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100 General Administration (GA)
Policy GA 101: The Authority and Purpose of the Institutional Review Boards

1. Purpose
The purpose of this policy is to:

- State the institutional authority under which the IRBs are established and empowered;
- Define the purpose of the IRBs;
- State the principles governing the IRBs to insure that the rights and welfare of research subjects are protected;
- State the authority of the IRBs;
- Define the relationship of the IRBs to other University committees and to University officials.

2. Responsibility for Executing the Policy
The Director/Associate Director, Office of Human Research (OHR)
Senior Institutional Official(s)

3. Policy Statement
This policy pertains to the activities of all IRBs operating under the authority of Thomas Jefferson University’s Federalwide Assurance (FWA).

3.1. Statement of Institutional Authority
The Institutional Review Boards are established and empowered under the authority of the President of Thomas Jefferson University and the University’s FWA with the Department of Health and Human Services.

Thomas Jefferson University requires that all research involving human subjects, or material or personal information from living humans, be reviewed and approved by one of the University’s IRBs prior to initiation of any research activities. This includes recruitment and screening activities.

3.2. Purpose of the IRBs
The purpose of the IRBs is to protect the rights and welfare of human subjects participating in biomedical and behavioral research conducted at Thomas Jefferson University. The IRBs are responsible for the review, approval and oversight of such research to assure that it meets the ethical principles established for human subjects research, and that it complies with federal regulations that pertain to human subjects protection at 45 CFR, Part 46 and 21 CFR, Part 56 and any other pertinent regulations and guidance.
3.3. Governing Principles
The IRBs will be guided by the ethical principles regarding research involving human subjects as espoused in the report of the National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research entitled: Ethical Principles and Guidelines for the Protection of Human Subjects in Research (“The Belmont Report”). The defining principles in the Belmont Report are:

- **Beneficence**— The sum of the benefit derived by the subject from participation and the importance of the knowledge to be gained from the study to outweigh the risks to the subject as to warrant a decision to allow the subject to accept the risks.

- **Autonomy**— Legally and ethically effective informed consent is obtained unless the requirements for waiver of informed consent are met by adequate and appropriate methods that meet the provisions of applicable regulations.

- **Justice**— The selection of subjects is equitable and is representative of the group of subjects that will benefit from the research.

3.4. IRB Authority
3.4.1. The function of the IRBs is to review and approve biomedical and behavioral research involving human subjects that is conducted by faculty of the separate colleges of the University regardless of the source of funding and the location at which the research is performed. The authority to carry out this mandate is stated in 21 CFR 56.108(a)(1); 108(b)(3); 109(a)(f); 113 and 45 CFR 160,164. Consequently, the IRBs will review all research that:

- is sponsored by Thomas Jefferson University

- is conducted by or under the direction of any faculty of the University in connection with his/her institutional responsibilities

- is conducted by or under the direction of faculty of the University using any property or facility of the University

- involves the use of the University’s or the University Hospital’s nonpublic information to identify and contact human research subjects

- involves the use or disclosure of protected health information.

3.4.2. Each Thomas Jefferson University IRB has the authority to ensure that human subjects research is designed and carried out in a manner that protects the rights, welfare and privacy of the subjects. Consequently each IRB has the authority to:
• Approve, require modifications to secure approval, or disapprove all human subjects research activities overseen and conducted by the organization (45 CFR 46.109(b))

• Suspend or terminate approval of research not being conducted in accordance with the IRB’s requirements or that has been associated with unexpected serious harm to participants (45 CFR 46.113)

• Observe, or have a third party observe, the consent process (21 CFR 56.109(f))

• Observe, or have a third party observe, the conduct of the research (21 CFR 56.109(f))

4. Policy Specifics

4.1. Federally Funded Research

If the study is part of an application to a sponsoring federal agency, the protocol involving human subjects must be reviewed by the IRB when the application is reviewed by the Office of Research Administration and prior to the submission of the application to the agency. In the case of the NIH, review may be carried out on a just in time basis. In any case, it must be done prior to the expenditure of any grant funds. (45 CFR 46.103(f))

4.2. Relationship of the IRBs to University Officials and Committees

4.2.1. Research covered by this policy that has been approved by an IRB may be subject to further appropriate review and approval or disapproval by officials of the institution. However, those officials may not approve the research if it has not been approved by an IRB. (45 CFR 46.112)

4.2.2. The IRBs function independently of, but in coordination with, University officials and other committees. If IRB members or IRB staff becomes aware of any undue influence on the IRB review process, they should notify the Director or Associate Director, OHR, immediately. The allegation will be referred to the Office of University Counsel which will be responsible for investigating the allegation and taking corrective actions, as necessary.
4.2.3. Before the IRB conducts its review of a research study, the IRB staff will check for a completed financial disclosure form from all individuals in the design, conduct, or reporting of the research. If the financial disclosure forms are not completed, IRB review will not proceed until complete financial disclosure forms are submitted. If a significant financial interest is disclosed, the IRB review will not occur until after the University’s Conflict of Interest Committee has completed its review of the significant financial interest and proposed management plan, and included its review in the study application. IRB staff will be periodically trained on procedure.

4.3. Use of Policies and Procedures
The Office of Human Research and each IRB must maintain and follow all written policies and procedures consistent with federal regulations, good clinical practice, and the ethics of human subjects protection when reviewing proposed research.

4.4. Number of IRBs
The senior administration of the University has authorized three IRBs to review and approve research involving human subjects conducted by faculty and students of the Colleges of the University.
1. **Purpose**
   To describe specific activities that require IRB review and, conversely, those that do not require IRB review.

2. **Responsibility for Executing the Policy**
   Director/Associate Director, OHR
   IRB Chairs, Vice Chairs

3. **Definitions**
   3.1. **DHHS**
   - **Research**: A systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge.
   - **Human Subject**: A living individual about whom an investigator (whether professional or student) conducting research obtains data through intervention or interaction with an individual or identifiable private information.
   - **Interaction**: Communication or interpersonal contact between an investigator or his or her research staff and the research subject or their private identifiable information.
   - **Intervention**: Physical procedures by which data are gathered (e.g., venipuncture) and manipulations of the subjects' environment that are performed for research purposes.
   - **Private Information**: 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 (for example, a medical record). Private 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) in order for obtaining the information to constitute research involving human subjects.
3.2. FDA

- **Clinical Investigation**: 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 Food and Drug Administration under section 505(i) or 520(g) of the Federal Food, Drug, and Cosmetic Act, or need not meet the requirements for prior submission to the Food and Drug Administration under these sections of the Federal Food, Drug and Cosmetic Act, but the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The terms research, clinical research, clinical study, study, and clinical investigation are synonymous for purposes of FDA regulations. (21 CFR 50.3(c), 21 CFR 56.102(c))

- **Human Subject**: an individual who is or becomes a subject in research, either as a recipient of the test article or as a control. A subject may be either a healthy individual or a patient. For research involving medical devices a human subject is also an individual on whose specimen an investigational device is used.

3.3. **Generalizable Knowledge**: Knowledge that is drawn from systematic qualitative or quantitative investigation that may be applied outside of the investigation from which it was derived.

4. **Policy Statement**

No intervention or interaction with human subjects in research, including recruitment, may begin until the IRB has reviewed and approved the research protocol. “Human subjects research is any activity that either 1) meets the HHS definition of ‘research’ involving ‘human subjects’ as defined at 45 CFR 46.102(d)(e)(f) or 2) meets the FDA definition of ‘clinical investigation’ involving ‘human subjects’ as defined at 21 CFR 56.102(c)(e).”

All research of any kind, and in any field, that involves human subjects as defined by HHS or FDA regulations, regardless of sponsorship, must be reviewed and approved by a Thomas Jefferson University IRB. Under certain conditions, TJU may rely on another institution’s IRB through execution of an IRB Authorization Agreement (IAA). An IAA can be initiated by contacting the Director/Associate Director, OHR.

5. **Policy Specifics- Activities Requiring IRB Review**

All research involving human subjects, unless declared exempt by appropriate OHR personnel as per Policy RR 403, must have review and approval by the IRB.

5.1. Specific activities that require IRB review include but are not necessarily limited to:
5.1.1. 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 section 505(i) or 520(g) of the Food, Drug and 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.

5.1.2. Collection of data about a series of standard procedures or treatments for dissemination or generalization if the activity meets the definition of "human subjects research."

5.1.3. Patient care or the assignment of normal participants to any intervention that is altered for research purposes in any way.

5.1.4. A diagnostic procedure for research purposes that is added to a standard treatment.

5.1.5. "Systematic investigations" involving innovative procedures or treatments. For example, if any investigator plans to collect information about an innovative procedure for scientific purposes or will repeat the innovation with other participants in order to compare it to the accepted standard.

5.1.6. Emergency use of an investigational drug or device (see OHR Policy GA 112). One-time emergency uses of an investigational drug or device may proceed without prospective IRB review. When emergency medical care involves an investigational article, the research does not require prospective IRB review and approval; the patient is a research subject as defined by FDA regulations, but may not be considered a research subject as defined by HHS regulations, and data generated from such care cannot be included in any prospectively conceived report of an HHS-regulated research activity.

5.1.7. Planned Emergency Research See Policy IC 708, "Research in Emergency Settings (Prospective Review)" which describes the exception from informed consent requirements for emergency research and the requirement for prospective review (note: this is not the same as Emergency use of an investigational drug or device as noted in 5.1.6 above).

5.1.8. Data, Human Cell or Tissue Repository: Data, human cell or tissue research typically involves repositories that collect, store, and distribute these materials for research purposes. (See "OHRP Issues to Consider in the Use of Stored Data or Tissues", November 1997) Consult the OHR19

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form to determine whether your research involving data, human cells or tissue requires IRB review.

5.1.9. Investigator-Initiated Research: A Principal Investigator who initiates and conducts a research project or clinical trial involving human subjects has the responsibility to keep the OHR informed of all problems that require prompt reporting to the IRB as described in Policy GA 120.

5.1.10. Student Conducted Research: All activities that meet the definition of research with human subjects, and that are conducted by students for a class project or for work toward a degree must be reviewed by the IRB. These include masters and doctoral theses/dissertations that involve research with human subjects and projects that involve human research subjects and for which findings may be published or otherwise disseminated. Some projects involving participants may meet IRB exemption qualification as defined in 45 CFR 46.101(b)(1-6).

5.1.11. Case Studies: When case studies are compiled in such a way as to allow generalization of knowledge from the data collected, that activity constitutes research and must be reviewed by the IRB. One or two case reviews do not require IRB review unless they meet the criterion of providing generalizable knowledge. They should, however, be reviewed and approved by the University Privacy Officer located in the Office of University Counsel.

5.1.12. Access to protected health information: Investigators within any of the covered entities of Thomas Jefferson University who require protected health information for the conduct of research must provide the IRB with appropriate information to obtain approval of the activity prior to access of the protected health information.

5.1.13. Collaborative Research. Collaborative research requires IRB review by each performance site unless an IRB Authorization Agreement is in place, by which one institution’s IRB can accept the review and approval from another institution’s IRB.

5.2. Activities Not Subject to IRB Review. Activities that do not meet the regulatory definition of human research or clinical investigation do not require IRB approval.

Proposals that lack definite plans for involvement of human subjects will not require IRB review. Additionally, activities such as quality improvement, assurance or quality control, programs and fiscal audits, and certain disease monitoring activities as prescribed by the Public Health Department generally do not qualify as research unless the activity meets either FDA or HHS definitions of research involving participants.
The investigator must obtain documentation from the IRB that the activity is not subject to IRB review.

5.3. Research on Decedents
Research on decedents is usually not subject to IRB review. However, if the research on decedents involves tissue (specimen) from a participant in an FDA-regulated device trial, either as the recipient of the device or as a control, then the research is subject to IRB review. (21 CFR 812.3 (p))

HIPAA does require review of research on decedents and the TJU Privacy Officer in the Office of University Counsel should be consulted regarding protected health information (PHI) and privacy issues.

5.4. Determining Whether an Activity Already Begun or Completed Represents Human Subjects Research (for example a quality improvement or assurance exercise). If an investigator: (1) has begun a project without prospective IRB review and approval and later learns that the project required IRB approval or; (2) realizes that data that has been obtained will contribute to generalizable knowledge and should be published, the investigator must immediately consult with the OHR to determine whether the project represented human subjects research, and thus requires a proposal to be submitted to the IRB.

Prior to beginning research activities, investigators must seek an official determination about whether an activity qualifies as research involving human subjects if they are unsure about whether IRB review is required. The proposal must be sent to the appropriate personnel in the OHR using IRB forms OHR-19 or OHR-23 as applicable. The OHR Director or Associate Director will review it and determine whether it involves human subjects research. If the Director/Associate Director has any questions about whether the activity qualifies as research involving human subjects, the IRB chair may be consulted for a final determination. OHR will notify the investigator in writing as to whether the proposal involves human subjects research or whether the activity is not subject to review and approval by the IRB.

If the proposal qualifies as human subject research, it will be forwarded to the IRB for review and approval unless the research qualifies for exemption. If the study is approved, it must also be determined whether data collected prior to the Board’s approval may be used for publication.

Finally, if it is determined that the investigator conducted human subjects research prior to IRB approval, it must also be determined whether there are issues of non-compliance that need to be investigated. These determinations will be made in accord with University Policy 110.15, “IRB Review of Noncompliance issues.”
6. References

Federalwide Assurance
45 CFR 46.102(d)(f)
21 CFR 50.3(c)(d)(g)
21 CFR 56.102(c)(d)(e)
21 CFR 56.108(b)(1)
21 CFR 812.3(p)
45 CFR 46.103(b)(4)
21 CFR 312
21 CFR 50.24

FDA Information Sheets for IRBs and Investigators
OPRR Reports: Emergency Medical Care, May 15, 1991
OPRR Reports: October 31, 1996
OHRP Guidance: Research Involving Coded Private Information or Biological Specimens, August 10, 2004
OHRP Guidance: Decision Charts; Human Subjects Regulations Decision Charts, September 24, 2004
OHR-19
OHR-23
1. Purpose
The purpose of this policy is to state the commitment of the OHR and the IRBs to maintain and follow up-to-date policies and procedures that adhere to ethical principles and federal and other required regulations pertaining to research with human subjects.

