturned by Institutional Officials.

When the IRB suspends or terminates a research study, it considers whether the suspension or termination requires that subjects be withdrawn from the study and/or places them at risk of harm.

- When subjects must be withdrawn from a study, the IRB considers the safety, rights, and welfare of subjects and determines necessary termination procedures (e.g., drug tapering, final visit, lab tests, other follow-up, and/or arrangements for continued care).
- 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 determines 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:
  o All subjects who have been or who are currently enrolled;
  o Only subjects who are currently enrolled and active; or
  o Only subjects who participated in a certain aspect of the study.
  • Research personnel may request to attend an IRB meeting to discuss a suspension or termination in order to provide clarification of the issues.

3.10. Transition to 2018 Requirements
Revisions to 45 CFR 46 (Common Rule) are effective January 21, 2019 (2018 requirements). Beginning July 19, 2018, research which is federally-funded or otherwise subject to the Common Rule will be subject to the 2018 Requirements. Previously-approved non-exempt research will be transitioned at time of renewal and the IRB will document the application of the 2018 Requirements at that time.

As of July 19, 2018, non-exempt research which meets all of the following criteria will be transitioned and considered in compliance with and subject to the 2018 Requirements:
  • Federally-funded
  • Progressed to the point that the involves only data analysis, including analysis of identifiable private information or identifiable biospecimens (i.e., data analysis only)
  • not also subject to FDA or VA regulations
A list of this research will be maintained by the HRPP.

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 debarment from engaging in research with human subjects at IU.

5.0 History
Revision to submission requirements (i.e., grant proposal) and renewal requirements; addition to section 3.3; new sections 2.13 and 3.9 - moved information from previous IU SOPs for Research Involving Human Subjects; new section 3.10; minor corrections to formatting and wording throughout

6.0 Related Information
AAHRPP Standards
  • Standard I-7, Elements I.7.A, I.7.B,
  • Standard II-1, Elements II.1.C, II.1.D, II.1.E
  • Standard II-2, II.2.D, II.2.E, II.2.G,
  • Standard II-4, Elements II.4.A

IU HRPP Documents
  • Policies:
    o Exempt Research
    o Informed Consent
Recruitment of Human Subjects

• Guidance:
  - Additional Review by Non-IRB Committees
  - Data Safety Monitoring
  - Expedited Research
  - Seeking Opinion from FDA Regarding Drug Exemption

• Forms:
  - Drug or Biological Product Form
  - Medical Device Form

KC IRB Questionnaires (see KC Crosswalk)

• Conflicts of Interest
• A – Level of Review Assessment
• B – Lay Summary & Research Design
• C – Sites & Collaborations
• D – Recruitment Materials
• E – Risks, Benefits, Protections
• F – Data Safety Monitoring
• G1 – Children
• G2 – Individuals Lacking Consent Capacity
• G3 – Prisoners
• G4 – Transnational Research
• H – Informed Consent Process
• J – Child Assent & Parental Consent Process
• K – HIPAA
• L – VA Research
• Amendment
• Renewal
• Reportable Event (FYI)
• Study Closure/Closure Report

Regulatory References

• 21 CFR 56
• 21 CFR 312
• 21 CFR 812
• 45 CFR 46
• DoD Instruction 3216.02 – Protection of Human Subjects and Adherence to Ethical Standards in DoD-Supported Research

• FDA Guidance:
  - Information Sheet Guidance for IRBs, Clinical Investigators, and Sponsors: Significant Risk and Nonsignificant Risk Medical Device Studies
  - Guidance for Clinical Investigators, Sponsors, and IRBs: Investigational New Drug Applications (INDs) – Determining Whether Human Research Studies Can Be Conducted Without an IND
  - Guidance for Clinical Investigators, Sponsors, and IRBs: IRB Responsibilities for Reviewing the Qualifications of Investigators, Adequacy of Research Sites, and the Determination of Whether an IND/IDE is Needed

• International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH): Guideline for Good Clinical Practice E6(R2), especially section 3
- OHRP Guidance:
  - Approval of Research with Conditions
  - Continuing Review
  - Expedited Review Procedures

- VHA Handbook 1200.05 – Requirements for the Protection of Human Subjects in Research
KC IRB

1.0 Scope

This policy applies to the conduct of human subjects research under the jurisdiction of the IU Human Research Protection Program (HRPP). This includes research under the oversight of the IU IRBs and research for which IU or its affiliates are relying on an external IRB for oversight.

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 Procedures

3.1 KC IRB System Controls

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.

Roles and Permissions

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<th>Role</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>Access is <strong>not</strong> protocol-based (i.e., role allows access to data/actions as defined below)</td>
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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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<td><strong>HSO Staff:</strong> Research Compliance Consultants, Associates, and Assistants</td>
<td>✔</td>
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<tr>
<td><strong>Office of Research Compliance:</strong> Persons in the Office of the Vice President for Research, Radiation Safety, Biosafety, Conflict of Interest, Office of Research Administration, Quality Improvement Office, Research Integrity Office</td>
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<tr>
<td><strong>Office of Research Compliance Other Advanced:</strong> Organization contacts/affiliates in the Clinical and Translational Sciences Institute, VA, etc.</td>
<td>✔</td>
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<tr>
<td>Access is <strong>protocol-based</strong> (i.e., role allows access to data/actions as defined below)</td>
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<tr>
<td><strong>IRB Member</strong></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>
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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>
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<tr>
<td><strong>Principal Investigator (PI):</strong> PI, Site-specific PI, Student, Fellow, Resident PI</td>
<td>✔</td>
<td>✔</td>
<td>✔</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>
<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>
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</tbody>
</table>

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

**Role Management**
Requests for and assignments of roles are the responsibility of HSO management. The HSO maintains a list of personnel assigned to roles.

**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

**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.

**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.
  - In general, protocol statuses that are considered “inactive” include “Deleted,” “Abandoned,” and “Amendment or Renewal Incorporated into Protocol”.

**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.
  - Review Not Required
  - 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.
  - Approve
  - Close
  - Disapprove
  - Expedited Approval
  - Response Approval
  - Specific Minor Revisions (Provisional Approval)
  - Substantive Revisions Required (Table)
  - Suspend
  - 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).

**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.

**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, research personnel can conduct study activities through 11:59 p.m. July 19, 2016.

### 3.2. 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.

Research personnel 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.

3.3. KC IRB Screening and Pre-Review Process
Upon submission, a preliminary review (“pre-review”) by a 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 (3.2).

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 (3.2).

3.4. 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.
  o Above-listed individuals (3.2) **except** the IRB Admin “Intake” Group receive notification of approval.

### Exempt Submissions

  o The KC Protocol, including Questionnaires and attached documents, is reviewed by a qualified HSO staff member directly within the KC IRB system.
  
  o 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.
  
  o “Grant Exemption” action generates a notice of exemption letter containing the reviewer’s signature, which can be retrieved from the KC Protocol.
  
  o Above-listed individuals (3.2) **except** the IRB Admin “Intake” Group receive notification of approval.
  
  o PI and Student, Fellow, and/or Resident PI receive notification, if the study intends to include children

### Expedited and Full Board Submissions (including HUD, Amendments, Renewals, and FYI Submissions)

  o 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 retrieved from the KC Protocol.
  
  o 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.

• Emergency Use
  o The KC IRB Protocol, including attached documents, is reviewed by a qualified HSO staff member directly within the KC IRB system.
  o Reviewer takes “Review Not Required” action, which indicates confirmation of receipt of notification of emergency use.
  o Above-listed individuals except the IRB Admin “Intake” Group receive notification of approval.

* 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

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 XXXXXXXXX IRB Approved
• For studies that are Closed to Enrollment → Protocol XXXXXXXXX IRB Approved for re-consenting only
• For studies in Data Analysis Only → Protocol XXXXXXXXX IRB Approved – Do Not Enroll Subjects
• For disapproved studies → Protocol XXXXXXXXX Disapproved
• For expired studies → IRB Approval of Protocol XXXXXXXXX Expired DD-Month-YYYY
• For closed studies → Protocol XXXXXXXXX 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.

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”.

IU HRPP Policy: KC IRB
Version Date: 07/19/2018
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<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&lt;br&gt;Signed Protocol Summary&lt;br&gt;Informed Consent with Watermark (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&lt;br&gt;Signed Protocol Summary**&lt;br&gt;Amendment Questionnaire**</td>
</tr>
<tr>
<td>Renewal – Full Board or Expedited</td>
<td>Approval Letter&lt;br&gt;Signed Protocol Summary**&lt;br&gt;Renewal Questionnaire**&lt;br&gt;Changes &amp; Amendments Questionnaire**</td>
</tr>
<tr>
<td>Reportable Event</td>
<td>Approval Letter&lt;br&gt;Signed Protocol Summary**&lt;br&gt;Reportable Events Questionnaire**</td>
</tr>
<tr>
<td>Closure</td>
<td>IRB Closure Notice/Letter&lt;br&gt;Signed Closeout Report Questionnaire</td>
</tr>
<tr>
<td>Reliance Request</td>
<td>Notice of Reliance</td>
</tr>
<tr>
<td>Not Human Subject Research (Research Not Subject to Human Subjects Regulations)</td>
<td>Notice of Determination - Administratively Reviewed</td>
</tr>
<tr>
<td>Waiver – Informed Consent / Parental Consent</td>
<td>Approval Letter</td>
</tr>
<tr>
<td>Waiver – HIPAA Authorization</td>
<td>Approval Letter&lt;br&gt;Signed Protocol Summary**&lt;br&gt;Signed KC IRB Questionnaire K and/or L**</td>
</tr>
</tbody>
</table>

**Collated together into a single document**

3.5. **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.

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
debarment from engaging in research with human subjects at Indiana University, or to sanctions relating to their participation in review of research with human subjects.