2. Responsibility for Executing the Policy
The Director/Associate Director, OHR
OHR Administrative Staff
Institutional Official(s)
IRB Chairs/Vice Chairs

3. Policy Statement
Adherence to the regulations and guidance from the Office of Human Research Protections (45 CFR 46 103(b)(4)(5),108), the FDA (21 CFR 56.[108(a)(1), (b)(3), 115, 116] and the International Congress of Harmonization, as well as institutional policies and procedures, will assure that the participants in human subjects research will be protected in a uniform manner regardless of changes in personnel listed in item 2.

Assurance of this protection will be documented by having in place written policies so that IRB review ensures research is ethically and scientifically sound.

OHR Internal Forms are used to ensure that OHR policies are integrated into the daily human subjects research operations and review. They also enable the OHR administrative staff and IRB members to manage and track review functions consistently and efficiently.

4. Policies, Procedures and Forms
4.1. Review, revision and approval of Policies, Procedures and Forms

4.1.1. Changes to federal or state regulations/guidelines or to good research practice, as well as to the policies and procedures of the University, may require the OHR to create or revise policies, procedures and/or forms.

4.1.2. Policies, procedures and forms will be reviewed by the Director, OHR on an ongoing basis.

4.1.3. The Director, OHR must approve all new or revised policies, procedures and forms. The Director, OHR will obtain the appropriate input from the Associate Provost for Research Support Services and University Counsel as necessary.
4.2. Policy Dissemination and Training of Affected Individuals

4.2.1. Following approval, the appropriate individuals and departments/divisions will be informed of the new or revised policies, procedures and forms. When IRB members are notified at an IRB meeting, this will be noted in the minutes for the meeting.
100 General Administration (GA)
Policy GA 105: Conducting Research Involving Non-Jefferson Performance Sites

1. Purpose
To outline the assurance process when Thomas Jefferson University participates in human subjects research with other performance sites “engaged” in human subjects research. (Individuals and/or the University/Hospital are “engaged in human subjects research” when any of the activities requiring IRB review, as defined in OHR Policy GA 102, are initiated irrespective of source of research funding.)

2. Responsibility for Executing the Procedure
When a performance site(s) will “engage” in human subjects research, it is the responsibility of the Principal Investigator who will collaborate with that performance site to insure that appropriate approvals and/or agreements are completed at the time when the human subjects research is conducted at the site.

The performance site “engaged” in research may have the research approved by its own IRB or the Thomas Jefferson University IRB through an IRB Authorization Agreement.

It is the responsibility of the IRB of Record as well as the institution holding the FWA to assure that the resources and facilities are appropriate for the conduct of the research under its jurisdiction.

3. Procedures
The Principal Investigator at the TJU site will obtain documentation that approval has been granted for a performance site “engaged” in human subjects research with the University. The investigator will also ensure that the performance site has an approved FWA.

In the case of an Unaffiliated Investigator Agreement, the Principal Investigator at TJU will submit to the OHR a signed Unaffiliated Investigator Agreement for any investigator who is not covered by another institution’s FWA. The Investigator will maintain documentation of any agreement.

The Director or Associate Director, OHR, or OHR administrative staff under their supervision, will ensure that IRB Authorization Agreements and Unaffiliated Investigator Agreements are properly executed and verify that applicable FWAs are current with OHRP.
OHR administrative staff, will consult the OHRP web site to confirm that all performance sites “engaged” in research with the University have an approved FWA and will verify that the appropriate IRB Authorization Agreements and Unaffiliated Investigator Agreements for performance sites have been submitted to OHR for approval. If omissions are found in the documentation, the Associate Director will contact the investigator specifying the required documentation needed from the performance site in order for approval.

The Director/Associate Director, OHR, will sign authorization agreements for the Institution and will maintain a file of current authorizations for those performance sites “engaged” in research where Thomas Jefferson University has agreed to serve as the IRB of Record. The Director, OHR will make all final determinations regarding the willingness of one of the University’s IRBs to serve as IRB of Record for a performance site “engaged” in research.

If a requested performance site is not routinely "engaged" in research (e.g. physicians practice), the investigator at this performance site may be covered under the University’s FWA provided the investigator submits an Unaffiliated Investigator Agreement to and receives approval from the Director, OHR.

The Director, OHR, will register the University with the OHRP and a University IRB will serve as the IRB of Record for an external performance site for research involving human subjects that is conducted in collaboration with Thomas Jefferson University.

The Director/Associate Director, OHR, on behalf of the IRBs, will report promptly to the appropriate Institutional officials at the performance site all actions taken by an IRB of Record for that site regarding any serious noncompliance by the investigator(s), and any suspension or termination for cause of IRB approval of the study in accordance with the TJU OHR and IRB policies and procedures.

4. Definitions
4.1. IRB of Record: An IRB is considered the IRB of Record when it assumes responsibility for human subjects protection for another institution, and is designated to do so through an approved Federalwide Assurance (FWA) with The Office of Human Research Protections (OHRP). An IRB Authorization Agreement is required designating Thomas Jefferson University to serve as the IRB of record.

4.2. IRB Authorization Agreement: A formal agreement between Thomas Jefferson University and another institution that identifies Thomas Jefferson University as the IRB of Record for that entity and defines the responsibilities for both Thomas Jefferson University and the other institution in the conduct of collaborative human subjects research.
4.3. **Unaffiliated Investigator Agreement:** A formal agreement between Thomas Jefferson University and a single independent investigator not routinely “engaged” in research that allows such a single investigator to conduct collaborative human subjects research under the provisions of Thomas Jefferson University’s FWA.

4.4. **Performance Site:** A site where research is performed.

4.5. **Performance site(s) "Engaged" in Research:** A performance site becomes “engaged” in human subjects research when its employees or agents intervene or interact with living individuals, tissue, or personal data from individuals for research purposes. Further, a performance site is considered to be “engaged” in human subjects research when it receives direct federal or commercial support for the research.

4.6. **Performance Site Not "Engaged" in Research:** A performance site is not “engaged” in human subjects research if its employees or agents do not interact with living individuals for research purposes or do not obtain individually identifiable private health information for research purposes.
1. Purpose
To define the process for determining whether personnel participating in the review or conduct of human subjects research have a conflict of interest (COI) with such research.

2. Responsibility for Executing the Policy
IRB Members
IRB Chairs/Vice Chairs
OHR Data Coordinator
Office of University Counsel Corporate Compliance Division
University Conflict of Interest Committee (COIC)

3. Policy Statement and Procedures
3.1. Researcher COI:
All Jefferson employees are required to abide by TJU Policy 107.03, “Conflicts of Interest for Employees” which includes, at a minimum, yearly disclosure of financial COI (FCOI) via the COI-SMART electronic reporting system. The determination as to whether an investigator or key study personnel has a conflict of interest with a particular study will be evaluated by the Office of University Counsel Corporate Compliance Division (“COI Officer”) at the time of initial and continuing review and for amendments adding personnel. The COI Officer confirms that there is a current conflict of interest disclosure on file for each study personnel and assesses individual responses to the COI questions on the appropriate forms (e.g. OHR-1 and OHR-9). The COI Officer will report any potential or managed FCOI to the IRB via an attachment to the electronic Portal agenda for the relevant IRB meeting. The Chair or Vice Chair will introduce it for discussion. If the submission is reviewed as exempt or expedited, the Chair or Vice Chair will ensure that the assigned reviewer is aware of the communication from the COI Officer.

Following its discussion, the IRB may approve or not approve the management plan and may impose additional requirements that are more but not less stringent than those required by the COIC. Furthermore, the IRB will determine whether the COI should be disclosed in the consent form.

The criteria used by the IRB to determine whether a management plan is adequate are described in TJU Policy 107.03 and include:

- Whether the financial interests will adversely affect the safety and/or welfare of participants; and
• Whether the financial interest will adversely affect the integrity of the research.

The plan, approved by both the IRB and the COIC is then submitted to the University Provost for approval. Following approval by the Provost, the IRB may then approve the research or release the approval letter if the study was previously approved contingent upon the Provost’s approval.

With respect to on-going IRB-approved research, investigators and key study personnel must also report any new potential FCOI or changes in existing FCOI within 5 business days of the inception of the potential conflict.

Non-employees involved in human subjects research must complete disclosure on the COI-SMART system. They must contact JeffCOISmart@jefferson.edu and provide their name, email address, institution or school and their role (i.e. clinician, student, therapist, etc.). COI-SMART will transmit instructions to allow researchers to submit answers to questions that are appropriate to their role and level of participation in the research.

3.2. IRB Reviewers
Non-TJU employees who are serving as consultants to the IRB are required to complete the Conflict of Interest Disclosure Form found on the forms page of the OHR website. COI for IRB consultants is addressed in OHR Policy OP 203, “Use of Consultants for Review of Studies”.

3.3. COI for IRB Members
Please see OHR Policy GA 122, “Conflict of Interest Disclosure for IRB Members”

4. Tools
OP 203 Use of Consultants for Review of Studies
TJU Conflict of Interest Policy 107.03
1. Purpose
To describe management policies and procedures designed to promote the long-term commitment of administrative staff of the Office of Human Research, and to ensure the efficient and effective administration and enforcement of IRB decisions.

2. Responsibility for Executing the Policy
Director/Associate Director, OHR
OHR Administrative Staff

3. Policy Statement
The OHR administrative staff provides expertise, constancy and administrative support for the University's three IRBs, and serves as a daily link between the OHR, the IRBs and the clinical trials research community. The OHR administrative staff represents the most vital component in the effective operation of the University's human subjects protection program. The highest level of professionalism and integrity on the part of the administrative staff is expected.

4. Procedures

4.1. Job descriptions and performance evaluations
A description of the responsibilities expected of the specific position of each member of the OHR administrative staff will be provided to the staff member.

The performance of each member of the OHR administrative staff will be reviewed annually at the time of review for merit salary increase using the University's Human Resources Performance Appraisal form.

4.2. Staff Positions
Staffing Levels and allocation of function will be determined by university policy, management assessment of support requirements and budget constraints.

4.3. Hiring and terminating OHR administrative staff
Recruiting, hiring and terminating OHR administrative staff will be conducted according to the human resource policies of the University.
4.4. Delegation of authority or responsibility
    Delegation of a specific function, authority or responsibility to an administrative staff member (e.g., responsibility as administrative secretary for an IRB or as a member of the QA/QI team) must be authorized by the Director, OHR and provided to the staff member in writing. Delegation of responsibility as a secretary for an IRB must be noted on the membership roster for that IRB.

4.5. Documentation
    The policies of the University’s Human Resource Department determine the policies for identifying, documenting and retaining formal staff appointments in the OHR.

5. Tools
    Human Resources Performance Appraisal Form
1. Purpose
   To determine whether the use of database information constitutes research and requires IRB review and/or patient consent.

2. Responsibilities for Executing the Policy
   Office of Human Research

3. Policy Statement
   There has been much confusion in the research community regarding the use of information compiled in databases or contained in existing databases and whether IRB review and/or patient consent is required to access such information.

   The following guidelines are to be used to determine whether the use of database information constitutes research and requires IRB review.

4. Procedures
   4.1. Prospective Data Collection
   If the collection of identifiable data is for a non-research use (e.g. quality assurance, outcome analysis, financial analysis), the act of collecting this information is not research and patient consent is not required.

   If the investigator collects data with a specific intent to test a hypothesis or publish the information, and the collection involves data that identifies the patient, the activity is research and requires IRB approval. However, the consent requirement may be waived by the IRB if the protocol meets the criteria for waiver (45 CFR46.116(c) (d)). Those criteria are: 1) the research presents no more than minimal risk to the subjects; 2) the waiver will not adversely affect the subjects’ rights and welfare; 3) the research could not practicably be carried out without the waiver; and 4) whenever appropriate, the subjects will be provided with additional pertinent information after participation.

   If the investigator collects data with a specific intent to test a hypothesis or publish the information, and the collection is without identifiers or links to identifiable information, the activity is research and requires IRB approval. However, the consent requirement may be waived by IRB if the protocol meets the criteria for waiver. Additionally, the research may qualify for expedited review.
4.2. Retrospective Data Review

If the investigator has a specific intent to test a hypothesis or publish the information, and the review of existing data and the recording of that data occurs without identifiers or links to identifiable information, the activity is research, but qualifies as exempt from IRB review (45 CFR 46.101 (4)). Accordingly, subject consent is not required. However the study must still be presented to the IRB to make the determination that the activity is exempt.

The review of existing data and recording of data with identifiers or links to identifiable information with the specific intent to test a hypothesis or publish is research that is not exempt and requires IRB approval. The research may qualify for expedited review if the data was originally collected for non-research purposes and meets other criteria for expedited review (45 CFR 46 110). Additionally, consent may be waived by the IRB if protocol meets criteria for waiver.

Contact the OHR if you should have any questions about these procedures or how they apply to your project.
1. Purpose
To describe the roles and responsibilities of the Principal Investigator, Co-investigator, Study Coordinator, Key Personnel, and the department chair and/or division head, in the responsible conduct of human subjects research.

2. Responsibility for Executing the Policy
Principal Investigator (PI)
Co-investigator(s) (Co-I)
Study Coordinator(s)
Key Personnel
Department Chair/Division Head

3. Policy Statement
The responsibilities delegated by the PI to the Co-I and other key personnel must coincide with the experience and the training of that particular team member. The PI should document in writing the responsibilities delegated to all members of the team. Any change in Principal Investigator or other team member during the study must be promptly reported to the IRB as an amendment to the protocol using the OHR-12B and OHR-12C.