5.0 **History**
Minor corrections to formatting and wording throughout

6.0 **Related Information**
AAHRPP Standards
- N/A

IU HRPP Documents
- IU HRPP Policies
- Guidance
  - [Quick Guides: Kuali Coeus (KC) IRB](#)

KC IRB Questionnaires (see [KC Crosswalk](#))

Regulatory References
- [www.kuali.org](http://www.kuali.org)
Pregnant Women, Fetuses, and Neonates in Research

1.0 Scope
This policy applies to the conduct of non-exempt human subjects research involving pregnant women, fetuses, and/or neonates under the oversight of the IU IRBs.

This policy does not apply to the conduct of research with viable neonates. A neonate, after delivery, that has been determined to be viable falls under the IU HRPP Policy on Children in Research.

Pregnant minors cannot, by virtue of their pregnant status alone, consent on their own behalf to participate in research; as such, research involving children who are pregnant must comply with both this policy and IU HRPP Policy on Children in Research.

2.0 Policy Statement
Research involving women who are or may become pregnant requires special consideration from the IRB to ensure ongoing safety of subjects during pregnancy, avoid unnecessary risk to the fetus, and ensure informed consent is obtained from the appropriate persons.

2.1 Research involving pregnant women or human fetuses
Pregnant women or human fetuses may be involved in research if all of the following conditions are met:

- 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
- 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

IU HRPP Policy: Pregnant Women, Fetuses, and Neonates in Research
Version Date: 07/19/2018
the purpose of the research is the development of important generalizable knowledge that cannot be obtained by any other means

- Any risk is the least possible for achieving the objectives of the research
- 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 or informed consent is waived in accordance with the IU HRPP Policy on Informed Consent
- 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 or waived in accordance with the IU HRPP Policy on Informed Consent, 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
- Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate
- No inducements, monetary or otherwise, will be offered to terminate a pregnancy
- Individuals engaged in the research will have no part in determining the viability of a neonate

2.2. Research involving neonates

Neonates of uncertain viability and nonviable neonates may be involved in research if all of the following conditions are met:

- Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates
- Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate
- Individuals engaged in the research will have no part in determining the viability of a neonate
- The requirements for neonates of uncertain viability or nonviable neonates listed below have been met, as applicable

Neonates of uncertain viability

Until it has been ascertained whether a neonate is viable, a neonate may not be involved in research unless the following additional conditions have been met:

- 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
- 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, except that the consent of the father or his LAR need not be obtained if the pregnancy resulted from rape
or incest

**Nonviable neonates**

After delivery, a nonviable neonate may not be involved in research unless all of the following additional conditions are met:

- Vital functions of the neonate will not be artificially maintained
- The research will not terminate the heartbeat or respiration of the neonate
- There will be no added risk to the neonate resulting from the research
- The purpose of the research is the development of important generalizable knowledge that cannot be obtained by other means
- The informed consent of both parents of the neonate is obtained in accordance with the IU HRPP Policy on Informed Consent
  - Waiver or alteration of the consent process is not available for research involving nonviable neonates
  - 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
    - 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

2.3. **Research not otherwise approvable**

The IRB may approve research which does not meet the requirements described in 2.1 or 2.2 only if 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.

For federally-funded research which meets this criteria, the DHHS Secretary or his/her designee, 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, must determine either:

- that the research in fact satisfies the conditions of 2.1 above; or
- 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; the research will be conducted in accord with sound ethical principles; and informed consent will be obtained in accord with the informed consent provisions of 46 CFR 46 and subpart A.

2.4. **Research subject to VA regulations**

- Research that involves provision of in vitro fertilization services cannot be conducted by VA research personnel 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.
- 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 research personnel 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.
• VA research personnel cannot conduct interventions in research that enrolls newborns within four weeks of birth while on official duty, at VA facilities, or at VA-approved offsite facilities. Prospective observational and retrospective record review studies that involve neonates or neonatal outcomes are permitted.

• Women who are known to be pregnant and/or their fetuses may be involved in research if all the requirements of 2.1 above are met and the VA medical facility Director certifies that the medical facility has sufficient expertise in women’s health to conduct the proposed research.

### 3.0 Procedures

#### 3.1. IRB submission and review

For studies proposing to enroll pregnant women, fetuses, and/or neonates, the study team completes the IRB application and provides protocol-specific information related to research with these populations. The IRB considers the information in the IRB application and documents its determinations as appropriate.

#### 3.2. When a current subject becomes pregnant during the research

When a human subject involved in ongoing research becomes pregnant during the course of the study, and the relevant research study was not previously approved by the IRB for the inclusion of pregnant women, fetuses, or neonates:

- All research procedures with the pregnant subject, including interactions and interventions and collection identifiable private information, must immediately cease.
- If research personnel wish to have the pregnant subject continue to participate in the research, the study team must submit an amendment to the IRB requesting inclusion of pregnant women, and the IRB must approve the inclusion in accordance with this policy. The pregnant woman may continue to participate in research procedures once the amendment is approved.
- If research personnel believe it is in the best interest of the pregnant woman to continue to receive research procedures before such an amendment can be reviewed, the IRB Chair may determine that the pregnant woman may continue to participate in the research until the above requirements are met if the potential benefits of continued treatment for the woman outweigh the risks of ongoing fetal exposure to the investigational drug, of discontinuing maternal therapy, and/or of exposing the fetus to additional drugs if placed on an alternative therapy.

### 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 debarment from engaging in research with human subjects at Indiana University.

### 5.0 History

Replaces portions of the IU SOP for Research Involving Human Subjects – Vulnerable Populations (v2/2017)
6.0 Related Information

AAHRPP Standards
- Element II.4.A
- Element II.4.B

IU HRPP Documents
- Policies
  - Children in Research
  - Informed Consent
  - IRB Review Process
- Guidance
  - Determining viability of newborns for research

KC IRB Questionnaires (see KC Crosswalk)
- QU G3 – Pregnant Women/Fetuses/Neonates

Regulatory References
- 45 CFR 46 Subpart B, §46.201-207
- VHA Handbook 1200.05 – Requirements for the Protection of Human Subjects in Research, especially section 17
Prisoners in Research

1.0 Scope
This policy applies to the conduct of non-exempt human subjects research involving prisoners under the oversight of the IU IRBs.

2.0 Policy Statement
Since prisoners are likely to be vulnerable to coercion or undue influence, additional protections must be applied to protect the rights and welfare of these subjects.

2.1 IRB review
The IRB shall approve research involving prisoners only if it finds all of the following:
- 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
- The risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers
- 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 (PI) 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.
- The information is presented in language understandable to the subject population
- 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
- Research personnel 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
- For federally-funded research, the research represents one of the categories of research or waiver permissible under section 2.2 below

### 2.2. Federally-funded research

Pursuant to 45 CFR 46.306(a)(2), federally-funded biomedical or behavioral research may involve prisoners as subjects only if the IRB determines the research falls under one or more of the following categories:

- 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;
- 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;
- 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
- 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 published notice in the Federal Register of the intent to approve such research.

Per notice in the federal register, the requirement that the research represent one of the categories of research listed above may be waived when DHHS conducts or supports certain important and necessary epidemiologic research on prisoners that meet all of the following criteria:

- 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
- 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:
  - The research presents no more than minimal risk and no more than
inconvenience to the prisoner-subjects, and
  - Prisoners are not a particular focus of the research

2.3. **Research subject to VA regulations**
Research involving prisoners cannot be conducted by VA research personnel 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 conducted in accordance with 45 CFR 46, Subpart C.

2.4. **Research conducted within an Indiana Department of Corrections (DOC) facility**
The use of prisoners for medical, pharmaceutical, or cosmetic experiments is prohibited, per DOC Policy and Administrative Procedure 01-02-101, Section XVI.

2.5. **Research subject to Department of Defense (DoD) regulations**
Research involving detainees as human subjects is prohibited. Detainees include any individual captured by, or transferred to the custody or control of DoD personnel pursuant to the law of war. This does not include persons being held solely for law enforcement purposes, except where the US is the occupying power.

In addition to allowable categories of research on prisoners in 45 CFR 46, Subpart C, epidemiological research is also allowable when:
- The research describes the prevalence or incidence of a disease by identifying all cases or studies potential risk factor association for a disease;
- The research presents no more than minimal risk;
- The research presents no more than an inconvenience to the subject
- Prisoners are not a particular focus of the research.

2.6. **Research subject to Department of Justice (DOJ) regulations**
For research conducted with the Bureau of Prisons (BOP), the requirements of 28 CFR 512 must be followed.

3.0 **Procedures**

3.1. **IRB submission and review**
For studies proposing to enroll prisoners, the study team completes the IRB application and provides protocol-specific information related to research with this population. The IRB considers the information in the IRB application and documents its determinations as appropriate.

When research is conducted in detention or correctional facilities, research personnel must obtain approval or permission to conduct the research from the facilities involved in the research and provide documentation to the IRB.

3.2. **When a current subject becomes a prisoner during the research**
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:
- All research procedures with the now-incarcerated prisoner-subject, including interactions and interventions and collection of identifiable private information, must immediately cease.
• If research personnel wish to have the prisoner-subject continue to participate in the research, the study team must submit an amendment to the IRB requesting inclusion of prisoners and the IRB must approve the inclusion in accordance with this policy. The prisoner-subject may continue to participate in research procedures once the amendment is approved.

• If research personnel believe it is in the best interest of the prisoner-subject to continue to receive research procedures before such an amendment can be reviewed, the IRB Chair may determine that the prisoner-subject may continue to participate in the research until the above requirements are met.

• IRB approval for inclusion of prisoners is not required if research procedures will not occur during the incarceration period.

3.3. Juvenile prisoners
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 in the IU HRPP Policy on Children in Research.

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 debarment from engaging in research with human subjects at Indiana University.

5.0 History

6.0 Related Information

AAHRPP Standards
• Element II-4

IU HRPP Documents
• Policies
  o Children in Research
  o IRB Meetings and Minutes
  o IRB Review Process
• Guidance
  o Research enrolling prisoners as subjects

KC IRB Questionnaires (see KC Crosswalk)
• Questionnaire G4 – Prisoners

Regulatory References
• 28 CFR 512
• 45 CFR 46 Subpart C, §46.301-306
• DoD Instruction 3216.02 – Protection of Human Subjects and Adherence to Ethical Standards in DoD-Supported Research, Section 7(b)
• Indiana DOC Policy and Administrative Procedure 01-02-101, Section XVI
• OHRP Guidance:
- Approving Research Involving Prisoners (2000)
- Prisoner Involvement in Research (2003)
- Prisoner Research Certification
- Prisoner Research FAQs

- **VHA Handbook 1200.05 – Requirements for the Protection of Human Subjects in Research**, especially section 18
Recruitment of Human Subjects

1.0 Scope
This policy applies to the conduct of non-exempt human subjects research under the oversight of the IU IRBs.

2.0 Policy Statement
A criterion for approval of research is that selection of subjects is fair and equitable. The IRB evaluates this criterion by considering both the selection criteria and proposed plans for recruitment of subjects for each research study. Recruitment represents the beginning of the consent process; as such, all recruitment methods and materials must meet ethical guidelines and must be reviewed and approved by the IRB before recruitment begins.

The IRB must ensure that recruitment methods and materials, including payment amount and timing of disbursement to subjects, are not coercive, misleading, or unduly influential. If the circumstances of the research could give rise to any level of undue influence (e.g., payment for subjects’ participation, instructors recruiting their own students, supervisors recruiting their direct reports, health care professionals recruiting their own patients), the study team must provide appropriate safeguards and/or assurances that the decision to participate will not affect the relationship.

2.1 Recruitment materials
Recruitment materials directed to potential subjects must be reviewed and approved by the IRB prior to use to ensure they are not unduly influential or misleading. Materials directed to other audiences (e.g., materials given to health care providers, teachers, or schools who will facilitate recruitment of subjects; news articles not intended for recruitment of subjects; financial page information for investors) and listings on clinical trial websites which provide basic information limited to title, purpose, study summary, basic eligibility criteria, locations, and contact information do not need to be reviewed.
Recruitment materials must include information prospective subjects need to determine their eligibility and interest. Materials should be written in a language understandable to the subjects, and may not:

- Emphasize the payment or payment amount by such means as larger or bold type
- Include exculpatory language
- State or imply certain favorable outcomes or other benefits beyond what is outlined in the informed consent document and the protocol
- Claim that an investigational drug, biological product, or device is safe or effective for the purposes under investigation, or that the test article is known to be equivalent or superior to any other drug, biological product, or device
- Use terms such as “new treatment” or “new drug” without explaining that the test article is investigational
- Promise free medical treatment when the intent is only to say that subjects will not be charged for taking part in the study
- 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.

3.0 Procedures

3.1. IRB submission and review

Recruitment methods are described and justified in the IRB application, including:

- identification of potential subjects
- plans for contacting potential subjects
- payment arrangements for subjects’ participation
- potential undue influence

Recruitment materials directed to potential subjects are attached to the IRB application.

For FDA-regulated research, the IRB must review and approve the final versions of any printed, audio, or video advertisements; however, the IRB may review and approve the wording prior to taping or final design.

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 debarment from engaging in research with human subjects at Indiana University.

5.0 History

Replaces IU SOP for Research Involving Human Subjects - Recruitment of Human Subjects (07/2015)

6.0 Related Information

- AAHRPP Standards
  - Element II.3.C
  - Element III.1.E
IU HRPP Documents

- Policies
  - IRB Review Process

- Guidance
  - Research using online tools & mobile devices: Guidelines for using online tools in research
  - Students: Recruiting students as research subjects

KC IRB Questionnaires (see KC Crosswalk)

- B – Lay Summary & Research Design
- D – Recruitment Methods

Regulatory References

- 45 CFR 46.111
- IU Policy on Drawings, Games, and Prizes
- OHRP Guidance: Clinical Trial Website: When is IRB review required and what should IRBs consider with reviewing?
Reliance

1.0 Scope

This policy applies to the conduct of human subjects research under the jurisdiction of the IU Human Research Protection Program (HRPP). This includes research under the oversight of the IU IRBs and research for which IU or its affiliates are relying on an external IRB for oversight.

2.0 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 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 the 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 research personnel are only engaged in minimal risk research activities.

### 3.0 Procedures

#### 3.1. HRPP submission and review

Study teams may request reliance on an external IRB for any of the above reasons by submitting a Reliance Request to the HRPP. HRPP 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 HRPP determines that reliance is not appropriate, the study must be submitted to the IU IRB for review.

Research personnel conducting VA research utilizing the VA CIRB are not required to submit a Reliance Request.

#### 3.2. Qualification of external IRBs

Reviewing, external IRBs are evaluated and deemed qualified based on a balance of the following factors:

- 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 research personnel
3.3. Reliance on the IU IRB

Study teams may request that the IU IRB provide IRB approval for non-affiliated research personnel. 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 research personnel 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 research personnel. 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 research personnel must obtain IRB approval from an appropriate, external IRB for their participation in the research.

When non-affiliated research personnel 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 research personnel’s participation.

3.4. 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 research personnel who are not conducting research on behalf of an institution, or when IU extends its Federalwide Assurance to cover non-affiliated research personnel, the responsibilities of the reviewing IRB and the non-affiliated research personnel are documented through a Non-Affiliated Investigator Agreement.

3.5. 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 PI 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 research personnel 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 research personnel 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:
  - Serious and/or continuing noncompliance
  - Restriction/suspension of research activities
  - Audits, including findings and corrective actions
  - Communication with regulatory agencies
  - Legal claims
  - 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 (UPIRTSO), serious/continuing noncompliance, suspensions and terminations.
- Review reports of audits conducted by the ORC Human Subjects Auditors.

Research personnel responsibilities
IU-affiliated research personnel conducting research for which an external, reviewing IRB has provided approval must fulfill all responsibilities outlined by the IU HRPP Policy on Research Personnel Responsibilities, plus the following:

- Submit Reliance Request to the HSO
- Obtain IRB approval for conduct of the research by IU-affiliated research personnel 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 research personnel 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

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 debarment from engaging in research with human subjects at Indiana University.

5.0 History
Minor corrections to formatting and wording throughout; addition to section 3.1.

6.0 Related Information
AAHRPP Standards
- Standard I-9

IU HRPP Documents
- Policies
  - Research Personnel Responsibilities
- Guidance:
  - Quick Guide: Reliance on External IRBs
  - Quick Guide: IU IRB review for non-affiliated investigators or external sites
  - Quick Guide: Understanding responsibilities under reliance
  - Quick Guide: Submitting an applicable NIH grant requiring sIRB
  - Quick Guide: Participating in as a site in a study requiring sIRB
• Templates/Forms
  o IU HRPP Reliance Forms
    • IRB Qualification Request
    • Investigator Responsibilities
    • Relying Site Local Context Checklist
    • Relying Site Personnel List
  o IU-PU-ND Request for Deferral Form
  o Non-Affiliated Investigator Agreement

KC IRB Questionnaires (see KC Crosswalk)
• Reliance Request
• Questionnaire C – Sites & Collaborations

Regulatory References
• NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research
• SMART IRB master reliance agreement and online reliance system
• VHA Handbook 1200.05 – Requirements for the Protection of Human Subjects in Research, especially 1200.05(5)(d)(1)
1.0 Scope
This policy applies to:

- The conduct of human subjects research under the oversight of the IU IRBs
- Clinicians under the oversight of the IU IRBs wishing to use a Humanitarian Use Device (HUD) for treatment or diagnosis, and the IU IRBs approving the use of the HUD

2.0 Policy Statement
In accordance with federal regulations and the IU HRPP Policy on the IRB Review Process, the IRB must ensure the relationship of risks to benefits to subjects remains reasonable throughout the conduct of the study, subjects are provided with the information necessary to make an informed decision about participation or continuation in the study, and data is adequately monitored to ensure ongoing safety of subjects. To that end, investigators conducting human subjects research and clinicians using a HUD must report events which may represent unanticipated problems and/or serious and/or continuing noncompliance (i.e., reportable events) to the IRB.

2.1 Promptly reportable events
The following reportable events may constitute unanticipated problems involving risks to subjects or others or serious and/or continuing noncompliance and 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) or the study status (i.e. Open to Enrollment, Closed by Investigator, etc.):

- Conduct of human subjects research without IRB approval, including:
  - Conduct of research without submitting for IRB review
  - Conduct of research prior to receiving IRB notification of final approval
  - 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 human subjects application
and/or protocol without prior IRB approval, including changes
necessary to eliminate apparent immediate hazards to the subject
  o Inclusion of vulnerable subject populations without specific IRB
    approval
  o Conduct of research when IRB approval has expired or been
    suspended or terminated
  o Subject interactions or review of identifiable research data by
    individuals who have not completed appropriate investigator
    requirements (e.g., COI disclosure and CITI training)
• 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) suggesting that the research places subjects or others at
  greater risk of harm than was previously known
• Unanticipated adverse device effects
• Use of a HUD which caused or contributed to a death or serious injury (i.e.,
  injury or illness that is life threatening, results in permanent impairment of a
  body function or permanent damage to a body structure, or necessitates
  medical or surgical intervention to preclude permanent impairment of a body
  function or permanent damage to a body structure)
• 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
• Consent and/or authorization issues, including:
  o Failure to obtain consent and/or authorization from subjects, including
    obtaining consent from someone who cannot legally consent for the
    subject
  o 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
  o Enrolling subjects using a consent which does not include all known
    risks, or continuation of subject participation without notification of
    newly identified risks
  o Other major deficiencies in the informed consent or HIPAA
    authorization process or documentation
  o Minor deficiencies in the informed consent or HIPAA authorization
    process or documentation, occurring within a one-year period and
    affecting ten (10) or more subjects
• Subject complaints that indicate an unexpected risk and/or that affect the
  rights and welfare of human subjects
• Study suspensions or holds related to risk, safety, or compliance issues
• Incidents that may compromise information security, subject privacy, and/or
  confidentiality (i.e., subject data breach)
• Local audit reports (i.e., Quality Improvement Office audits, VA audits)
• Failure to submit amendments which update risks, benefits, or procedures
  within sixty (60) days of receipt, or promptly report events when required per
  IU HRPP Policies.