Anyone proposing to conduct human subject research involving Jefferson patients, facilities or resources must submit a proposal to the IRB for review. This includes investigators from outside the University who intend to collaborate with a Jefferson Principal Investigator.

If the site of performance for a protocol is not a part of Thomas Jefferson University or Thomas Jefferson University Hospital and its Divisions, either the Jefferson IRB or an external IRB must approve the study. If an external IRB is used, the Office of Human Research must be contacted to arrange an appropriate IRB Authorization Agreement to assure compliance with 45 CFR Part 46. These documents must be reviewed and signed by all institutions participating in the project.

4. Policy Specifics
4.1 Procedures for investigators and department chairs
4.1.1 Determination of human subject involvement:
The OHR relies on investigators and department chairs to identify activities that will involve human subjects in research as defined in 45 CFR 46 and/or 21 CFR 50, and as per Policy GA102. When it is not clear whether the activity involves human subjects in research, the investigator should contact the OHR for a determination.

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4.1.2. Requirement for a Co-investigator:
All interventional human subjects research (generally involving a drug, biologic, vaccine or device) must have at least one co-investigator as an alternative contact.

4.1.3. Preparation of protocol:
PIs shall prepare or provide a protocol giving a complete description of the proposed research. In the protocol, the PI shall make provisions for the adequate protection of the rights and welfare of prospective research subjects, and insure that pertinent laws and regulations are observed. This requirement is applicable even in cases where the research is exempt under 45 CFR 46. Investigators shall include the protocol, any investigator brochure, proposed informed consent form(s), any advertisements to recruit subjects and other pertinent information the IRB might need to make a proper determination. The requirement for a written protocol may be waived at the discretion of the IRB.

4.1.4. Scientific merit and ethical consideration of review:
Department heads, through procedures established within their respective departments, centers, or institutes, are responsible for reviewing research protocols for ethical considerations and scientific merit prior to IRB submission.

4.1.5. Submission of a protocol to the Institutional Review Board:
Once it is determined that an investigator wants to initiate a human research study, the investigator and department head shall be responsible for ensuring that the study is submitted to the IRB for review and approval prior to its initiation.

4.1.6. Complying with IRB decisions:
Investigators shall be responsible for complying with all IRB decisions, conditions, and requirements.

4.1.7. Obtaining informed consent:
Investigators shall be responsible for obtaining and documenting informed consent in the manner approved by the IRB and in accordance with 45 CFR 46.116, 21 CFR 50.23 and OHR policies as follows:
- Policy IC 701: Informed Consent and HIPAA Authorization: General Requirements
- Policy IC 702: Documentation, Waiver and Alteration of Informed Consent
4.1.8. Submission of progress reports on the research:
Research investigators are responsible for reporting the progress of the research for review as often as required by the IRB, but no less than once a year [45 CFR 46.109(e); 21 CFR 56.109(f)]. Sufficient time prior to the expiration date should be allowed for processing and IRB review. Submission of a completed OHR-9 form is required for continuing review.

4.1.9. Submission of reports concerning adverse events, unanticipated problems, or risks:
Research investigators are responsible for promptly reporting to the IRB any serious adverse events or unanticipated problems involving risk to subjects or others as per Policy GA 120.

4.1.10. Reporting changes in the research:
Research Investigators are responsible for submitting proposed changes in a research protocol using form OHR-12, OHR-12B and/or OHR-12C. When investigators are added and removed, the OHR-12B and OHR-12C must be submitted to the IRB. However, if the addition/removal of investigator is the only change, a revised consent form does not have to be submitted with the OHR-12B and OHR-12C. The addition/removal of investigators will be made to the consent form with the next required consent amendment or continuing review, whichever comes first.

Changes in research during the period for which IRB approval has already been given shall not be initiated by research investigators without prior review and approval by the IRB, except where necessary to eliminate apparent immediate hazards to the subject. In these situations, an amendment should subsequently be submitted as appropriate to the IRB for review and approval.

4.1.11. Reporting of noncompliance:
Research Investigators and department heads are responsible for promptly reporting to the IRB any serious or continuing noncompliance with the requirements of the University’s FWA or the determinations of the IRB.

4.1.12. Attending IRB meetings:
To facilitate the review of research and the protection of the rights and welfare of human subjects, research investigators may be asked to attend an IRB meeting at which their study is being discussed, and only at the invitation of the IRB.

5. Definitions
5.1. Principal Investigator (PI):
Person with ultimate responsibility for the conduct of the study and adherence to regulations. Qualified individuals are:
Those with a faculty appointment (instructor or higher in one of the Colleges of the University)

TJU or TJUH Employees without a faculty appointment in one of the Colleges of the University but who have appropriate training and expertise as determined by the IRB (in general those who hold advanced degrees such as PhD, MS, MA, PharmD, MSN, MRH, etc.)

Residents, at the discretion of the IRB, for certain minimal risk studies as long as there is a faculty co-investigator to facilitate any outstanding IRB requirements if the resident PI leaves TJUH prior to submission of the final report

Individuals from other institutions who hold an adjunct appointment allowing limited activities at TJU are not eligible per Jefferson by-laws to be a Principal Investigator on a research grant or clinical study conducted at Jefferson. However, they can be listed as co-investigators or key personnel.

5.2. Co-investigators (Co-Is):
For biomedical studies, individuals meeting the qualifications of a PI who are responsible for performing study-related procedures and making important study-related decisions, and who may be designated to obtain informed consent from the study subject are designated as co-I’s. A co-I must be able to answer all study questions and conduct the study in the absence of the Principal Investigator.

On some studies involving minimal risk, other personnel, such as non-faculty members and students may be designated as co-investigators. Examples of this are chart reviews and database studies.

5.3. Study Coordinator:
A research professional who works for and under the direction of the PI. The study coordinator may be responsible for screening and recruiting of subjects, collecting and recording clinical data, maintaining clinical supplies, and if qualified, drawing blood and dispensing medication.

5.4. Key Personnel:
All other individuals contributing to the conduct of the study including, but not limited to, nurses, nurse practitioners, coordinators, residents, fellows, technicians, and students (see also OHR Policies GA 116 and G 601). Key Personnel must be listed on the OHR-1, submit a conflict of interest statement and take all required human subjects training. Other individuals not listed as Key Personnel (i.e., students and residents) may assist in protocol-related procedures only if they do so under the direct supervision of the Principal Investigator or a Co-Investigator.
6. References

45 CFR 46 and 21 CFR 50
GA 102, “Activities Requiring IRB Review”
GA 116 “Use of Students and Employees as Key Personnel and Subjects in Clinical Trials”
GA 125, “Investigator Responsibilities and Delegation of Responsibility”
G 601 “Definition of Key Personnel in Human Subjects Research”
1. Purpose
   To describe the signatory authority given to personnel of the Office of Human Research, for all actions of the IRBs.

2. Responsibility for Executing the Policy
   Associate Provost for Research Support Services
   Director/Associate Director, OHR
   OHR Administrative Staff

3. Policy Statement
   The Director/Associate Director, OHR, are authorized to sign all documents in connection with the review and approval of research involving human subjects. Such research shall have been reviewed and approved according to University policies and procedures by an IRB.

   In all cases, individuals signing documents pertaining to the business of the Division and/or the IRBs, must sign their own name and no other and indicate their title.

4. Procedures
   4.1. Authorization for Signatory Authority
       Authorization to sign documents not described in this policy may be determined by the Director, OHR, and provided in writing to the individual.

   4.2. Results of Reviews, Actions and Decisions
       Results of reviews and actions taken by the IRB, whether by a convened Board or expedited review, may be signed by the Director, Associate Director, or OHR Administrative Staff as designated by the Director.

   4.3. Routine Internal Correspondence
       Routine internal correspondence is any written communication between OHR staff and University/Hospital personnel that does not imply, or appear to imply IRB approval. This correspondence may be issued without the signature of the Director/Associate Director, OHR.

   4.4. Correspondence with External Agencies
       Any letter(s), memo(s) or email(s) sent to any agency of the federal government, as well as to other funding agencies, whether public or private or their agents will be signed by the Director or Associate Director of the OHR.
4.5. Decisions Made by Chairpersons of the Constituent IRBs
Any letter(s), memo(s) or email(s) representing the decisions or opinions of the chairpersons of the constituent IRBs or their respective designees, may be signed by the appropriate designated IRB staff, if so designated by the IRB Chair or a majority in a convened IRB, provided that the correspondence does not imply review and approval of a research study.

5. References
45 CFR Part 46.103 (b) (5)
45CFR Part 46.115(a) (6)
21CFR Part 56.108(b)
1. **Purpose**
   To set forth the policy and procedure for reporting adverse events associated with gene transfer protocols involving human subjects.

2. **Responsibility for Executing the Policy**
   - Principal Investigators
   - Sponsors
   - Director/Associate Director, OHR
   - IRB Chairs/Vice Chairs

3. **Policy Statement**
   Adverse events that meet the reporting criteria for unanticipated problems involving risks to subjects or others will be reported as outlined in Policy GA 120.

   Additional reporting responsibilities apply in gene transfer studies. The Principal Investigator is required to report all serious adverse events to the appropriate offices/agencies listed below regardless of whether they are thought to be related to the gene transfer intervention.

   Section I-E-7 of the NIH Guidelines for Recombinant DNA Research states: “A 'serious adverse event' is defined as any expected or unexpected adverse event, related or unrelated to the intervention, occurring at any dose that results in any of the following outcomes; death, a life-threatening event, in-patient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening or require hospitalization also may be considered to be a serious adverse event when, based on appropriate medical judgment, they may jeopardize the human gene transfer subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition."

4. **Procedures**
   Section E-1-7, Appendix M-Vii-C-1-3, of the NIH Guidelines requires that Principal Investigators (or their designated sponsors) conducting gene transfer clinical trials immediately report serious adverse events to the local Institutional Review Board (IRB), Institutional Biosafety Committee (IBC), Office of Human Research Protections (if applicable), NIH/OBA (Office of Biotechnology Activities) and the Food and Drug Administration (FDA) followed by the submission of a written report filed with each group.
"Immediate" written reporting of serious adverse events is to occur as soon as possible, but no later than 15 days after the event has occurred.

Serious adverse event reports must not contain any trade secret or commercial or financial information that is privileged or confidential as defined under the Freedom of Information Act, 5 USC 552. Serious adverse event reports should be stripped of individually identifiable patient information.

Reports of serious adverse events for gene transfer studies must follow the format provided in the Adverse Event Reporting Form available on the NIH/OBA's website at http://oba.od.nih.gov/oba/rac/adverse_event_template.pdf
1. Purpose
To define emergent use of a test article (drug, biologic, or device) and to define the procedure for notifying the IRB of such use.

2. Responsibility for Executing the Policy
Principal Investigators
Practicing Physicians
Director/Associate Director, OHR

3. Policy Statement
Emergency use means the use of a test article on a human subject in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval [(21 CFR 56.102(d)].

FDA regulations allow emergent use without prior IRB approval provided there is not sufficient time to call a meeting of the IRB (21 CFR 56.102(d)), and the emergency use is reported to the IRB within 5 working days after its initiation/administration. Any subsequent use of the test article must have prior review by the full IRB (21 CFR 56.104). Under FDA regulations, emergency use of a test article is research, the patient is a subject, and the data obtained must be reported to the sponsor and the FDA for research purposes.

DHHS regulations require that all non-exempt research involving human subjects receive IRB review and approval. However, DHHS recognizes that physicians do have the authority to provide emergency medical care to their patients [45 CFR 46.116(f)]. Furthermore, DHHS guidance stipulates that, whenever emergent care is initiated without prior IRB review and approval, the patient may not be considered to be a research subject and the outcome of such care may not be included in any report of a prospectively conceived research activity.

While FDA and DHHS regulations appear to be in direct opposition, the particulars allow for both to be satisfied.

4. Policy Specifics
When possible, contact the OHR Associate Director (215-503-8966) or Director (215-503-0203) as soon as you contemplate emergent use of a study in order that they can determine that the circumstances would follow FDA regulations, and that the emergent use is not research as defined by HHS regulations.

4.1. Investigational Drugs and Biologicals
4.1.1. Procedures to follow
Determine if the proposed use meets the regulatory definition for emergency use of an investigational drug or biologic. Emergency uses must meet ALL of the following criteria:

- The subject has a disease or condition that is life threatening or severely debilitating¹
- No generally acceptable alternative for treating the patient is available
- The subject’s disease or condition requires intervention with the investigational drug or biologic before review at a convened IRB meeting is feasible

The physician is expected to follow as many subject protection procedures as possible. These include:

- Obtaining an independent assessment of necessity by an uninvolved physician;
- Obtaining informed consent from the participant or participant’s legally authorized representative, in accordance with and to the extent required by FDA regulations, and appropriately documenting consent in accordance with and to the extent required by FDA regulations, or determining that use meets the exception to the requirement for consent (see section 6 below);
- Notifying the Institutional Review Board (IRB)

4.1.2. Obtaining the drug/biologic
The Investigator should contact the manufacturer of the drug/biologic to determine if it can be provided under an existing IND or, if not available through the manufacturer, the investigator should contact the FDA for an Emergency IND. If there is insufficient time for an IND, FDA may authorize shipment of the test article in advance of the IND application. Requests for authorization may be made by telephone or other rapid communication means (21 CFR 312.36).

Some manufacturers may require an “IRB approval letter” before releasing the test article. If it is not possible to convene a quorum of IRB members, the Associate Director or Director, OHR will provide the sponsor a letter stating that the IRB is aware of the proposed use and considers the use to meet the emergent use category at 21 CFR 56.104(c). This does not represent IRB approval but it may allow shipment to proceed.
4.2. Investigational Medical Devices

Requirements for emergency use of a medical device are similar to those for use of drugs and biologics. The investigator is referred to the 1998 FDA information sheet, entitled "Medical Devices" [http://www.fda.gov/oc/ohrt/irbs/devices.htm](http://www.fda.gov/oc/ohrt/irbs/devices.htm) for specific instructions.

Each of the following conditions must exist to justify emergency use:

- The patient is in a life-threatening or severely debilitating condition that needs immediate treatment²

- No generally acceptable alternative for treating the patient is available

Because of the immediate need to use the device, there is no time to use existing procedures to get FDA approval for the use.

In the event that a device is to be used in circumstances meeting the criteria listed above, the device developer should notify the Center for Devices and Radiological Health (CDRH), Program Operation Staff by telephone (301-594-1190) immediately after shipment is made. (Note: an unapproved device may not be shipped in anticipation of an emergency.) Nights and weekends, contact the FDA Office of Emergency Operations (HFA-615) 301-443-1240.

The physician is expected to follow as many subject protection procedures as possible. These including:

- Obtaining an independent assessment of necessity by an uninvolved physician;

- Obtaining informed consent from the participant or participant’s legally authorized representative, in accordance with and to the extent required by FDA regulations, and appropriately documenting consent in accordance with and to the extent required by FDA regulations, or determining that use meets the exception to the requirement for consent (see section 6 below);

- Notifying the Institutional Review Board (IRB); and

- Obtaining authorization from the IDE holder, if an approved IDE for the device exists.

5. Procedures to Follow After Emergent Use of a Test Article

Following the emergent use of a drug, biologic or device, the physician is expected to do the following:
• Report the emergent use to the OHR in writing within five (5) working days of use, providing copies of all paperwork related to the emergent use and a synopsis of patient outcome if applicable. The letter should address the following:
  1. Identification of the patient (name, age)
  2. A brief medical history of the patient regarding emergency use of the test article including why the condition is/was considered “life threatening” and what other options, if any, may have been employed
  3. Any information on the outcome of the emergent use.

• Provide the OHR with a copy of the independent physician assessment.

• Provide a copy of the signed consent form. If obtaining informed consent from the subject or a legally authorized representative is not possible, certify that the conditions for exception to the informed consent requirements are met (see section 6 below).

• Evaluate the likelihood of a similar need for recurring use of the test article, and if future use is likely, immediately initiate efforts to obtain IRB approval and an approved IND or IDE for subsequent use.

Based on this information, the Associate Director and/or Director will determine whether the emergent use met FDA regulations and will ensure that the use is not research under HHS regulations (see Section 3 of this Policy).

The OHR will maintain a record of each emergent use of a test article and record the following information: Investigator/physician; drug, biologic or device used; name of patient; use of agent; date of use; and number of times test article has been used at TJU/TJUH.

The Associate Director or Director, OHR will present the emergent use to a convened Board. After Board review, the OHR will notify the investigator in writing as to whether or not the circumstances met FDA criteria for emergent use and that the test article may not be used a second time without the submission of a protocol to the IRB for review and approval.

6. Exceptions to the Informed Consent Requirement

Although emergency use of a test article is permissible without prior IRB approval, every effort should be made to obtain informed consent from the subject or his/her legally authorized representative. The obtaining of informed consent shall be deemed feasible unless, before use of the test article, both the investigator and a physician who is not otherwise participating in the clinical investigation certify in writing all of the following:
1. The human subject is confronted by a life-threatening situation necessitating the use of the test article.

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

3. Time is not sufficient to obtain consent from the subject's legally authorized representative.

4. There is available no alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the subject.

If immediate use of the test article is, in the investigator's opinion, required to preserve the life of the subject, and time is not sufficient to obtain the independent determination, the determinations of the clinical investigator shall be made and, within 5 working days after the use of the article, be reviewed and evaluated in writing by a physician who is not participating in the clinical investigation.

The documentation required in this section shall be submitted to the IRB within 5 working days after the use of the test article.

7. Subsequent Emergent Use of a Test Article
After an initial emergent use, FDA regulations require that any subsequent use of the test article must be subject to prospective IRB review. However, the FDA has also acknowledged that the emergency use exception to IRB approval should not be so narrowly construed as to deny emergency treatment to a second patient, and that it would be inappropriate to deny such treatment to a patient if the only obstacle is that the IRB has not had sufficient time to convene and review the issue.

The following are consistent with the policy:
7.1. Additional Doses: The term "use" should be interpreted as "course of treatment" rather than "a single dose" of a drug. This interpretation provides for those instances where more than one dose of a drug is required (e.g., daily or twice daily doses, or a course of chemotherapy) before the IRB can be convened and is consistent with the spirit of the "emergent use" doctrine. Accordingly, additional doses of a test article may be given to a patient only until the IRB is able to convene, provided that the above-stated procedures are followed and all of the conditions for emergency use continue to be met.

7.2. Emergency Treatment of a Second Patient: Should a situation arise which would require the emergency use of the same test article for a second patient, either by the same or another physician, subsequent use should not be withheld solely for the purpose of obtaining IRB approval provided all of the above-stated procedures are followed and conditions for emergency use are met.
7.3. **Recurrent Use of a Test Article Under Emergent Conditions.** It is not permissible to administer a test article repeatedly as an emergent use and thereby avoid prospective IRB review. If a test article is administered a second time under the Emergent Use policy, the investigator should develop a new protocol or amend an existing one to cover future uses. The matter may also be referred to the convened IRB for resolution. The physician/investigator will be required to take one of the following actions before any additional uses of the test article will be permitted:

- When there is an existing protocol covering the intended use of the test article, the protocol should be amended to include a rescue arm. The rescue arm should list all possible providers who will likely administer the test article as co-investigators, and the existing consent form should be amended to include details of the rescue protocol.

- When there is no existing protocol covering the intended use of the test article, a full protocol should be submitted to the IRB and should include at minimum completed OHR-1, OHR-2, and OHR-8 forms.

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¹ **Life Threatening:** Diseases or conditions in which the likelihood of death is high unless the course of the disease is interrupted and diseases with potentially fatal outcomes. The disease need not be immediately life threatening.

² **Severely Debilitating:** Diseases or conditions that cause major irreversible morbidity. Examples include blindness, loss of arm, leg, hand or foot, loss of hearing, and stroke.
1. **Purpose**
   To describe how the findings and actions concerning all research submitted to the IRB are to be communicated to investigators.

2. **Responsibility for Executing the Policy**
   - Associate Director, OHR
   - OHR Administrative Staff
   - IRB Chairs/Vice Chairs

3. **Policy Statement**
   It is imperative that the OHR maintains open and frequent communication with the investigators and their research staffs.

4. **Procedures**
   4.1. Investigator Notifications
      4.1.1. **Initial Submission**: The IRB secretary will notify the Principal Investigator by email of the IRB’s review comments and study approval status in general within the week following the IRB meeting. The IRB secretary will specify the requirements to secure approval. The correspondence will specify whether the protocol has been approved or not approved as described in Policy OP 206.

      For a study reviewed by an expedited procedure, the process is the same except that the IRB administrative secretary will compile the written comment from the two IRB members charged with expedited review.

      The IRB allows the PI a 30 day window to reply. If there are extenuating circumstances (e.g., sponsor delay, staff turnover) the PI may request additional time. If 30 days elapses without communication from the PI, the study will be administratively deactivated.

      4.1.2. **Renewals and Revisions**: The PI and study coordinator will be notified by email as soon as possible as to the actions taken by the IRB for any continuing review or amendment to the study.

      4.1.3. **Notification of Study Approval**: The approval letter and any other relevant, stamped study materials are sent by email to the study contact(s) as soon as possible after IRB approval. The IRB secretary archives approval letters electronically on the OHR server.
4.1.4. Final Reports: Final Reports are received and handled by the administrative secretaries for continuing review, and are reviewed by the IRB Chair or Vice Chair. If the final report is satisfactory, the administrative secretary will issue a letter to the PI acknowledging closure of the study.

4.2. Other Notifications
At the discretion of the IRB, the Associate Provost for Research Support Services and the Provost may be notified of studies that the IRB feels may pose significant risk to the subjects or the University. See also Policy GA 101 for the role of University officials in the approval or disapproval process.

If the IRB determines that conflict of interest requirements are not being met, as part of IRB requirements in order to approve the study, the Associate Provost for Research Support Services and the Chair of the COI Committee will be notified by the Director or Associate Director of the Office of Human Research.
1. Purpose
   To describe the IRB actions and determinations that must be communicated to other entities within the University and with federal agencies.

2. Responsibility for Executing the Policy
   Director/Associate Director, OHR
   OHR Administrative Staff
   IRB Chairs/Vice Chairs

3. Policy Statement
   The IRB is required by federal regulations and institutional policy to communicate certain actions to entities that may have an interest in the status of the research being conducted. This policy defines the activities and the individuals and/or agencies that must be notified, if appropriate.

   The DHHS and FDA regulations require prompt reporting of three situations:
   1. An unanticipated problem involving risks to participants or others (see OHR Policy GA120).
   2. An incident of serious or continuing non-compliance or failure to meet IRB requirements (see TJU Policy #110.15).
   3. A suspension or termination of previously approved research (see OHR Policy RR407).

4. The Reporting Process
   The Director, OHR will draft the report for submission to the IRB which may approve, modify or disapprove the report. The report will contain a complete description of the nature of the event, the findings related to the event, the actions taken by the IRB, the reasons such actions were taken, and description of any continuing investigation or corrective action plan. The report will be submitted to the IRB that originally reviewed the protocol. Thus, the maximum time lapse for Board review will be 2 weeks. Boards meet on all Thursdays except 5th Thursdays in a month and official holidays and in those instances the elapsed time may be 3-4 weeks.

5. Distribution of the Report
   The Director, OHR shall be responsible for distribution of the final report to the following within 10 working days of approval of the report by a convened IRB:

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- The IRB
- The researcher
- University Counsel
- The Associate Provost for Research Support Services and/or the President as the case may require.
- Department Chair or Dean as appropriate
- OHRP
- Other federal agencies when the research is subject to oversight by those agencies, and they require reporting separate from that to OHRP
- FDA when the research is FDA-regulated.

If federal agencies have received reports of the event(s) via other sources, such as the investigator, sponsor, or another organization, reporting to these agencies is not required of TJU.
1. **Purpose**
   To delineate the procedure whereby a research subject in a clinical trial, a relative of or advocate for a research subject, a member of a study team (investigator or coordinator), government agency, or the University itself may report their concerns about any clinical trial.

2. **Responsibility for Executing the Policy**
   Associate Director, OHR  
   IRB Chairs/Vice Chairs

3. **Policy Statement**
   The University's IRBs have the responsibility to oversee the safety and welfare of human subjects participating in research, including compliance with applicable federal human subjects regulations. This policy and procedure provides a means whereby any individual may report to the IRB, through the OHR, any problem or issue of concern with on-going or completed clinical research, including potential noncompliance with federal human subject regulations.

4. **Procedures**
   4.1. The Director/Associate Director, OHR, or an IRB Chair or Vice Chair will act as reviewer for the complaint.
   
   4.2. The reviewer will determine whether the complaint involves noncompliance or an unanticipated problem involving risks to participants or others as defined in the respective policies.
   
   4.3. Complaints that involve non-compliance will be handled according the non-compliance policy (TJU Policy 110.15).
   
   4.4. Complaints that involve unanticipated problems involving risks to participants or others will be handled according to Policy GA 120.
   
   4.5. The reviewer will be available by telephone or in person to the complainant in order to address the issue in a confidential manner. The complainant will have the opportunity to discuss problems, concerns, and questions; obtain information; or offer input with an informed individual who is unaffiliated with the specific research protocol or plan (such as the University Ombudsman or the Senior Associate Dean for Faculty Affairs).
1. **Purpose**
   To provide guidance on how to avoid coercion when recruiting students as key personnel or as research subjects for human subjects research. This also applies to recruiting employees as research subjects for human subjects research.

2. **Responsibilities for Executing Policy**
   - Investigators
   - Research Coordinators
   - IRB Members
   - OHR Administrative Staff

3. **Policy Statement**
   Students are not usually considered a separate class of research participants from the standpoint of ethical standards or federal regulatory compliance. Students frequently act as key personnel under the direct supervision of the Principal Investigator on clinical trials or NIH sponsored studies to obtain experience and data for their advanced degree.

   In other situations some categories of research specifically target students as subjects. Students are mostly involved in research conducted in established or commonly accepted educational settings involving normal educational practices such as research on regular and special instructional strategies, or research on the effectiveness of, or the comparison among: instructional technique; curricula; or classroom management methods.

   The principal controversy about the use of students and employees as subjects in a research study involves whether or not the inducements to participate are considered coercive. These two groups are comparatively convenient, easy to recruit and may accept less remuneration for participation. 45 CFR 46.116 states that an investigator should seek consent “only under circumstances that provide the prospective subject sufficient opportunity to consider whether to participate and that minimize the possibility of coercion or undue influence.” Considering that students and employees may exist in a subordinate role, often to the investigators, the potential for coercion, intentional or unintentional, does exist.

   In addition to coercion, another major concern regarding student and employee participants is that of confidentiality. This applies particularly to the case where students are key personnel on a study that involves other students or employees who work together.
Extra care must be taken to insure subject confidentiality in these instances. The IRB must ensure that data is stored where access is restricted, and if students are involved in data collection and analysis, the IRB must ensure that the students understand the importance of maintaining the confidential nature of the information. The IRB shall also ensure that the process of data storage is acceptable so that the data is secure.

4. Procedure
The IRB shall carefully review recruiting inducements, particularly those related to the enrollment of students in the trial to count: 1) for participation in a course; 2) for course credit; 3) as writing a research paper, 4) as attendance at faculty research talks; 5) as direct payment for participation. The IRB shall also carefully review recruiting inducements for employees.