2.2. Additional reportable events for VA research
In addition to section 2.1, the following reportable events must also 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):
• Local research deaths which are unanticipated and related to the research must be reported verbally to the IRB immediately, followed by a written report
• Local serious adverse events (SAEs) which are unanticipated and related to the research
• Serious problems
• Apparent serious and/or continuing noncompliance
• Any suspension or termination of VA research by, or at the direction of, any entity external to the facility

Any other adverse events, SAEs, unanticipated problems involving risks to subjects or others, or apparent noncompliance must be reported to the IRB in accordance with Section 2.4.

2.3. Additional reportable events for HUDs
In addition to section 2.1, the following reportable events must also be reported to the IRB within five (5) business days of the clinician becoming aware of the event:
• When use of a HUD caused or contributed to a death serious injury

2.4. Reportable events that do not require prompt reporting
The following reportable events do not meet the criteria for prompt reporting must be reported to the IRB at the time of renewal, if applicable:
• Protocol deviations that do not affect subject safety or data integrity
• Minor noncompliance
• Adverse events that were not promptly reported, occurred at a site under the oversight of the IU IRB, and occurred at a greater frequency and/or severity than was previously expected based on the protocol, informed consent document, and/or investigator's brochure

Noncompliance which is determined by Human Subjects Office (HSO) staff to be not apparent serious or continuing noncompliance must be reported at the time of next study renewal, if applicable.

Studies that do not require renewal, including studies in Clinical Follow-Up or Data Analysis Only, may report these events at the time of study closure.

3.0 Procedures

3.1. IRB submission and review
Promptly reportable events are submitted via KC IRB. After submission, HSO staff verify whether the event represents a promptly reportable event pursuant to this policy. For items classified as noncompliance, the University Director, HRPP, a HSO Associate Director, or a HSO Senior Research Compliance Consultant will further review the item to determine if the report may constitute serious or continuing noncompliance. If the item is determined not to meet prompt reporting criteria or is determined to be not apparent serious or continuing noncompliance, HSO staff will communicate this to the study team and withdraw the item from further review. If staff determines that prompt reporting is appropriate, they submit the report to a convened IRB meeting for review and possible action.

The convened IRB reviews the report to determine whether the research protocol still satisfies the requirements for IRB approval under 45 CFR 46.111. In particular, the IRB
3.2. Research subject to VA regulations

Local research deaths

- The IRB must alert the Office of Research Oversight (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.
- 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.
- 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:
  - The death was both unanticipated and related to the research; or
  - There is insufficient information to determine whether the death was both unanticipated and related to the research; or
  - The death was not unanticipated and/or the death was not related to the research.
- Regardless of the determination under the above bullets, 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 research personnel 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.
- The IRB must notify the VA facility Director and the ACOS/R&D of its determinations under the above bullets within 5 business days of the determinations.
- The VA facility Director must report the determinations to ORO within 5 business days after receiving the IRB’s notification.

IRB review of Serious Adverse Events (SAEs) and serious problems

- Within five (5) business days after receiving written notification of a 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.
- The convened 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:
• The incident was serious and unanticipated and related to the research; or
• There is insufficient information to determine whether the incident was serious and unanticipated and related to the research; or
• The incident was not serious, and/or the incident was not unanticipated, and/or the incident was not related to the research.

• The convened IRB must also determine and document whether any protocol or informed consent modifications are warranted. If so, the convened IRB must determine and document whether or not research personnel 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.

• The IRB must notify the VA facility Director and the ACOS/R&D in writing within 5 business days after its convened meeting if:
  o Actions were taken to eliminate apparent immediate harm to subjects; or
  o 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
  o Protocol or informed consent modifications were warranted.

• The VA facility Director must report the situation to the ORO within 5 business days after receiving the IRB’s notification.

Apparent serious and/or continuing noncompliance

• The convened IRB must review any report of apparent serious and/or continuing noncompliance at the next convened IRB-01 meeting, 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.

• The convened IRB must determine and document whether or not serious and/or continuing noncompliance actually occurred. If the IRB determines that serious and/or continuing noncompliance occurred:
  o A documented IRB determination is also required as to whether remedial actions are needed to ensure present and/or future compliance.
  o IRB must notify the VA facility Director and the ACOS/R&D within 5 business days after making its determinations.
  o The VA facility Director must report the determination to ORO within 5 business days after receiving the IRB’s notifications.
  o If the apparent serious or continuing noncompliance was identified by a Research Compliance Office (RCO) audit, the IRB must notify the RCO within 5 business days after its determination.
  o The IRB must track the determinations for use in the VA facility Director Certification.

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 debarment from engaging in research with human subjects at Indiana University.

5.0 History

Replaces IU SOP for Research Involving Human Subjects – Reportable Events (v02/2017)
6.0  Related Information

AAHRPP Standards

- Element 1.5.D
- Element II.2.F
- Element II.2.D

IU HRPP Documents

- Policies
  - IRB Reporting
  - IRB Review Process
- Guidance
  - Reportable Events

KC IRB Questionnaires (see KC Crosswalk)

- Reportable Events
- Renewal

Regulatory References

- 45 CFR 46, especially 46.103(b)(5) and 46.111
- 21 CFR 56, especially 56.108(b)
- FDA Guidance: Guidance for Clinical Investigators, Sponsors and IRBs: Adverse Event Reporting to IRBs – Improving Human Subject Protection
- OHRP Guidance: Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events (2007)
- VHA Handbook 1058.01 – Research Compliance Reporting Requirements
- VHA Handbook 1058.03 – Assurance of Protection for Human Subjects Research
Research Data Management

About This Policy

Effective Date:
07/19/2018

Last Updated:
07/19/2018

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1.0 Scope
This policy applies to the conduct of human subjects research under the jurisdiction of the IU
Human Research Protection Program (HRPP). This includes research under the oversight of the
IU IRBs and research for which IU or its affiliates are relying on an external IRB for oversight.

2.0 Policy Statement
The Principal Investigator (PI) has primary responsibility for the collection, management,
custody, retention, and destruction of research data and must adopt an orderly system of
record keeping which is:

• Followed by all members of the research team
• Enables the reconstruction of the entire study process, including retention of source
documents
• Enables 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
• Ensures conduct of research without fabrication, falsification, or plagiarism

Research data include, but are not limited to, the following, as applicable:

• Grant application
• Documents related to budget and funding
• Financial disclosure and conflict of interest information
• Correspondence with regulatory agencies and sponsor and/or funding agencies
• Correspondence with review committees (e.g., IRB, Institutional Animal Care and Use
Committee, Research & Development Committee) including documents approved by
the review committees
• Research protocol and all amended versions of the protocol
• Lists of all subjects entered in the study and codes and keys used to de-identify and re-
  identify subjects
• Signed and dated informed consent forms and HIPAA authorization forms from each
  subject
• Data collection or case report forms and all source and supporting data
• Documentation on each subject including informed consent process, interactions with
  subjects by telephone or in person, observations, interventions, and other data
  relevant to the research study
• Data collected during the research including photos, video recordings, and voice
  recording, all derivative data, and derivative databases
• Subject compensation records
• Reports of adverse events, complaints, and protocol deviations
• Records related to the investigational agents such as drug or device accountability
  records
• Monitoring and audit reports such as Data Safety Monitoring Board Reports and audits
  by oversight entities
• Data analyses
• Reports (including, but not limited to, abstracts and other publications)

All data must be retrievable and identifiable. Audit trails, if required, must identify who made
any changes, when, and why they were made.

Specific obligations with respect to research data ownership, creation, distribution, and
retention may be defined by contract or agreement, and apply to the research covered by the
contract or agreement.

2.1. Ownership of research data
When research data is generated pursuant to a contract or agreement (e.g., clinical trial
agreement with sponsor), ownership of the data is defined by the contract or
agreement. 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.

Research data which is not generated pursuant to a contract or agreement that
explicitly details ownership is the property of IU.

If research is completed by individuals who are employees of, or conduct work at, both
a federal or state government agency (e.g., Roudebush VAMC) and IU, ownership is
generally shared between IU and the government agency. Research personnel should
seek guidance from administrative officials at both institutions.

2.2. Data retention
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 minimum of three
(3) years from the date of submission of the final expenditure report to the funding
agency or the date of study closure with the IRB, whichever is longer.

Records may need to be retained beyond this date, specifically:
• For studies subject to HIPAA, signed HIPAA authorization forms must be
  retained for a minimum of six (6) years from the date it was obtained.
• For studies conducted under an IND, records must be retained for two (2) years
  after approval of a marketing application for the drug for the indication for
which it is being investigated or, if no application is to be filed or if the application is not approved for such indication, until 2 years after the investigation is discontinued and FDA is notified.

- For studies conducted under an IDE or HDE, records must be retained during the investigation and for a period of two (2) years after the latest of either: 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 premarket approval application, a notice of completion of a product development protocol, a humanitarian device exemption application, a premarket notification submission, or a request for De Novo classification.

- For research subject to VA regulations, records must be retained for six (6) years following the federal fiscal year end (September 30th) after the study has closed by the VA.

- If the research involves intellectual property, data must be kept for as long as may be necessary to protect any intellectual property claims resulting from the work.

- 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.

- If the research is being conducted by a student, data must be retained at least until the degree is awarded, or it is clear that the student has abandoned the work.

- If the research is conducted pursuant to a contract or agreement, data must be retained in accordance with the contract or agreement.

After the specified period of time has elapsed, research personnel may dispose of the documentation relating to a research study in an appropriate manner, including encrypting, shredding, incinerating, mutilating, erasing, and otherwise rendering the information illegible or unusable. Source documentation must be retained in its original form until this time.

2.3. Research subject to FDA regulation

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.

Studies subject to FDA regulation must also comply with 21 CFR 11: Electronic Records; Electronic Signatures.

3.0 Procedures

3.1. Recording and transcription of Data

When recording source data and/or transcribing source documents to case report or data collection forms, the following procedures should be followed:

- For paper documents, record all observations/data in ink.
- 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 for the correction. 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.)
• Complete all fields on the forms according to sponsor or other predetermined specifications.

3.2. Data sharing
IU faculty, staff, and students may not disclose social security numbers (SSNs) outside IU except in limited circumstances outlined in IC 4-1-10.

Public access requests seeking documents containing information concerning research must be forwarded to the IU Office of Vice President and General Counsel for further review and analysis, including a determination as to whether the records requested are or are not publicly available.

Certificates of Confidentiality
Certificates of confidentiality protect human subjects by prohibiting disclosure of identifiable sensitive research information. Certificates of confidentiality are automatically applied to NIH-funded research and may be requested for research not funded by the NIH. When a certificate applies, the researcher shall not:

• Disclose or provide, in any Federal, State, or local civil, criminal, administrative, legislative, or other proceeding, the name of such individual or any such information, document, or biospecimen that contains identifiable, sensitive information about the individual and that was created or compiled for purposes of the research, unless such disclosure or use is made with the consent of the individual to whom the information, document, or biospecimen pertains; or
• Disclose or provide to any other person not connected with the research the name of such an individual or any information, document, or biospecimen that contains identifiable, sensitive information about such an individual and that was created or compiled for purposes of the research.

If disclosure of research data protected by a certificate is requested, research personnel should immediately consult the IU HRPP.

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

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

NIH data sharing policies
Effective October 1, 2003, NIH requires a written plan to share data with the public and general research community for certain grants.

Effective January 25, 2015, NIH-funded research must comply with the NIH Genomic Data Sharing Policy. Upon request, the IRB reviews the research and assures to the Institutional Signing Official that all of the following are true:

• The data submission is consistent, as appropriate, with applicable national, tribal, and state laws and regulations as well as relevant institutional policies.
• Any limitations on the research use of the data, as expressed in the informed consent documents, are delineated.
• The identities of research participants will not be disclosed to NIH-designated data repositories.
• An IRB has reviewed the investigator’s proposal for data submission and assures that:
  o The protocol for the collection of genomic and phenotypic data is consistent with 45 CFR Part 46;
  o Data submission and subsequent data sharing for research purposes are consistent with the informed consent of study participants from whom the data were obtained;
  o Consideration was given to risks to individual participants and their families associated with data submitted to NIH-designated data repositories and subsequent sharing;
  o 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; and
  o The investigator’s plan for de-identifying datasets is consistent with the standards outlined in the NIH Genomic Data Sharing Policy.

If all of the above are true, the Institutional Signing Official will provide a signed Institutional Certification.

3.3. When research personnel leave the institution
Departing research personnel 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 institution or IU department or school.

Responsibility for compliance with this policy may be transferred to another appropriate person willing to accept responsibility. If the study will remain open with the IRB, transfer must be made via 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.

If the study will close with the IRB, the PI may withdraw from responsibility with this policy.

• The departing PI is responsible for notifying his/her institution, department, or division who has agreed to accept this responsibility.
• The institution, department, or 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 auditors.
• In the absence of someone willing to accept responsibility for the documents, the IU department chairman will become responsible for assuring that documents are stored per regulatory and IU requirements.

For studies subject to FDA regulation, notice of such a transfer of responsibility shall be given to the sponsor and FDA within 10 working days after the transfer occurs.

For research subject to VA regulations
All research records are retained by the VA facility where the research was conducted. If a 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.
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 debarment from engaging in research with human subjects at Indiana University.

5.0 **History**
Replaces IU SOP for Research Involving Human Subjects – Data Management (v02/2017)

6.0 **Related Information**

**AAHRPP Standards**
- N/A

**IU HRPP Documents**
- Policies
  - Confidentiality and Privacy
  - Security of Research Data
- Guidance
  - N/A

**KC IRB Questionnaires (see [KC Crosswalk](#))**
- N/A

**Regulatory References**
- [21 CFR 11](#)
- [21 CFR 312.62(c)](#)
- [21 CFR 812.140(d)-(e)](#)
- International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH): Guideline for Good Clinical Practice E6(R2), especially section 4.9
- Indiana Code
  - 4-1-10
  - 16-39-7-1
  - 24-4-14
- [IU Policy on Research Misconduct](#)
- [NIH Certificates of Confidentiality Policy](#)
- [NIH Data Sharing Policy](#)
- [NIH Genomic Data Sharing](#)
- [VHA Records Control Schedule 10-1 (November 2017)](#)
Research Personnel Responsibilities

1.0 Scope
This policy applies to the conduct of human subjects research under the jurisdiction of the IU Human Research Protection Program (HRPP). This includes research under the oversight of the IU IRBs and research for which IU or its affiliates are relying on an external IRB for oversight.

2.0 Policy Statement
The Principal Investigator (PI) is responsible for making an initial determination of whether an activity meets the definition of human subjects research and is therefore subject to this policy. The PI is ultimately responsible for ensuring compliance with this policy and may delegate specific responsibilities to research personnel, except those described in section 2.1, provided the individuals are appropriately qualified and trained.

2.1. PI responsibilities
The following responsibilities are the sole responsibility of the PI and may not be delegated.

- Ensure research personnel are qualified to perform delegated tasks and procedures, including but not limited to appropriate training, education, expertise, credentials, and privileges.
- Take appropriate steps to ensure entities not under the control of the PI are qualified to perform any delegated task(s).
- Ensure research is designed in a manner which:
  - Minimizes risks to subjects: (i) By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and (ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.
o Ensures 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.

- Ensure appropriate resources are available to conduct the research and 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.

- Review potentially reportable events and determine whether they require prompt reporting to the IRB.

- Review adverse events and make an initial determination of relationship between the event and the research.

### 2.2. Research personnel training and qualification

- Complete appropriate human subjects protection training as required by the institution and any funding agencies/entities.

- Report any potential financial interest which could affect or be affected by the research, regardless of financial value, held by research personnel or immediate family member of research personnel.

### 2.3. General responsibilities

- Obtain all appropriate approvals before commencing the research, including but not limited to IRB, VA Research & Development, Scientific Review Committee (SRC), and departmental approvals.

- Ensure research is conducted properly and in compliance with all of the following as applicable:
  - IRB-approved human subjects application and protocol, and any conditions of approval imposed by the IRB
  - Ethical principles described in The Belmont Report
  - Applicable contracts and agreements
  - FDA-approved investigational plan and IND/IDE application
  - IU HRPP Policies
  - Institutional policies
  - All applicable federal, state, and local laws and regulations

- Ensure continuous and timely communication with all members/entities of the research team.

- Obtain ongoing review and approvals:
  - Prospectively request any changes to a research study in the appropriate manner, and implement those changes only after receiving approval.
    - If changes are necessary to eliminate apparent immediate hazards to subjects, implement the change and promptly report the exception to the IRB.
    - Submit amendments updating risks, benefits, or study procedures to the IRB for review within 60 days of receipt of the amendment.
  - Promptly report to the IRB any promptly reportable event in accordance with relevant policies.
  - If the IRB has not reviewed and approved a research study by the expiration date, ensure all research activities cease, including research
interventions or interactions, enrollment of new subjects, and analysis of identified data, unless the IRB finds that it is in the best interests of individual subjects to continue participating in the research interventions or interactions.

- Report study closure to the IRB for all research within a reasonable time frame. At a minimum, this must be completed prior to study expiration, if applicable.
- Notify the IRB if the PI is leaving the institution and either close active research studies or arrange for appropriate transfer of authority for all active research studies to other qualified investigators.

2.4. Enrollment of subjects

- Do not accept personal 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. 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). The IU Policy on Sponsored Programs (Grant and Contracts) and Gifts: Definitions and Administration clearly distinguishes gifts from sponsored research projects.
- Obtain specific IRB approval prior to enrollment of any of the following populations into non-exempt research, and ensure research is conducted in accordance with the relevant IU HRPP Policy.
  - Adult individuals lacking consent capacity
  - Children
  - Pregnant women, fetuses, neonates
  - Prisoners
- For non-exempt research, obtain and document informed consent from each potential subject, unless waived, in accordance with the IU HRPP Policy on Informed Consent.
  - If the subject cannot provide consent for him/herself, due to age or lack of consent capacity, obtain informed consent from the appropriate individual in accordance with the relevant IU HRPP Policy and the IRB-approved human subjects application.
  - For VA research, if someone other than the PI conducts the informed consent process and obtains consent, the PI must formally delegate this responsibility and ensure the person so delegated has received appropriate training.
- Ensure all study subjects meet the inclusion and exclusion criteria set forth by the approved human subjects application and protocol.
- Notify subjects of any significant new findings during the study that may affect their willingness to participate.
- Respond appropriately to questions, concerns, complaints, or requests for information from potential subjects, subjects in the recruitment process, current research subjects, and/or past research subjects.
- Ensure subjects are withdrawn from research in a manner that protects their safety, rights, and welfare, and notify subjects when follow-up after withdrawal is required for safety reasons.
2.5. Data management and security
- Maintain privacy of research subjects and confidentiality of research data.
- Ensure appropriate maintenance and retention of research records in accordance with the IU HRPP Policy on Data Management.
- Ensure only authorized research personnel have access to research data.
- Establish appropriate security oversight and implement appropriate safeguards to maintain the confidentiality, integrity, and availability of research data, including PHI.
- Immediately report any suspected or known security breach that compromise research data to the appropriate institutional privacy and/or security office.

2.6. Transnational Research
- Before research is conducted at an international site, determine whether the country has laws or guidance related to the protection of human subjects.
- If required and/or available, obtain IRB approval from a local ethical board or group.
- Where there is no equivalent board or group available, 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.
- Provide appropriate information about the transnational site’s local context, including customs, culture, and religious norms as applicable, to the IRB.