The IRB must discourage such recruiting methods and only approve methods that solicit participants by less coercive means such as using sign-up sheets or general announcements, rather than direct solicitation of individuals from the classroom or workplace environment. These options reduce the likelihood of “undue coercion” by making the request less direct and by decreasing the influence inherent in the faculty-student/supervisor/employee relationship.
1. **Purpose**
   It is not a sponsor’s obligation to determine IRB compliance with regulations. Because the clinical investigator works closely with the IRB, it is appropriate that the clinical investigator assure the sponsor that the IRB is operating according to regulations.

2. **Responsibility for Executing the Policy**
   Director/Associate Director, OHR
   Principal Investigators

3. **Procedure**
   Any correspondence between the IRB and the investigator should be made available to the sponsor by the investigator. The primary responsibility of the IRB member with respect to maintaining confidentiality is to the research subject. The IRB will respect the sponsor’s need to maintain confidentiality of information about procedures under development. Any disagreement between the sponsor and the IRB or the investigator and the IRB or any impasse about study procedures or consent form wording will be resolved through appropriate communication in writing between the respective parties. In the event of a true impasse it is the IRB’s responsibility to provide the oversight necessary to protect the human subjects, and the decision voted upon by the IRB will stand.
1. **Purpose**
To delineate the procedures whereby sponsors and Principal Investigators may petition for IRB approval of inclusion/exclusion waivers to enroll subjects on a clinical trial.

2. **Responsibility for Executing the Policy**
   Director/Associate Director, OHR
   Sponsor
   Principal Investigator

3. **Policy Statement**
   It is not uncommon for a sponsor, or the Principal Investigator in the case of an Investigator-Initiated Treatment Trial (IITT), to make allowances for certain subjects who fall outside of the protocol's inclusion/exclusion criteria to be enrolled on the study. These allowances are referred to as protocol inclusion/exclusion waivers. In general, such waivers are discouraged. However, there are circumstances in which they may be granted.

   Waivers may be approved by the IRB if:
   - The person’s inclusion would not place him or her at increased risk of harm
   - Participation in the study would be in the person’s best interest because alternatives are limited to less favorable options.
   - Scientific validity of the clinical trial would not be substantially compromised by the inclusion of the research subject

   Typical examples of waiver requests include:
   - Required imaging studies obtained days to weeks prior to that permitted by protocol
   - Potential subject is slightly older or younger than specified in protocol
   - Blood chemistries fall slightly outside the protocol permitted levels.

4. **Procedure**
   If the study is an IITT, and the PI feels that a protocol inclusion/exclusion waiver is appropriate, the PI must submit an OHR-31 with the justification and risk assessment sections completed in sufficient detail to allow an informed decision on the part of the IRB reviewer.
A protocol inclusion/exclusion waiver represents a one-time deviation from the protocol and should not be submitted to the IRB as an amendment to the protocol.

If the sponsor provides the PI with an inclusion/exclusion waiver for a subject, the PI will forward the notice of waiver attached to completed form OHR-31 to the IRB as per directions on the form for approval prior to enrolling the subject in question.

If the PI makes requests for a waiver for the same inclusion/exclusion criterion more than one time, the PI must formally amend the inclusion/exclusion criteria in the protocol.

5. References
   Form OHR 31
1. Purpose
To provide the rationale and procedures for review of gene transfer and vaccine studies by an ad hoc committee comprised of members of both an IRB and the Institutional Biosafety Committee (IBC) prior to review and approval by Committees proper.

2. Responsibility for Executing the Policy
Director, OHR
IRB
IBC
Institutional Biosafety Officer

3. Policy Statement
Human gene transfer and recombinant vaccine clinical protocols must be reviewed at four levels: 1) local IRB; 2) local IBC; 3) Recombinant DNA Advisory Committee (RAC); 4) FDA. Investigator-initiated studies must be submitted to the Recombinant DNA Advisory Committee of the NIH Office of Biotechnology Activities (OBA) and the FDA prior to local submission to the ad hoc committee. The investigator must provide comments from the RAC review to the ad hoc combined IRB/IBC Committee. Commercially sponsored gene transfer and vaccine protocols should be submitted to the RAC and FDA prior to submission to the ad hoc IRB/IBC Committee.

4. Procedures
Prior to review and approval of a gene transfer or recombinant vaccine protocol by the IRB and the IBC, the protocol must be reviewed and approved by an ad hoc combined IRB/IBC Committee composed of members with appropriate expertise from both committees to address the clinical, IRB and biosafety issues involved in the study.

Should the OBA/RAC determine that the protocol requires RAC review, the PI must address and respond to all RAC issues and provide documentation that this has been done in the submission to the IRB/IBC ad hoc committee. A copy of the RAC review must also be submitted. If the protocol does not require RAC review, the PI must provide the ad hoc committee with a letter from the RAC to that effect along with any comments the RAC might have about the protocol.
The Chair of the IBC will serve as the chair of the ad hoc review committee. The deliberations and final determination of the ad hoc committee will be provided in writing to the Principal Investigator so that the information required can be incorporated into subsequent submissions to the IRB and the IBC.

4.1. Submission to the ad hoc IRB/IBC Committee

Twelve (12) collated copies each of the following documents are to be submitted to the ad hoc committee for review and approval:

- IRB OHR-2 Internal Form (summary of the protocol);
- IBC-1 Registration for Research Form for recombinant DNA Research;
- Appendix M. Points to Consider; NIH recombinant DNA Guidelines
- Clinical Protocol and consent form;
- Investigator Brochure (if available);
- Any correspondence from the RAC

Documents should be submitted to the Secretary for the IBC.

4.2. Submission of the ad hoc Committee-Approved Protocol to the IRB and IBC

The protocol, revised according to the requirements of the ad hoc IRB/IBC Committee and any supporting documents, should be submitted concomitantly to the IRB and the IBC for review and approval according to standard submission requirements.

After review and approval of the study by both committees, each committee will provide the PI with a formal approval letter.
1. **Purpose**
   The purpose of this policy is to ensure prompt reporting to the IRB of Serious Adverse Events (SAEs) and Unanticipated Problems (UAPs) by principal investigators. Regulatory requirements of both DHHS (45 CFR 46.103(b)(5)) and FDA (21 CFR 56.108(b)(1)) require that “each IRB shall follow written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and the Department or Agency head of any unanticipated problems involving risks to subjects or others.”

2. **Responsibility for Executing the Policy**
   - Director/Associate Director, OHR
   - Sponsors
   - Principal and Co-Investigators/Research Coordinators
   - SAE Reviewers

3. **Definitions**
   3.1. **Adverse Event Grade** refers to severity as per the Common Terminology Criteria for Adverse Events (CTCAE) created by the US Department of Health and Human Services, National Institutes of Health, National Cancer Institute.
      - Grade 1 = Mild
      - Grade 2 = Moderate
      - Grade 3 = Severe
      - Grade 4 = Life-threatening or disabling
      - Grade 5 = Death

   3.2. An **Adverse Event (AE)** is judged to be grade 1 or 2. It includes any unfavorable and unintended occurrence including an abnormal laboratory finding or symptom or disease, temporally associated with the use of a medical treatment or procedure that may or may not be considered to be related to the medical treatment or procedure and that is mild or moderate in severity and has a short duration of occurrence.

   3.3. **Serious Adverse Event (SAE)** is judged to be grade 3, 4 or 5. and is defined (21 CFR 314.80) as any serious adverse drug experience that results in any of the following:
• Death
• Life threatening adverse drug experience
• Inpatient hospitalization or prolongation of existing hospitalization
• A persistent or significant disability /incapacity
• Congenital anomaly/birth defect

21 CFR 314.80 continues as follows: “Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered a serious adverse drug experience when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse.”

An Emergency Department (ED) visit should be reported as an AE or SAE if the PI determines the ED visit was possibly, probably, or definitely related to the study article or a study procedure. All ED visits that last more than 24 hours should be considered hospital admissions and reported as SAEs whether or not related to study article or procedure.

3.4. Unexpected Adverse Event is defined as “Any adverse drug experience, the specificity or severity of which is not consistent with the current investigator brochure; or, if an investigator brochure is not required or available, the specificity or severity of which is not consistent with the risk information described in the general investigational plan or elsewhere in the current application, as amended. For example, under this definition, hepatic necrosis would be unexpected (by virtue of greater severity) if the investigator brochure only referred to elevated hepatic enzymes or hepatitis. Similarly, cerebral thromboembolism and cerebral vasculitis would be unexpected (by virtue of greater specificity) if the investigator brochure only listed cerebral vascular accidents. “Unexpected,” as used in this definition, refers to an adverse drug experience that has not been previously observed (e.g., not included in the investigator brochure) rather than from the perspective of such experience not being anticipated from the pharmacological properties of the pharmaceutical product.” (21 CFR 312.32).

3.5. An Unanticipated Adverse Device Effect is any serious adverse effect on health or safety or any life-threatening problem or death caused by or associated with a device, if not identified in the device brochure, protocol, or consent form (21 CFR 812.3(s)).
3.6. A protocol deviation/violation is a departure from the IRB-approved protocol. Any further definition beyond this is up for debate, as there continues to be national discussion about the use of these terms, and a consensus has not been reached on how these terms should be defined and distinguished from each other. A frequent differentiation is that a deviation does not place subjects at increased risk, whereas a violation does. Our current thinking on the topic is that we do not find the aforementioned differentiation useful because the assignment of risk to an event is a downstream decision. What is germane is that an event has occurred and needs to be assessed, first by the PI, and then by the IRB. Thus, for the current time, we will use the joint term deviation/violation, which will capture all events under these terms and will direct all of them to the appropriate reporting channel.

3.7. Unanticipated Problems posing risks to subjects or others (UAPs) are unforeseen given the information contained in the protocol and other study related documents, and indicate that participants or others are at increased risk of harm (than was previously known or recognized) and are related or possibly related to the research. Examples include but are not limited to the following:

- An interim analysis of the data suggesting or indicating additional risk associated with a study procedure or test article.

- A report (journal article or abstract, etc.) that shows that the risks or potential benefits of the research might now be different from those initially presented to the IRB.

- A breach of confidentiality.

- Change in FDA labeling or withdrawal from marketing of a drug, device, or biological used in a research protocol.

- Change made to the research without prior IRB review to eliminate an apparent immediate hazard to a subject.

- Incarceration of a subject in a protocol not approved to enroll prisoners.

- An event that requires prompt reporting to the sponsor.

- Sponsor imposed suspension for risk.

- Complaint of a subject when the complaint indicates unexpected risks or cannot be resolved by the research team.

- A change to a protocol or procedure that is not pre-approved by the IRB.
• Protocol violation (an accidental or unintentional change to the IRB-approved protocol) that may harm subjects or others or that indicates that subjects or others may be at increased risk of harm.

• Other unanticipated information that indicates participants or others might be at increased risk of harm.

3.8. Some events do not qualify as AEs, SAEs or Unanticipated Problems posing risks to subjects or others. Most of these are events or circumstances encountered in the usual course of receiving medical attention. Examples of these are pain or minimal bleeding/bruising at the time of venipuncture, drowsiness after sedation, boredom while waiting for the scheduled visit or procedure, or other similar scenarios.

Please note, protocol deviations/violations not posing risks to subjects or others are not considered unanticipated problems involving risk and should not be reported to the IRB at the time they occur. For IITs or other non-commercially sponsored studies for which there is no study monitor, it is recommended that you keep a log of protocol deviations/violations in the study file for inclusion in the continuing review submission or final report. For commercially sponsored studies, the sponsor or the PI should provide a log of these with the continuing review or final report.

4. Review of SAEs and UAPs

Electronically submitted on-site SAE reports are forwarded for review to selected pharmacists and physicians or other practitioners as a spread sheet containing the relevant study information on the first of each month summarizing the SAEs of the previous month. Reviewers will note either no concerns or issues or will note unusual events, concerns, or trends and report findings to the Director and Associate Director OHR for further evaluation and determination of any actions that may be necessary. Reports will be archived on the server dedicated to the OHR.

Reports of unanticipated problems will be previewed by the Director and/or Associate Director, OHR, (or their designees) as they are reported, to determine whether the problem meets the definition of an “unanticipated problem involving risks to subjects or others” before deciding what, if any, action should be taken. The Director and Associate Director will also receive a spreadsheet on the first of each month summarizing the previous months' UAPs. The spreadsheet will provide relevant information about the event and the research. If the pre-review indicates an unanticipated problem involving substantive risks to subjects or others, the Director/Associate Director, OHR, will present the unanticipated problem to a convened IRB or assign a primary reviewer based on expertise and experience who will present the information to the IRB. The primary reviewer and all IRB members will receive the OHR-20 and any other materials pertinent to the unanticipated problem. Immediate actions may also be necessary to eliminate any immediate
hazards to subjects or others. If this is the case, the Director/Associate Director, OHR, will notify the IRB of the actions taken.

If the unanticipated problem involves failure to follow federal or institutional human subjects regulations, further action as per TJU Policy 110.15 “Institutional Review Board Review of Noncompliance Issues” will be initiated.

5. Actions for Consideration by the Convened IRB
The convened IRB will consider the following actions during its deliberations:
- Modification of the protocol
- Modification of the information disclosed during the consent process
- Providing additional information to past subjects
- Notification of current subjects when such information might relate to their willingness to continue participation in the study
- Requirement that current subjects be re-consented
- Modification of the continuing review schedule
- Monitoring of the research and/or consent process by the OHR QA/QI program
- Suspension of the research
- Termination of the research
- Referral to other organizational entities for further investigation

6. Reporting of Adverse Events, Serious Adverse Events, and Unanticipated Problems (also see decision tree attached)
6.1. AEs and SAEs are reportable from the time the patient consents to 30 days after the last study intervention, or as specified in the protocol (usually based on drug half-life).