2.7. Research with investigational test articles
- Ensure the investigation is conducted in accordance with the signed investigator statement, the investigational plan (i.e., IRB-approved human subjects application and protocol), and any conditions of approval imposed by the FDA.
- Ensure appropriate storage and control of test articles, including ensuring test articles are used and distributed only in accordance with the IRB-approved human subjects application and protocol.
- Maintain adequate records of the disposition of test articles, including dates, quantity, and use by subjects, and return unused supplies to the sponsor or provide for appropriate disposition.
- Prepare and maintain adequate and accurate research records in accordance with the IU HRPP Policy on Data Management.
- Provide appropriate reports to the sponsor, including adverse events.

Sponsor-investigators
In addition to the above, sponsor-investigators must also:
- Submit appropriate IND or IDE application to the FDA, and ensure approval before beginning the investigation.
- Select qualified investigators and provide them with the information needed to conduct the investigation properly, including investigational plan and reports of prior investigation.
- Ensure IRB review and approval is obtained and that the IRB and FDA are promptly informed of significant new information.
- Obtain signed agreement from each investigator which includes the investigator curriculum vitae, statement of relevant experience, explanation of any involvement in previously-terminated research, statement of commitment, and financial disclosure.
• Ensure proper monitoring of the investigation, including selection of qualified monitors.
• Review and evaluate evidence relating to safety and effectiveness, including adverse events and unanticipated device effect, and terminate investigations which present an unreasonable risk to subjects.
• Prepare and submit complete, accurate, and timely sponsor reports, as applicable.
• Maintain accurate, complete, and current sponsor records, as applicable.

2.8. Research subject to HIPAA
Ensure all members of the research team are knowledgeable about the appropriate uses and disclosures of PHI per the IU HRPP Policy on Use of PHI in Research and protocol-specific requirements.

2.9. Research subject to Department of Defense (DoD) regulations
Notify the Human Research Protection Office (HRPO) of the following:
• When significant changes to the research protocol are approved by the IRB
• Results of the IRB continuing review
• If the IRB used to review and approve the research changes to a different IRB
• When the institution is notified by any Federal department or agency or national organization that any part of its HRPP is under investigation for cause involving a DoD-supported research protocol
• IRB determination of unanticipated problem involving risk to subjects or others or serious and/or continuing noncompliance, or IRB suspension or terminations, regarding DoD-supported research involving human subjects

3.0 Procedures

3.1. IRB submission and pre-review
When submitting items to the HSO for review and approval:
• Ensure all applicable pre-submission requirements have been met before the item is submitted for review (e.g., conflict of interest disclosures, Collaborative Training Initiative [CITI] training, Good Clinical Practice [GCP] training, SRC approval obtained).
• Ensure the human subjects application is complete and all relevant documents are attached.
• Respond to HSO requests for additional information and/or clarification within two (2) weeks. If a response is not received within two (2) weeks, the submission may be withdrawn and the study team may resubmit at their convenience.
• For items reviewed at a convened IRB meeting, respond to requested provisions within two (2) weeks. If a response is not received within two (2) weeks, the item may be withdrawn and the study team may resubmit at their convenience.
• Promptly notify the IRB when a research study is to be withdrawn from further IRB review.

3.2. Required research personnel training
Unless determined otherwise by the IRB, IU-affiliated research personnel who are designated key personnel and research personnel directly interacting with human
subjects must:
  • Complete one of the following human subjects protection courses via the CITI program every three years:
    o Biomedical Researcher, Stage 1, or refresher
    o Social/Behavioral/Educational Researchers, Stage 1, or refresher
    o VA Human Subjects Protection course

IU-affiliated PIs and Student, Fellow, and/or Resident PIs of interventional clinical trials must:
  • Complete the CITI GCP course every three years.

Research funded by the NIH Investigators and clinical trial site staff responsible for the conduct, management, and/or oversight of trials (i.e., key personnel) must:
  • Complete GCP training via applicable class/course, academic training program, or certification from a recognized clinical research professional organization.

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 debarment from engaging in research with human subjects at Indiana University.

5.0 History
Replaces IU SOP for Research Involving Human Subjects – Investigator Responsibilities (07/2015)

6.0 Related Information
AAHRPP Standards
  • Element I.1.D
  • Element I.1.E
  • Element I.1.G
  • Element I.4.A
  • Element II.3.F
  • Element III.1.A
  • Element III.1.C
  • Element III.1.D
  • Element III.1.F
  • Element III.1.G
  • Element III.2.A
  • Element III.2.B
  • Element III.2.C
  • Element II.2.D

IU HRPP Policies and Guidance
  • All

KC IRB Questionnaires (see KC Crosswalk)
  • N/A
Regulatory References

- 21 CFR 312, especially Subpart D
- 21 CFR 812, especially Subpart C and Subpart G
- 42 CFR 11
- 45 CFR 46
- International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH): Guideline for Good Clinical Practice E6(R2), section 4
- OHRP Investigator Responsibilities FAQs
Use of Education Records in Research

About This Policy

Effective Date: 07/19/2018

Last Updated: 07/19/2018

Policy Contact:
IU Human Subjects Office
(317) 274-8289
irb@iu.edu

1.0 Scope

This policy applies to the conduct of human subjects research involving student education records under the jurisdiction of the IU Human Research Protection Program (HRPP). This includes research under the oversight of the IU IRBs and research for which IU or its affiliates are relying on an external IRB for oversight.

This policy does not apply to directory information.

2.0 Policy Statement

Student education records may be used for research purposes only when one of the following is true:

- The records do not include personally identifiable information
- The institution whose student education records will be used determines that the records will be used by school officials with legitimate educational interest.
- The student (or the student’s parent or guardian, when appropriate) provides written permission. Written permission must include all of the following:
  - Description of the records to be disclosed
  - Purpose of the disclosure
  - Party or class of parties to whom the disclosure may be made

3.0 Procedures

3.1. Human subjects submission and review

The study team describes the use of student education records in the human subjects application and provides the following, if applicable:
• Documentation that the institution has determined that the records will be used by school officials with legitimate educational interest, except for use of IU student education records under section 3.2 below
• If the researcher is obtaining written permission from students (or the students’ parent or guardian, when appropriate) to access student education records, the document used to secure such permission

The reviewer ensures that all requirements consistent with this policy are met.

3.2. Use of IU personally identifiable educational records without written permission
IU researchers may be considered school officials with legitimate educational interests and may use student education records of IU students for research purposes without written permission if all of the following are true:

• The research is designed to study the effectiveness of an instructional technique or method
• The researcher will access identifiable information only from students in their own courses
• The researcher will present only aggregate data in publications and presentations

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 debarment from engaging in research with human subjects at Indiana University.

5.0 History
New Policy

6.0 Related Information
AAHRPP Standards
• N/A

IU HRPP Documents
• Policies
  o N/A
• Guidance
  o FERPA and research with student education records

KC IRB Questionnaires (see KC Crosswalk)
• Exempt Questionnaire
• Questionnaire D – Recruitment Methods

Regulatory References
• The Family Education Rights and Privacy Act (FERPA), 20 U.S.C. § 1232g; 34 CFR 99
• IU Policy on Release of Student Information
Use of PHI in Research

1.0 Scope

This policy applies to the conduct of human subjects research subject to the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule under the jurisdiction of the IU Human Research Protection Program (HRPP). This includes research under the oversight of the IU IRBs and research for which IU or its affiliates are relying on an external IRB for oversight.

2.0 Policy Statement

The use of Protected Health Information (PHI) is always allowable for treatment, payment, and health care operations. PHI may also be used for research purposes, including recruitment, in the circumstances as described below.

2.1. Authorization from the research subject

PHI may be used for research purposes when the subject provides authorization. An authorization to use and disclose PHI must be written in plain language and must include all of the following elements:

- Name and address of the subject, if the study team is seeking release of medical records
- A specific and meaningful description of the information to be used or disclosed, written in a language understandable to the subject
- 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)
- 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., research personnel and other individuals who are part of the research team, described as broadly as possible to cover all possible circumstances)
• A description of the purpose of each use or disclosure of identifiable health information
• An expiration date for the authorization, such as a date, an event, or a statement like, “end of research study”
• The individual’s signature (or that of his/her legally authorized representative, including a description of that representative’s authority to act on behalf of the individual, if applicable) and the date, unless the Privacy Board waives this requirement
• A statement that the individual may revoke the authorization in writing to a member of the research team, except to the extent that research personnel had already acted in good faith on the signed authorization
• 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
• 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

2.2. Waiver or alteration of authorization
PHI may be used or disclosed for research purposes when a Privacy Board approves a waiver of authorization. In addition, the Privacy Board may approve an alteration to the authorization requirements described in 2.1 above. The Privacy Board may approve such a waiver or alteration if it determines all of the following:
• 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:
  o An adequate plan exists to protect the identifiers from improper use and disclosure
  o An adequate plan exists 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
  o There is 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 HIPAA Privacy Rule
• The research could not practicably be conducted without the waiver
• The research could not practicably be conducted without access to and use of the PHI

An IRB may serve as the Privacy Board for purposes of granting waivers of authorization pursuant to this section. Uses or disclosures of PHI made pursuant to a waiver of authorization or alteration of authorization requirements are subject to the minimum necessary rules.

2.3. De-identified health information
De-identified health information is not considered PHI and may be used or disclosed for research purposes without authorization from the research subject or a waiver of authorization from a Privacy Board.
Research personnel using de-identified information must be able to provide documentation, upon request, that the health information was de-identified by one of the following two methods/processes:

- **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, 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 documents in writing the methods and results of the analysis that justifies such determination.