6.2. On-site Serious Adverse Events: On-site SAEs should be reported using the electronic SAE reporting system (eSAEy) accessed via a link on the OHR homepage at [http://www.jefferson.edu/human_research/irb/index.cfm](http://www.jefferson.edu/human_research/irb/index.cfm).
On-site SAEs (Grades 3-5) that are unexpected and deemed to be at least possibly or definitely related to the study article should be reported within 2 working days of knowledge of the event, except that death should be reported within one working day. Unrelated SAEs should be reported within 5 working days. SAEs occurring in drug studies must be reported whether or not considered drug-related and whether or not the event is listed in the Protocol, Investigator Brochure or consent form.

There is often medical judgment involved regarding whether an event represents a SAE. Severe anemia may not require reporting as a SAE in study subjects with diagnoses often associated with severe anemia. For example, severe anemia would not be reported in a subject with Thalassemia, unless in the medical judgment of the PI or Co-I, the severe anemia represents a process separate from the disease. An example of the latter would be a subject with Thalassemia who develops severe anemia from a gastrointestinal hemorrhage with attribution to the study drug or concomitant medication.

The occurrence of events that are clearly part of a disease process should be noted in the protocol and, if possible, specific SAE reporting requirements established.

SAEs that occur in device studies should be reported to the IRB if they are not identified in the device brochure, protocol, or consent form.

6.3. On-site AEs: Grade 1 AEs should not be reported to the IRB. Grade 2 AEs should NOT be reported at the time of continuing review or final report unless, in the opinion of the investigator, they represent events that exceed expected frequency or in some other way are judged to be unexpected and possibly associated with increased risk. If protocol or consent requires changes, an amendment should be submitted with the continuing review. Grade 2 AEs that fit these criteria may also be submitted to the IRB as they occur. Grades 1 and 2 AEs should be kept in the study file if required by study sponsor.

6.4. Off-site AEs/SAEs: Off-site AEs/SAEs or IND safety reports that require a change to the protocol and/or consent form should be submitted for review within 5 working days of knowledge of the event and be accompanied by a completed OHR10 off site report form and an OHR-12 form to effect the required amendment. Off-site AEs/SAEs or IND safety reports that do not require a change in the protocol or consent should not be reported to the IRB. A summary or itemized listing of these events should be included with the continuing review for the study.

6.5. AE Grading: AEs should be categorized for severity using the current version of the CTCAE. The CTCAE is incorporated into the eSAEy reporting system. The current CTCAE version can be accessed at http://ctep.cancer.gov/.
6.6. **Unanticipated Problems:** Unanticipated problems (UAPs) that pose risk to subjects or others, and that are not AEs/SAEs should be reported within 10 working days using the electronic reporting system (eazUP) accessed via a link on the OHR homepage at [http://www.jefferson.edu/human_research/irb/index.cfm](http://www.jefferson.edu/human_research/irb/index.cfm). For UAPs that do not pose risk to subjects or others, complete the report in the eazUP system, but do not submit it for investigator signature. Print the report, obtain the investigator signature and retain the form for your records. Submit all unanticipated problem reports with the next continuing review.

6.7. Submit an OHR-12 for review if an amendment is required.

6.8. Events that meet the reporting criteria in Policy GA 120 will be handled according to Policy GA 114, Reporting of Unanticipated Problems, Terminations, Suspensions and Non-compliance.

7. **Attachment**

AE reporting decision tree

8. **References**

   OHR Guidance G-602, “Reporting Adverse Events and Unanticipated Problems Involving Risks to Subjects or Others - Guidance for Problem Issues”
   OHRP Guidance: “Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events” January 15, 2007
   21 CFR 312.64(b) Safety Reports
   21 CFR 812.3 (s) Unanticipated adverse device effect
   21 CFR 314.80 Post marketing reporting of adverse drug reactions
Appendix: Decision Tree for reporting adverse events

1. Adverse Event
   - Is the *adverse event SERIOUS? NO
     - NO
   - YES
     - Is the adverse event **UNEXPECTED? NO
       - NO
       - PI judgment: The adverse event must be included in the AE log and reported at continuing review. Please keep in mind ultimately it is the responsibility of the PI to determine relationship to the treatment or procure and provide a viable justification.
     - YES
       - Is the adverse event related/possibly related to the study treatment or procedure? NO
         - NO
         - The event must be reported to the IRB within 48 hours (working days) *(24 hours if it is a grade 5)* from the time of notification or knowledge using the eSAEy system:
           - http://www.jefferson.edu/human_research/irb/index.cfm
     - YES
       - Adverse Event must be included in AE log along with CTC grade (if applicable), attribution, action, length and outcome and submitted at continuing review.

*Serious Adverse Event is judged to be grade 3, 4 or 5 and is defined but not limited to any untoward occurrence that results in any of the following: death, a life-threatening adverse experience, inpatient hospitalization or prolongation of an existing hospitalization, persistent or significant disability or incapacity, or a congenital anomaly or birth defect. As well as any important medical events that may be considered an SAE when based upon appropriate medical judgment they may jeopardize the subject and require medical or surgical intervention to prevent the outcomes listed in this definition.

**Unexpected adverse events are those that are NOT included in the protocol, consent and/or investigational brochure.

All expected adverse events should still be listed in the OHR-8.
1. **Purpose**
   To describe the requirements for management of all OHR and IRB documents including: document retention; administrative documents; and archiving.

2. **Responsibility for Executing the Policy**
   Director/Associate Director, OHR
   OHR Administrative Staff

3. **Policy Statement**
   Each study file maintained by the OHR must contain a complete history of IRB actions related to review and approval of the particular study. This would include: scientific reviews, if any, continuing reviews; amendments; renewals following expiration; and reports of adverse events and unanticipated problems. The OHR will also maintain a list of IRB members for each Board as per 45 CFR 46.103(b) (3); 115(a) (5). All records received by the IRB regarding a study, whether approved or not, must be retained in an appropriately secure manner as required by regulatory requirements [(45 CFR 46.103(a)] and/or institutional policy.

   Records must be accessible for inspection and copying by authorized representatives of a sponsor, funding department or agency as well as by institutional audits at reasonable times and in a reasonable manner [45 CFR 46.115 (b)].

   Required documents must be submitted to any appropriate requesting funding entity, as required.

4. **Policy Specifics**
   4.1. **Document Retention**
      IRB-approved studies must be retained by OHR for 3 years after closure of the research by submission of a Final Report. Studies receiving IRB review that are not approved must be retained for at least 3 years from the date of last review. Studies that are closed due to cancellation without subject enrollment or termination by the IRB must also be retained for 3 years after the date of closure [(45 CFR 46.115(b); 21 CFR 56.115(b)].

      If the study, or an individual involved with the study, is the subject of litigation, all IRB records pertaining to the study will be retained until the issue is resolved.

   4.1.1. **Study related documents:**
      Adequate documentation for each study will be prepared, maintained, and retained including:
• Records of initial, continuing and amendment review activities, both full and expedited, and exempt studies, including appropriate submitted materials, reviewer determinations and determinations required by regulations and protocol-specific findings supporting those determinations for:
  o Waiver or alteration of consent process
  o Research involving pregnant women, fetuses, and neonates
  o Research involving prisoners
  o Research involving children

• One copy of the original submission;

• A copy of the most recently approved OHR-2;

• A copy of the latest protocol

• A copy of the original approved consent form, and any approved revised consent form;

• Scientific evaluations;

• Progress reports submitted by investigators;

• All reported protocol deviations as submitted;

• Reports of injuries to subjects

• Approval period for each initial and continuing review

• DHHS-approved sample consent document and protocol, when applicable

• Copies of all submitted monitoring reports, site visit reports and other continuing review activities;

• Copies of all correspondence between the IRB and investigators;

• Statements of significant new findings provided to subjects as submitted by the investigator;

• For exempt studies, the specific exemption category

• IRB records for initial and continuing review reviewed by the expedited procedure must include:
4.2. IRB Administration Documents:

In addition, the following IRB administrative documents will be retained:

4.2.1. Rosters of regular and alternate IRB members identified by name, earned degrees, scientist/non-scientist status, representative capacity, indications of experience sufficient to describe each regular and alternate member’s chief anticipated contributions to the IRB’s deliberations; and any employment or other relationship between each member and the IRB and/or the University (e.g., full-time employee, part-time employee, member of a governing panel or Board, stockholder, paid or unpaid consultant), affiliation status, capacity of member (member, chair, ex officio), and voting status.

Alternate members shall be included on the roster. In addition to the above information, the roster shall indicate the regular member for whom the alternate will substitute [(45 CFR 46.115(a)(5); 21 CFR 56.115(a)(5)],

4.2.2. Current copies of the Standard Operating Policies and Procedures.

4.2.3. Agendas and minutes of all IRB meetings (Policy OP 206);

4.2.4. Reports of any complaints received from participants, regulatory agencies and their resolution.

4.2.5. Delegation of specific functions, authorities, or responsibilities by the Director/Associate Director, OHR, or an IRB Chairperson must be in writing and maintained in the OHR.

4.3. Purging Files

Files exceeding the three year retention limit will be purged annually. Final entry into the study history in the data base will be made indicating that the file has been purged. The study folder and its materials will be discarded by shredding.
1. **Purpose**
   To establish a conflict of interest (COI) policy for Members serving on an IRB.

2. **Responsibility for Executing the Policy**
   Director/Associate Director, OHR
   IRB Chair/Vice Chair
   Members of the IRB

3. **Policy Statement**
   A conflict of interest exists when an IRB member, or a member of the member’s “immediate family”, possesses a significant financial interest in an entity that sponsors or may sponsor human subjects research at TJU, or is involved in the design, conduct or reporting of the research, or has an interest that the IRB member believes conflicts with his or her ability to objectively review a protocol.

   The term “may sponsor” encompasses not only the sponsor but also any company that competes with the sponsor of the research, if the financial interests of such a company would reasonably appear to be affected by the research.

   3.1. **Financial Interest Related to the Research** means financial interest in the sponsor, product or service being tested, or competitor of the sponsor or product or service being tested.

   3.2. **Immediate Family** means spouse, dependent children, and all other persons living in the same household, and any associated entity.

   3.3. **Associated Entity** means any trust, organization or enterprise other than the University over which the covered individual, alone or together with his / her immediate family, exercises a controlling interest.

   3.4. **Significant Financial Interest** is defined as any of the following interests of the IRB member and his/her immediate family:
      - Ownership interest, stock options, or other financial interest related to the research unless it meets four tests:
         - Less than $5,000 when aggregated for the immediate family.
         - Publicly traded on a stock exchange.
Office of Human Research
Office of Human Research Policy and Procedure
Manual

- Value will not be affected by the outcome of the research.
- Less than 5% interest in any one single entity when aggregated for the immediate family.

- Compensation related to the research unless it meets two tests:
  - Less than $5,000 in the past year when aggregated for the immediate family.
  - Amount will not be affected by the outcome of the research.

- Proprietary interest related to the research including, but not limited to, a patent, trademark, copyright or licensing agreement.

- Board or executive relationship related to the research, regardless of compensation.

- Consulting fees; honoraria; gifts or other financial compensation; or "in kind" compensation from a financially interested company for any purpose not directly related to the reasonable cost of conducting the research (as specified in the research agreement) or engaging in the activity; that when aggregated for the covered individual and his/her immediate family in the prior calendar year exceeded, or in the next calendar year are expected to exceed, $5,000.

- Royalties or inventor’s share of royalty income pursuant to the University’s Patent Policy, or the right to receive future royalties or such inventor’s share under a patent license or copyright agreement or any other type of agreement, where the research or activity is directly related to the licensed technology or work.

- Any non-royalty payments (or entitlements to payments) in connection with the research or activity that are not directly related to the reasonable costs of the research (as specified in the research agreement between the sponsor or company providing research funding and the University) or activity. This includes any bonus or milestone payments to investigators in excess of reasonable costs incurred, whether such payments are received from a financially interested company or from the University.

3.5. “Non-financial COI” is defined as an interest other than financial that could directly and significantly affect or be affected by the design, conduct or reporting of a research activity. Examples include but are not limited to:

- Personal beliefs

- Personal relationships

- Institutional relationships
• Career advancement

Individuals who are responsible for research development are prohibited from serving as members or ex-officio members on the IRBs. These individuals include employees in the TJU Office of Technology Transfer and Business Development or other administrators with business development interests.

IRB members cannot participate in the review of any research, including the review of unanticipated problems involving risks to subjects or others, non-compliance, expedited review, or review of exempt research when they have a significant financial or non-financial conflict of interest. IRB members must notify the Director or Associate Director, OHR if they are assigned to review research when they have a conflict of interest (see also reviewer questionnaire RQ-1).

Individuals with “significant financial or non-financial COI” may not be present at Board meetings during discussion, deliberation or voting on the relevant study as per OHR Policy GA106, paragraph 4. As stated in that policy, the conflicted member may be asked to temporarily return to the meeting to answer a question(s) raised by the Board. The IRB minutes shall document the foregoing actions taken in response to an IRB member with a conflicting interest.

IRB members with a conflict of interest are not counted towards quorum when a vote is taken on protocols for which a conflict exists.

IRB members with a conflict are documented in the minutes as being absent with an indication that a conflict of interest was the reason for the absence.

This Policy will be distributed to each IRB member annually and will be available for review at all IRB meetings. At the beginning of each IRB meeting the IRB Chair will require financial interest and conflict of interest disclosure, consistent with the above criteria, from each IRB member prior to conducting IRB reviews of studies.
1. **Purpose**
   To state the policy and outline the procedures regarding confidential information that is processed in the OHR office and reviewed by IRB members in and out of IRB meetings.