- **Safe Harbor Method:** The following identifiers concerning the individual or of the individual’s employer, relatives, and household members are removed:
  - Names
  - All geographic subdivisions smaller than a state, including street address, city, county, precinct, ZIP code
  - Elements of dates (except year) directly related to an individual including birth date, admission date, discharge date, death date, and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older
  - Telephone numbers
  - Fax numbers
  - Electronic mail addresses
  - Social Security numbers
  - Medical record numbers
  - Health plan beneficiary identifiers
  - Account numbers
  - Certificate/license numbers
  - Vehicle identifiers and serial numbers, including license plate numbers
  - Device identifiers and serial numbers
  - Web universal resource locators (URL)
  - Internet protocol (IP) address numbers
  - Biometric identifiers, including finger and voice prints
  - Full face photographic images and any comparable images
  - Any other unique identifying number, characteristic, or code

The following demographic information may be used and still be considered de-identified:

- Age with dates limited to the year (age 90 and over must be aggregated to 90+ to prevent the identification of very old individuals)
- Aggregated ZIP codes in the form of the initial three-digit ZIP codes that contain more than 20,000 people
- Race
- Ethnicity
- Marital status
- Codes that can be affixed to the research record that will permit the information to be reidentified by the covered entity if necessary, provided that the key to such a code is not accessible to the research personnel 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
Research personnel must be able to provide documentation upon request that the individual creating the de-identified data set has legitimate access to the PHI.

2.4. **Limited data set**
A Limited Data Set excludes direct identifiers and may be used or disclosed for research purposes without authorization from the research subject or a waiver of authorization from a Privacy Board. A Limited Data Set may not include any of the identifiers which must be removed for the safe harbor method above, with the exception of the following direct identifiers:

- Town, city, county, precinct, state and ZIP code
- All elements of dates directly related to an individual, including birth date, admission date, discharge date, and date of death
- Unique identifying numbers, characteristics, and codes

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.

Uses or disclosures of PHI as Limited Data Sets for research purposes are subject to the minimum necessary rules.

2.5. **Research involving decedent PHI**
PHI of decedents deceased less than 50 years may be used or disclosed for research purposes without authorization from the research subject or a waiver of authorization from a Privacy Board. Research personnel must provide documentation of all of the following upon request:

- The use will be solely for research on the identifiable health information of decedents
- The PHI sought is necessary for the purposes of the research
- Documentation of the death of the individual about whom information is being sought

PHI of individuals deceased more than 50 years is not protected under the HIPAA Privacy Rule and not subject to this policy.

2.6. **Reviews preparatory to research**
PHI may be used for research purposes without authorization from the subject or a waiver of authorization from a Privacy Board for reviews preparatory to research (i.e., feasibility studies) when all the following are true:

- The use or disclosure of identifiable health information is solely to prepare a research protocol or for similar purposes that are preparatory to research
- Research personnel shall not record or remove the information from the covered entity. Research personnel may access PHI electronically in order to review the information, but may not record, store, or otherwise retain the information after the review.
- 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)
• 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 the study team’s ability to successfully recruit.

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

3.0 Procedures

3.1. IRB and Privacy Board submission and review
The study team describes the use of PHI in the human subjects application and submits the mechanism for obtaining HIPAA authorization, including any translated language, when applicable.

Subjects enrolled at the Roudebush VAMC must provide written HIPAA authorization, unless HIPAA authorization is waived, on VA Form 10-0493. The HIPAA authorization cannot be embedded in the consent form for these subjects.

A request for waiver or alteration of authorization requirements is submitted to the Privacy Board for review and approval. When the Privacy Board approves such a waiver or alteration, it must document all of the following:
• Privacy Board of record
• Date of Privacy Board approval of the waiver
• Statement that the waiver of HIPAA authorization satisfies the criteria described in 2.2 above
• A brief description of the PHI for which the Privacy Board has determined use or disclosure to be necessary
• Identification of the Privacy Board review procedure used to approve the waiver
• Signature of the Chair of the Privacy Board or a qualified voting member designated by the Chair

Protocol-specific mechanisms for ensuring confidentiality of research data, including PHI, are also described by the study team in the human subjects application. The IRB considers the information in the IRB application and documents its determinations as appropriate. IU and its affiliates have agreed that identified systems provide adequate provisions to protect confidentiality of research data. If research personnel will use only these systems to collect, transmit, store, compute, and archive research data, the IRB may find that adequate provisions exist to maintain confidentiality of data without additional information.

3.2. Recruitment
PHI may be used for recruitment purposes (i.e., identification and screening) without authorization from the subject or a waiver of authorization from a Privacy Board if the investigator is a part of the workforce of the covered entity who owns the PHI. If the investigator using PHI for recruitment purposes is not a part of the workforce of the covered entity, authorization from the subject or waiver of authorization from a Privacy Board for recruitment purposes is required.

When PHI will be created through self-report of detailed PHI, or interventions with
potential subjects that are being conducted solely for the purposes of determining eligibility for the research, authorization from the subject or a waiver of authorization from a Privacy Board is required.

3.3. **Psychotherapy notes**
Psychotherapy notes may only be used for research purposes, including recruitment, with authorization from the subject.

3.4. **Revisions to HIPAA authorization language**
HIPAA authorization language must be revised whenever there is a change in any of the core elements of the authorization described in 2.1 above, including a change to the persons or classes of persons who will receive PHI. Revisions to HIPAA authorization language must be reviewed and approved by the IRB prior to implementation. Newly enrolled subjects must sign the most recently approved version of the HIPAA authorization language.

3.5. **Individual’s access to PHI**
Subjects who participate in research have the right to access PHI (i.e., inspect and obtain a copy) about them which is stored as part of the research record. Subjects participating in treatment studies may be temporarily suspended from accessing their research records for as long as the research is in progress, provided that:
- The subject agreed to the denial of access in the HIPAA authorization
- The subject’s right of access will be reinstated upon completion of the research

3.6. **Revocation of HIPAA authorization**
A research subject may revoke 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.

When a subject revokes authorization, data collected on the subject to the point of the subject’s revocation remains part of the study records and may not be deleted. Copies of revocations of authorizations should be maintained as part of the research record.

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 debarment from engaging in research with human subjects at Indiana University.

5.0 **History**
Replaces portions of the IU SOP for Research Involving Human Subjects – Confidentiality and Privacy (v02/2017)

6.0 **Related Information**
AAHRPP Standards
- Element II.3.D
- Element II.3.E

IU HRPP Documents
- Policies
  - Research Data Management
• Guidance
  o HIPAA

KC IRB Questionnaires (see KC Crosswalk)
• K – HIPAA
• L – VA Research

Regulatory References
• 45 CFR 164, especially Subpart E
• Indiana Code 16-39-1-4
• IU University Compliance: HIPAA Privacy and Security Compliance
• Health Information Privacy, especially:
  o HIPAA for Professionals
  o Research
• VHA Handbook 1200.05 – Requirements for the Protection of Human Subjects in Research, especially section 23
IU HRPP Policy Definitions

1.0 Abbreviations

**CFR:** Code of Federal Regulations

**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

**IU HRPP:** IU Human Research Protection Program

**HHS:** U.S. Department of Health & Human Services

**IU:** Indiana University

**KC:** Kuali Coeus

**OHRP:** DHHS Office of Human Research Protections

**ORC:** IU Office of Research Compliance

**QIO:** IU Quality Improvement Office

**Roudebush VAMC:** Richard L. Roudebush VA Medical Center, Indianapolis, IN

**VA:** U.S. Department of Veterans Affairs

**VHA:** U.S. Veterans Health Administration

**VHA ORD:** VHA Office of Research and Development

**VA ORO:** Office of Research Oversight
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.

**adult:** An individual who has reached age of majority in the relevant state. In Indiana, a person at least eighteen (18) years of age.

**adult 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.

**adverse events:** Any untoward or unfavorable occurrence, including medical, physical, and psychological harms, in a human subject associated with the subject’s participation in the research, whether or not considered related to the subject’s participation in the research.

**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. Includes audits, monitoring visits, and compliance inspections.

- **for-cause (directed) audit:** internal audit requested by an IRB, IRB chair, the director of the Human Research Protection Programs, or the associate vice president of research compliance when circumstances require an on-site record review, generally related to reported or suspected noncompliance.

- **internal audit:** audit conducted by the IU Quality Improvement Office

- **not-for-cause (scheduled) audit:** internal audit which is a part of the IU HRPP audit plan.

**audit trail:** Documentation, including 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:** per the Privacy Rule, an individual’s permission to allow a covered entity to use or disclose the individual’s protected health information (PHI) described in the authorization for the purpose(s) and to the recipient(s) stated in the authorization.

**biological product/biologic:** As regulated by the FDA, a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein (except any chemically synthesized polypeptide), or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound), applicable to the prevention, treatment, or cure of a disease or condition of human beings; regulated as a drug.

**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.

**children (minor):** 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. In Indiana, persons less than 18 years of age.

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

**confidentiality:** The assurance that certain information about individuals, which may include a subject’s identity, health, behavior, or lifestyle information, or a sponsor’s proprietary information, will not be disclosed without permission from the subject or sponsor.

**corrective action:** Action taken to correct a noncompliant situation that has occurred.

**covered entity:** Health plan, health care clearinghouse, or health care provider who electronically transmits any health information in connection with transactions for which HHS has adopted standards.

**data use agreement:** Under the Privacy Rule, an agreement between a covered entity and the recipient of a *limited data set* which specifies permitted uses and disclosures of the limited data set, identifies who may use or receive the limited data set, and restricts further use and disclosure.

**de-identified:** information that is rendered not individually identifiable by either the Expert Determination method or Safe Harbor Method described in the IU HRPP Policy on Use of PHI in Research, section 2.3.

**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 provided by the Common Rule to the department or agency head has been delegated.

**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:

1. recognized in the National Formulary, or the United States Pharmacopeia, or any supplement to them;
2. 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
3. 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. See [FDA Guidance for Industry and FDA Staff on Classification of Products as Drugs or Devices and Additional Product Classification Issues](https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm).

**Directory information:** for education records, includes, but is not limited to, the student's name; address; telephone listing; electronic mail address; photograph; date and place of birth; major field of study; grade level; enrollment status (e.g., undergraduate or graduate, full-time or part-time); dates of attendance; participation in officially recognized activities and sports; weight and height of members of athletic teams; degrees, honors, and awards received; and the most recent educational agency or institution attended.

**drug:** As regulated by the FDA:
(A) articles recognized in the official United States Pharmacopoeia, official Homoeopathic Pharmacopoeia of the United States, or official National Formulary, or any supplement to any of them; and

(B) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and

(C) articles (other than food) intended to affect the structure or any function of the body of man or other animals; and

(D) articles intended for use as a component of any articles specified in clause (A), (B), or (C).

See FDA Guidance for Industry and FDA Staff on Classification of Products as Drugs or Devices and Additional Product Classification Issues.

**Education records**: Under FERPA, those records that are directly related to a student; and maintained by an educational agency or institution or by a party acting for the agency or institution. The term does not include:

- Records that are kept in the sole possession of the maker, are used only as a personal memory aid, and are not accessible or revealed to any other person except a temporary substitute for the maker of the record.
- Records of the law enforcement unit of an educational agency or institution, subject to the provisions of §99.8.
- Records relating to an individual who is employed by an educational agency or institution, that:
  - Are made and maintained in the normal course of business;
  - Relate exclusively to the individual in that individual’s capacity as an employee; and
  - Are not available for use for any other purpose.
- Records relating to an individual in attendance at the agency or institution who is employed as a result of his or her status as a student are education records and not excepted under paragraph (b)(3)(i) of this definition.
- Records on a student who is 18 years of age or older, or is attending an institution of postsecondary education, that are:
  - Made or maintained by a physician, psychiatrist, psychologist, or other recognized professional or paraprofessional acting in his or her professional capacity or assisting in a paraprofessional capacity;
  - Made, maintained, or used only in connection with treatment of the student; and
  - Disclosed only to individuals providing the treatment. For the purpose of this definition, “treatment” does not include remedial educational activities or activities that are part of the program of instruction at the agency or institution; and
- Records created or received by an educational agency or institution after an individual is no longer a student in attendance and that are not directly related to the individual’s attendance as a student.
- Grades on peer-graded papers before they are collected and recorded by a teacher.

**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.
**enrollment:** Enrollment begins at the time of consent for the study. For research for which consent is not required, enrollment begins at time of data collection or when the subject agrees to participate.

**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.

**federally-funded:** Supported, either directly or indirectly, by funds provided by the federal government. This includes federal pass-through funding (i.e., received as a subrecipient through subcontracts). Use of administrative services funded by a federal grant, alone, is not sufficient to consider research federally-funded.

**Federalwide Assurance (FWA):** written assurance of compliance with the Common Rule to OHRP from institutions engaged in non-exempt human subjects research conducted or supported by HHS.

**fetus:** The product of conception from implantation until delivery.

**generalizable knowledge:** Information that expands the knowledge base of a scientific discipline or other scholarly field of study.

**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.

**HIPAA:** The Health Insurance Portability and Accountability Act of 1996. See also Privacy Rule.

**human subject:** A living individual about whom an obtains 1) data through intervention or interaction with the individual, or 2) identifiable private information (as defined by 45 CFR 46.102(f)). For research subject to FDA regulations, 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. Synonymous with “subject,” “participant,” and “volunteer.”

**humanitarian device exemption (HDE):** FDA marketing application for an HUD.

**humanitarian use device (HUD):** As regulated by 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.”

**identifiers:** Information that can be used to link a sample or scientific result with a specific person or group of people, including any of eighteen (18) identifiers defined by the Privacy Rule and defined in the IU HRPP Policy on Use of PHI in Research, section 2.3, Safe Harbor Method.

**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 in accordance with the IU HRPP Policy on Informed Consent.

**in loco parentis:** The legal doctrine under which someone acts in the place of a parent.

**Institutional Review Board (IRB):** Appropriately constituted group formally designated review and monitor research involving human subjects to assure the protection of the rights and welfare of the subjects.

**interaction:** Includes communication or interpersonal contact between the investigator (or research personnel) and the subject.
**intervention**: Includes both physical procedures by which information or biospecimens are gathered (e.g., venipuncture) and manipulations of the subject or the subject’s environment that are performed for research purposes.

**investigational biologic, drug, device, or test article**: A drug or device that is the object of a clinical investigation.

**investigational device exemption (IDE)**: As regulated by the FDA, authorization allowing an investigational device to be used in a clinical investigation in order to collect safety and effectiveness data.

**Investigational New Drug Application (IND)**: request for authorization from the FDA to administer an investigational drug or biological product to humans.

**IRB-approved protocol**: refers to all IRB-approved study information, including the human subject application, formal protocol document, consents, etc.

**legally authorized representative (LAR)**: 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. For definition of LAR in Indiana, see IU HRPP Policy on Adult Individuals Lacking Consent Capacity.

**life-threatening**: (1) diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted, and (2) disease or conditions which potentially fatal outcomes, where the endpoint of the clinical trial analysis is survival.

**limited data set**: A limited set of identifiable protected health information which excludes some identifiers as described in the IU HRPP Policy on Use of PHI in Research.

**minimum necessary**: Standard under the Privacy Rule that PHI should not be used or disclosed when it is not necessary to satisfy a particular purpose or carry out a function.

**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 the same or similar instances of noncompliance, occurring in reasonably close proximity, which continues to occur after discovery of noncompliance and implementation of a preventive action plan, or results from failure to implement a preventive action plan approved by the IRB.
- **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.
- **observed or apparent noncompliance**: Noncompliance that does not require further information to confirm its occurrence.
- **serious noncompliance**: Noncompliance which:
- Significantly increases the probability and/or magnitude of risk to subjects beyond what was previously recognized for the study,
- Significantly compromises the rights and welfare of subjects,
- For greater than minimal risk research, compromises the research such that important conclusions can no longer be reached, or
- Results from significant disregard for policies and/or regulations intended to protect human subjects and results in actual harm to subjects.

For VA research, also includes noncompliance which (1) presents a genuine risk of substantive harm to the safety, rights, or welfare of human research subjects, research personnel, or others, including their rights to privacy and confidentiality of identifiable private information, or (2) substantially compromises a facilities’ HRPP.

**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. 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.

**nonscientist**: For the purposes of IRB membership, 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.

**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.

**parent**: A child’s biological or adoptive parent.

**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.

**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.

**preventive action**: A process implemented to prevent occurrence of an event in the future.

**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.
privacy: Refers to persons and their interest in controlling the access of others to themselves.

Privacy Board: Under the Privacy Rule, the group of individuals charged with the review and approval of waivers of authorization.

Privacy Rule: Federal Rule found at 45 CFR 160, and 164 subparts A and E, which establishes national standards for protection of individuals’ medical records and other personal health information; applies to covered entities.

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).

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 deviation: An alteration/modification to the IRB-approved protocol that is not approved by the IRB prior to its initiation or implementation.

major protocol deviation: may affect subject safety and/or the integrity of study data.

psychotherapy notes: notes recorded (in any medium) by a health care provider who is a mental health professional documenting or analyzing the contents of conversation during a private counseling session or a group, joint, or family counseling session and that are separated from the rest of the individual's medical record. Psychotherapy notes excludes medication prescription and monitoring, counseling session start and stop times, the modalities and frequencies of treatment furnished, results of clinical tests, and any summary of the following items: diagnosis, functional status, the treatment plan, symptoms, prognosis, and progress to date (45 C.F.R. § 164.501).

recruitment: initial identification and contact with potential subjects, which may include both direct interactions with individuals and/or accessing identifiable data or specimens for the purpose of determining whether an individual or their data or specimen may participate or be included in a 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 that agrees to accept IRB review and oversight from a reviewing IRB

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.
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.

- Synonomous with clinical investigation: For research subject to FDA regulations, any experiment that involves a test article 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 following activities are deemed not to be research under this definition:

- Scholarly and journalistic activities (e.g. oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information that focus directly on the individuals about whom the information is collected.

- Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. Such activities are limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products). Such activities include those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters).

- Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for the activities authorized by law or court order solely for criminal justice or criminal investigative purposes.

- Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions

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 personnel: Individuals engaged in human subjects research; specifically, individuals who interact or intervene with human subjects, or access identifiable information for research purposes. Also called investigators.

Investigator: In research subject to FDA regulations, an individual who actually conducts a clinical investigation, i.e., under whose immediate direction the test article is
administered or dispensed to, or used involving, a subject, or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team

**IU-affiliated investigator:** Indiana University faculty, staff, and students engaged in human subjects research, and employees and staff of IU affiliate institutions that 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:** Investigators, other than the PI, who are 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 a study that is greater than minimal risk (Full Board), Investigators listed on Form FDA 1572 or the investigator agreement.

**Non-key personnel:** Investigators conducting research procedures under the direction of the principal investigator or key personnel but are not considered responsible for the conduct and/or reporting of research.

**non-affiliated investigator:** Indiana University faculty, staff, and students engaged in human subjects research, and employees and staff of IU affiliate institutions that 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.

**Principal Investigator (PI):** responsible leader of a team of research personnel who has the ultimate responsibility for the conduct of the research.

**Student, Fellow, Resident PI:** Student responsible for design and/or conduct of the research under the mentorship of a PI in order to complete an education requirement.

**Site-Specific PI:** When the IU IRB is providing review and oversight for an external research site, the responsible leader of a team of investigators at that site who has the ultimate responsibility for the conduct of the research only at that site.

**reviewing IRB:** The IRB responsible for review and oversight of a research project. Also known as the IRB of record or the single IRB (sIRB).

**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.

**serious adverse event (SAE):** Any adverse event that results in death, a life-threatening experience, inpatient hospitalization, prolongation of hospitalization, persistent or significant disability/incapacity, congenital anomaly, or birth defect, or that requires medical or surgical intervention to prevent such an outcome.

**serious problem:** For research subject to VA regulations, 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.
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 research.

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).

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: 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.

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.

**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.

**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.

**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.