2. **Responsibility for Executing the Policy**
   - Director/Associate Director, OHR
   - IRB Chairs/Vice Chairs
   - IRB Members
   - OHR Administrative Staff
   - Investigators

3. **Policy Statement**
   Confidentially pertains to the treatment of information that an individual has disclosed in a relationship of trust and with the expectation that it will not be divulged to others in ways that are inconsistent with the understanding of the original disclosure without further permission from the individual.

   Confidentiality is supported by “Respect for Persons” and “Beneficence”, two of the principles of research ethics identified in the *Belmont Report*. Both 45 CFR §46.111 and 21 CFR §56.111 require the investigator and the IRB to determine, that the research subject’s confidentiality are protected.

   HIPAA adds further regulatory protections as to how confidentiality of subject data is to be protected. Much of what follows stems from HIPAA.

4. **Procedures**
   4.1. **Protection of Confidentiality by the Investigator**
      4.1.1. Storage and Retention of Confidential Data:
      The investigator must consider confidentiality as part of his regulatory and ethical duty to protect the rights and welfare of human subjects. He must consider the degree of privacy of the information being collected and establish methods for protecting the confidentiality of the information obtained during the recruitment process, during the research, and after the research is completed.

      The Investigator must provide information to the IRB on how the confidentiality of the research data will be protected.
The investigator also must indicate how long the records will be retained and whether they will be destroyed when the research is complete. Research data can, however, be retained indefinitely if reasonable justification can be provided.

The investigator must inform the subject through the consent document and during the consent process of the extent to which confidential records identifying the subject will be maintained and that the FDA potentially may inspect the subject’s confidential research record, if the study is FDA-regulated.

4.1.2. Protection of Confidentiality during the Recruitment Process:

The investigator must also consider the protection of confidentiality during the subject recruitment process. Care must be taken by research staff in the manner in which subjects are identified and approached for participation in a study. Along with obtaining appropriate IRB approval, research staff should also obtain appropriate departmental permission before searching medical records and/or databases to which they ordinarily would not have clinical access;

The FDA has addressed the issue of confidentiality during the screening process (FDA Information Sheet, Recruiting Study Subjects). In this regard the investigator must address the following issues in the protocol:

- What will happen to the personal information obtained by phone if the caller ends the interview or hangs up?
- Are the data being gathered by a marketing company; if so are identifiers and/ or health information being sold?
- Are names of noneligibles being maintained in case they qualify for another study?
- Are paper copies of the records shredded?

The acceptability of the procedures would depend on the sensitivity of the data gathered. For particularly sensitive information the investigator may wish to obtain a Federal Certificate of Confidentiality (OHR Guidance Document G 607).

4.2. Protection of Confidentiality by the IRB and OHR Staff

The IRB is responsible for ensuring that those issues listed in Section 4.1 are addressed by the investigator in the IRB application.
4.2.1. The IRB and the Sponsor:
The IRB is responsible for ensuring that the consent document adequately provides the subject with information concerning the extent to which confidentiality of the research and medical records will be maintained. Both 45 CFR § 46.116 and 21 CFR § 50.52 require that the consent document contain a statement describing the extent, if any, to which confidentiality of research records identifying subjects will be maintained. The IRB must ensure that required HIPAA language is included in the consent form.

FDA regulations require, in addition, that subjects are informed of the possibility that the FDA may inspect the records for the study, if it is FDA-regulated. The consent form should also indicate whether the sponsor or research monitors hired by the sponsor will have access to the subject health information in order to monitor for accuracy.

4.2.2. Confidentiality Issues during Waiver or Documentation of Informed Consent:
The IRB must consider confidentiality in its analysis of the criteria to be met in order to allow research without the consent of the subjects. The IRB must determine whether the research represents minimal risk to the subjects and does not adversely affect the rights and welfare of the subjects. Some research that represents no physical risk may still represent more than minimal risk because of potential breaches of privacy and confidentiality as in the case of genetic research. This type of risk of harm is more likely if the research records are kept with the medical records, where employers or insurers could accidentally or intentionally have access.
1. **Purpose**

Investigators and supporting personnel when conducting research involving human subjects must operate under Good Clinical Practice Guidelines. Good Clinical Practice (GCP) was promulgated by an International Congress of Harmonization, *Harmonized Tripartite Guideline for Good Clinical Practice*. GCP represents an international ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the participation of human subjects in the research. Compliance with this standard assures the public that the rights, safety and well-being of clinical trial subjects are being protected consistent with the principles of both the Declaration of Helsinki and the Belmont Report.

2. **Responsibility for Understanding the Policy**

- Investigators
- Research Coordinators
- Clinical Trial Nurses and Practitioners

3. **Policy**

The European Agency for the Evaluation of Medicinal Products (EMEA), *Human Medicines Evaluation Unit*, developed the Guideline with consideration of the current good clinical practices of the European Union, Japan and the United States, as well as those of Australia, Canada, the Nordic countries and the World Health Organization to facilitate the mutual acceptance of clinical trial data by the regulatory authorities in those jurisdictions. It was published in 1998. The following information has been reproduced directly from the EMEA ICH Guideline.

4. **Investigator Responsibilities under the Policy**

4.1. Investigator’s Qualifications and Agreements

   4.1.1. The investigator(s) should be qualified by education, training, and experience to assume responsibility for the proper conduct of the trial, should meet all the qualifications specified by the applicable regulatory requirement(s), and should provide evidence of such qualifications through up-to-date curriculum vitae and/or other relevant documentation requested by the sponsor, the IRB, and/or the regulatory authority(ies).

   4.1.2. The investigator should be thoroughly familiar with the appropriate use of the investigational product(s), as described in the protocol, in the current Investigator's Brochure, in the product information and in other information sources provided by the sponsor.
4.1.3. The investigator should be aware of, and should comply with, GCP and the applicable regulatory requirements.

4.1.4. The investigator/institution should permit monitoring and auditing by the sponsor, and inspection by the appropriate regulatory authority(ies).

4.1.5. The investigator should maintain a list of appropriately qualified persons to whom the investigator has delegated significant trial-related duties.

4.1.6. When the researcher is the lead researcher of a multi-site study, applications include information about the management of information that is relevant to the protection of participant, such as:
   - Unanticipated problems involving risks to participants or others.
   - Interim results.
   - Protocol modifications.

4.2. Adequate Resources
4.2.1. The investigator should be able to demonstrate (based on retrospective data) a potential for recruiting the required number of suitable subjects within the agreed recruitment period.

4.2.2. The investigator should have sufficient time to properly conduct and complete the trial within the agreed trial period.

4.2.3. The investigator must have a co-investigator as well as an adequate number of qualified staff and adequate facilities for the foreseen duration of the trial to conduct the trial properly and safely.

4.2.4. The investigator should ensure that all persons assisting with the trial are adequately informed about the protocol, the investigational product(s), and their trial-related duties and functions.

4.3. Medical Care of Trial Subjects
4.3.1. A qualified physician (or dentist, when appropriate), who is an investigator or a sub-investigator for the trial, should be responsible for all trial-related medical (or dental) decisions.

4.3.2. During and following a subject's participation in a trial, the investigator/institution should ensure that adequate medical care is provided to a subject for any adverse events, including clinically significant laboratory values, related to the trial. The investigator/institution should inform a subject when medical care is needed for intercurrent illness(es) of which the investigator becomes aware.
4.3.3. It is recommended that the investigator inform the subject's primary physician about the subject's participation in the trial if the subject has a primary physician and if the subject agrees to the primary physician being informed.

4.3.4. Although a subject is not obliged to give his/her reason(s) for withdrawing prematurely from a trial, the investigator should make a reasonable effort to ascertain the reason(s), while fully respecting the subject's rights.

4.4. Communication with IRB

4.4.1. Before initiating a trial, the investigator/institution should have written and dated approval/favorable opinion from the IRB/IEC for the trial protocol, written informed consent form, consent form updates, subject recruitment procedures (e.g., advertisements), and any other written information to be provided to subjects.

4.4.2. As part of the investigator's/institution's written application to the IRB/IEC, the investigator/institution should provide the IRB/IEC with a current copy of the Investigator's Brochure. If the Investigator's Brochure is updated during the trial, the investigator/institution should supply a copy of the updated Investigator's Brochure to the IRB/IEC.

4.4.3. During the trial the investigator/institution should provide to the IRB/IEC all documents subject to review.

4.5. Compliance with Protocol

4.5.1. The investigator/institution should conduct the trial in compliance with the protocol agreed to by the sponsor and, if required, by the regulatory authority(ies) and which was given approval/favorable opinion by the IRB/IEC. The investigator/institution and the sponsor should sign the protocol, or an alternative contract, to confirm agreement.

4.5.2. The investigator should not implement any deviation from, or changes of the protocol without agreement by the sponsor and prior review and documented approval/favorable opinion from the IRB/IEC of an amendment, except where necessary to eliminate an immediate hazard(s) to trial subjects, or when the change(s) involves only logistical or administrative aspects of the trial (e.g., change in monitor(s), change of telephone number(s)).

4.5.3. The investigator, or person designated by the investigator, should document and explain any deviation from the approved protocol.
4.5.4. The investigator may implement a deviation from, or a change of, the protocol to eliminate an immediate hazard(s) to trial subjects without prior IRB/IEC approval/favorable opinion. As soon as possible, a description of the implemented deviation or change, the reasons for it, and, if appropriate, the proposed protocol amendment(s) should be submitted:

- to the IRB/IEC for review and approval/favorable opinion;
- to the sponsor for agreement and, if required;
- to the regulatory authority(ies).

4.6. Investigational Products

4.6.1. Responsibility for investigational product(s) accountability at the trial site(s) rests with the investigator/institution.

4.6.2. Where allowed/required, the investigator/institution may/should assign some or all of the investigators/institution's duties for investigational product(s) accountability at the trial site(s) to an appropriate pharmacist or another appropriate individual who is under the supervision of the investigator/institution.

4.6.3. The investigator/institution and/or a pharmacist or other appropriate individual, who is designated by the investigator/institution, should maintain records of the product's delivery to the trial site, the inventory at the site, the use by each subject, and the return to the sponsor or alternative disposition of unused product(s). These records should include dates, quantities, batch/serial numbers, expiration dates (if applicable), and the unique code numbers assigned to the investigational product(s) and trial subjects. Investigators should maintain records that document adequately that the subjects were provided the doses specified by the protocol and reconcile the quantities of all investigational product(s) received from the sponsor.

4.6.4. The investigational product(s) should be stored as specified by the sponsor (see ICH E6 5.13.2 and 5.14.3) and in accordance with applicable regulatory requirement(s).

4.6.5. The investigator should ensure that the investigational product(s) are used only in accordance with the approved protocol.
4.6.6. The investigator, or a person designated by the investigator/institution, should explain the correct use of the investigational product(s) to each subject and should check, at intervals appropriate for the trial, that each subject is following the instructions properly.

4.7. Randomization Procedures and Unblinding
The investigator should follow the trial's randomization procedures, if any, and should ensure that the code is broken only in accordance with the protocol. If the trial is blinded, the investigator should promptly document and explain to the sponsor any premature unblinding (e.g., accidental unblinding, or unblinding due to a serious adverse event) of the investigational product(s).

4.8. Informed Consent of Trial Subjects
4.8.1. In obtaining and documenting informed consent, the investigator should comply with the applicable regulatory requirement(s), and should adhere to GCP and to the ethical principles that have their origin in the Declaration of Helsinki. Prior to the beginning of the trial, the investigator should have the IRB/IEC's written approval/favorable opinion of the written informed consent form and any other written information to be provided to subjects.

4.8.2. The written informed consent form and any other written information to be provided to subjects should be revised whenever important new information becomes available that may be relevant to the subject's consent. Any revised written information consent form, and written information should receive the IRB/IEC's approval/favorable opinion in advance of use. The subject or the subject's legally acceptable representative should be informed in a timely manner if new information becomes available that may be relevant to the subject's willingness to continue participation in the trial. The communication of this information should be documented.

4.8.3. Neither the investigator, nor the trial staff, should coerce or unduly influence a subject to participate or to continue to participate in a trial.

4.8.4. None of the oral and written information concerning the trial, including the written informed consent form, should contain any language that causes the subject or the subject's legally acceptable representative to waive or to appear to waive any legal rights, or that releases or appears to release the investigator, the institution, the sponsor, or their agents from liability for negligence.
4.8.5. The investigator, or a person designated by the investigator, should fully inform the subject or, if the subject is unable to provide informed consent, the subject's legally acceptable representative, of all pertinent aspects of the trial including the written information given approval/ favorable opinion by the IRB/IEC.

4.8.6. The language used in the oral and written information about the trial, including the written informed consent form, should be as non-technical as practical and should be understandable to the subject or the subject's legally acceptable representative and the impartial witness, where applicable.

4.8.7. Before informed consent may be obtained, the investigator, or a person designated by the investigator, should provide the subject or the subject's legally acceptable representative ample time and opportunity to inquire about details of the trial and to decide whether or not to participate in the trial. All questions about the trial should be answered to the satisfaction of the subject or the subject's legally acceptable representative.

4.8.8. Prior to a subject's participation in the trial, the written informed consent form should be signed and personally dated by the subject or by the subject's legally acceptable representative, and by the person who conducted the informed consent discussion.

4.8.9. If a subject is unable to read or if a legally acceptable representative is unable to read, an impartial witness should be present during the entire informed consent discussion. After the written informed consent form and any other written information to be provided to subjects, is read and explained to the subject or the subject's legally acceptable representative, and after the subject or the subject's legally acceptable representative has orally consented to the subject's participation in the trial and, if capable of doing so, has signed and personally dated the informed consent form, the witness should sign and personally date the consent form. By signing the consent form, the witness attests that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the subject or the subject's legally acceptable representative, and that informed consent was freely given by the subject or the subject's legally acceptable representative.

4.8.10. Both the informed consent discussion and the written informed consent form and any other written information to be provided to subjects should include explanations of the following:

- That the trial involves research.
- The purpose of the trial.
• The trial treatment(s) and the probability for random assignment to each treatment.

• The trial procedures to be followed, including all invasive procedures.

• The subject's responsibilities.

• Those aspects of the trial that are experimental and those that are standard of care.

• The reasonably foreseeable risks or inconveniences to the subject and, when applicable, to an embryo, fetus, or nursing infant.

• The reasonably expected benefits. When there is no intended clinical benefit to the subject, the subject should be made aware of this.

• The alternative procedure(s) or course(s) of treatment that may be available to the subject, and their important potential benefits and risks.

• The compensation and/or treatment available to the subject in the event of trial related injury.

• The anticipated prorated payment, if any, to the subject for participating in the trial.

• The anticipated expenses, if any, to the subject for participating in the trial.

• That the subject's participation in the trial is voluntary and that the subject may refuse to participate or withdraw from the trial, at any time, without penalty or loss of benefits to which the subject is otherwise entitled.

• That the monitor(s), the auditor(s), the IRB/IEC, and the regulatory authority(ies) will be granted direct access to the subject's original medical records for verification of clinical trial procedures and/or data, without violating the confidentiality of the subject, to the extent permitted by the applicable laws and regulations and that, by signing a written informed consent form, the subject or the subject's legally acceptable representative is authorizing such access.
• That records identifying the subject will be kept confidential and, to the extent permitted by the applicable laws and/or regulations, will not be made publicly available. If the results of the trial are published, the subject's identity will remain confidential.

• That the subject or the subject's legally acceptable representative will be informed in a timely manner if information becomes available that may be relevant to the subject's willingness to continue participation in the trial.

• That the person(s) to contact for further information regarding the trial and the rights of trial subjects, and whom to contact in the event of trial-related injury.

• The foreseeable circumstances and/or reasons under which the subject's participation in the trial may be terminated.

• The expected duration of the subject's participation in the trial.

• The approximate number of subjects involved in the trial.

4.8.11. Prior to participation in the trial, the subject or the subject's legally acceptable representative should receive a copy of the signed and dated written informed consent form and any other written information provided to the subjects. During a subject's participation in the trial, the subject or the subject's legally acceptable representative should receive a copy of the signed and dated consent form updates and a copy of any amendments to the written information provided to subjects.

4.8.12. When a clinical trial (therapeutic or non-therapeutic) includes subjects who can only be enrolled in the trial with the consent of the subject's legally acceptable representative (e.g., minors, or patients with severe dementia), the subject should be informed about the trial to the extent compatible with the subject's understanding and, if capable, the subject should sign and personally date the written informed consent.

4.8.13. Except as described in 4.8.14, a non-therapeutic trial (i.e. a trial in which there is no anticipated direct clinical benefit to the subject), should be conducted in subjects who personally give consent and who sign and date the written informed consent form.

4.8.14. Non-therapeutic trials may be conducted in subjects with consent of a legally acceptable representative provided the following conditions are fulfilled:
• The objectives of the trial cannot be met by means of a trial in subjects who can give informed consent personally.

• The foreseeable risks to the subjects are low.

• The negative impact on the subject's well-being is minimized and low.

• The trial is not prohibited by law.

• The approval/favorable opinion of the IRB/IEC is expressly sought on the inclusion of such subjects, and the written approval/favorable opinion covers this aspect.

Such trials, unless an exception is justified, should be conducted in patients having a disease or condition for which the investigational product is intended. Subjects in these trials should be particularly closely monitored and should be withdrawn if they appear to be unduly distressed.

4.8.15. In emergency situations, when prior consent of the subject is not possible, the consent of the subject's legally acceptable representative, if present, should be requested. When prior consent of the subject is not possible, and the subject's legally acceptable representative is not available, enrolment of the subject should require measures described in the protocol and/or elsewhere, with documented approval/favorable opinion by the IRB/IEC, to protect the rights, safety and well-being of the subject and to ensure compliance with applicable regulatory requirements. The subject or the subject's legally acceptable representative should be informed about the trial as soon as possible and consent to continue and other consent as appropriate (see ICH E6 4.8.10) should be requested.

4.9. Records and Reports

4.9.1. The investigator should ensure the accuracy, completeness, legibility, and timeliness of the data reported to the sponsor in the CRFs and in all required reports.

4.9.2. Data reported on the CRF, that are derived from source documents, should be consistent with the source documents or the discrepancies should be explained.
4.9.3. Any change or correction to a CRF should be dated, initialed, and explained (if necessary) and should not obscure the original entry (i.e. an audit trail should be maintained); this applies to both written and electronic changes or corrections (see ICH E6 5.18.4(n)). Sponsors should provide guidance to investigators and/or the investigators' designated representatives on making such corrections. Sponsors should have written procedures to assure that changes or corrections in CRFs made by sponsor's designated representatives are documented are necessary, and are endorsed by the investigator. The investigator should retain records of the changes and corrections.

4.9.4. The investigator/institution should maintain the trial documents as specified in Essential Documents for the Conduct of a Clinical Trial (see ICH Guidelines for Good Clinical Practice, Section 8, or attachment A to this policy) and as required by the applicable regulatory requirement(s). The investigator/institution should take measures to prevent accidental or premature destruction of these documents.

4.9.5. Essential documents should be retained until at least 2 years after the last approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications in an ICH region or at least 2 years have elapsed since the formal discontinuation of clinical development of the investigational product. These documents should be retained for a longer period however if required by the applicable regulatory requirements or by an agreement with the sponsor. It is the responsibility of the sponsor to inform the investigator/institution as to when these documents no longer need to be retained (see ICH E6 5.5.12).

4.9.6. The financial aspects of the trial should be documented in an agreement between the sponsor and the investigator/institution.

4.9.7. Upon request of the monitor, auditor, IRB/IEC, or regulatory authority, the investigator/institution should make available for direct access all requested trial-related records.

4.10. Progress Reports
4.10.1. The investigator should submit written summaries of the trial status to the IRB/IEC annually, or more frequently, if requested by the IRB/IEC.

4.10.2. The investigator should promptly provide written reports to the sponsor, the IRB/IEC (see ICH E6 3.3.8) and, where applicable, the institution on any changes significantly affecting the conduct of the trial, and/or increasing the risk to subjects.
4.11. Safety Reporting

4.11.1. All serious adverse events (SAEs) should be reported immediately to the sponsor except for those SAEs that the protocol or other document (e.g., Investigator's Brochure) identifies as not needing immediate reporting. The immediate reports should be followed promptly by detailed, written reports. The immediate and follow-up reports should identify subjects by unique code numbers assigned to the trial subjects rather than by the subjects' names, personal identification numbers, and/or addresses. The investigator should also comply with the applicable regulatory requirement(s) related to the reporting of unexpected serious adverse drug reactions to the regulatory authority(ies) and the IRB/IEC.

4.11.2. Adverse events and/or laboratory abnormalities identified in the protocol as critical to safety evaluations should be reported to the sponsor according to the reporting requirements and within the time periods specified by the sponsor in the protocol.

4.11.3. For reported deaths, the investigator should supply the sponsor and the IRB/IEC with any additional requested information (e.g., autopsy reports and terminal medical reports).

4.12. Premature Termination or Suspension of a Trial

If the trial is prematurely terminated or suspended for any reason, the investigator/institution should promptly inform the trial subjects, should assure appropriate therapy and follow-up for the subjects, and, where required by the applicable regulatory requirement(s), should inform the regulatory authority(ies). In addition:

4.12.1. If the investigator terminates or suspends a trial without prior agreement of the sponsor, the investigator should inform the institution where applicable, and the investigator/institution should promptly inform the sponsor and the IRB/IEC, and should provide the sponsor and the IRB/IEC a detailed written explanation of the termination or suspension.

4.12.2. If the sponsor terminates or suspends a trial (see ICH E6 5.21), the investigator should promptly inform the institution where applicable and the investigator/institution should promptly inform the IRB/IEC and provide the IRB/IEC a detailed written explanation of the termination or suspension.

4.12.3. If the IRB/IEC terminates or suspends its approval/favorable opinion of a trial (see ICH E6 3.1.2 and 3.3.9), the investigator should inform the institution where applicable and the investigator/institution should promptly notify the sponsor and provide the sponsor with a detailed written explanation of the termination or suspension.
4.13. Final Report(s) by Investigator
Upon completion of the trial, the investigator, where applicable, should inform the institution; the investigator/institution should provide the IRB/IEC with a summary of the trial's outcome, and the regulatory authority(ies) with any reports required.

5. Sponsor
5.1. Quality Assurance and Quality Control
5.1.1. The sponsor is responsible for implementing and maintaining quality assurance and quality control systems with written SOPs to ensure that trials are conducted and data are generated, documented (recorded), and reported in compliance with the protocol, GCP, and the applicable regulatory requirement(s).

5.1.2. The sponsor is responsible for securing agreement from all involved parties to ensure direct access (see ICH E6 1.21) to all trial related sites, source data/documents, and reports for the purpose of monitoring and auditing by the sponsor, and inspection by domestic and foreign regulatory authorities.

5.1.3. Quality control should be applied to each stage of data handling to ensure that all data are reliable and have been processed correctly.

For other responsibilities of the sponsor under Good Clinical Practice, consult the Harmonized Tripartite Guideline for Good Clinical Practice.

6. Tools
ICH Guidelines for Good Clinical Practice
# Regulatory Binder Index

| 1. Protocol | • Study Protocol  
| | • Study Protocol Amendments  
| | • Protocol or Amendment Signature Pages  
| | • Non-Disclosure Agreement  
| | • Investigator Drug Brochure |
| 2. 1572/Regulatory Forms/CV | • Form FDA 1572 (If applicable)  
| | • Curriculum Vita of investigator(s)  
| | • Medical Licenses (US only, if applicable)  
| | • Financial Disclosure Agreement (if applicable)  
| | • Copies of IRB & HIPAA training certificates |
| 3. Original IRB-Approved Consent Form(s) | • Original Informed Consent(s) (with red IRB stamp) |
| 4. IRB Approval letters and Correspondence | • IRB/IBC/RAC Approvals for Protocol  
| | • Copies of OHR12 (Amendments, Advertisements), OHR9 (continuation)  
| | • Other IRB Correspondence (copies of OHR20 for deviations/violations, etc.) |
| 5. Laboratory | • Lab Certifications as applicable (CAP & CLIA)  
| | • Laboratory Normal Ranges  
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| 6. Study Logs | • Investigator Personnel Team Signature Page  
| | • Site Visit Logs  
| | • Site Signature Logs  
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| 7. Correspondence | • Study related correspondence between the site, sponsor, CRO, etc. |
| 8. Serious Adverse Events (SAE) | • Printouts of SAE reports  
| | • IND Safety Letters |
| 9. Drug / Device Accountability (if applicable) | • Receipt/packing invoices  
| | • Accountability Form  
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| 10. Miscellaneous | • Miscellaneous (CRF transmittal logs, etc.) |
1. **Purpose**  
This Policy defines the responsibilities of the Investigator and members of the study team in conducting human subjects research including FDA-regulated research. It also identifies areas of accountability and the process for delegating the transfer of the Investigator's responsibilities to other designated individuals.

2. **Responsibility for Executing the Policy**  
Principal Investigator  
Key Study Personnel

3. **Policy Specifics**  
This policy applies to the Principal Investigator and all other designated individuals involved in supervising, managing, or conducting human subjects related research in the University.

3.1. **Investigator Responsibilities**  
3.1.1. Consults with and obtains approval from the Office of Human Research (OHR) for clinical study activities prior to proceeding.

3.1.2. Establishes standard operating procedures (SOP) to ensure that the conduct of regulated human subject research proceeds in compliance with Sponsor requirements, GCP guidelines and all applicable regulations and institutional requirements.

3.1.3. Ensures that SOPs are developed, reviewed, approved, and modified in a controlled and accountable manner (References G 606, Investigator-Initiated Study Protocol Template; GA 124, Policy on Good Clinical Practice for Investigators).

3.1.4. Ensures that responsibilities and activities in the conduct of regulated human subject research that are delegated to others are understood by those who carry them out and are delegated to individuals who are qualified by training and experience to carry out those responsibilities and activities, with appropriate documentation of that delegation (Reference QA 304, Study Team Training).

3.1.5. Establishes training policies and procedures to provide all designated individuals with the opportunity to maintain and enhance their ability to carry out their delegated responsibilities; and ensures all individuals engaged in clinical research have met their training requirements (Reference QA 304, Study Team Training).
3.1.6. Ensures that financial and professional conflicts of interest are recognized, reported to the Office of University Counsel and any other appropriate authorities, and mitigated where possible (Reference GA 106, Policy and Procedure for Determining Conflicts of Interest).

3.1.7. Provides Sponsor with sufficient evidence of qualification of all key personnel and a commitment to conduct the study according to the Sponsor and Investigator's mutual agreement.

3.1.8. Ensures that all key study personnel are adequately prepared to participate in Sponsor-initiated site training on the regulations, the protocol and the investigational product (Reference QA 304, Study Team Training).

3.1.9. Ensures regular, timely, effective and well-documented communication among all individuals participating in the conduct of clinical research (Reference G 606, Investigator-Initiated Study Protocol Template; GA 124, Policy on Good Clinical Practice for Investigators).

3.1.10. Ensures the proper use, storage and accountability of investigational products [(Reference G 606, Investigator-Initiated Study Protocol Template; GA 124, Policy on Good Clinical Practice for Investigators, Section 4.6, Investigational Product(s)].

3.1.11. Maintains all required documents and records in the appropriate location and for a period of time specified by Sponsor and by regulatory requirements (Reference GA 124, Policy on Good Clinical Practice for Investigators, Section 4.9 Records and Reports).

3.1.12. Ensures compliance with the protocol and cooperation with the Sponsor's Monitors (Reference GA 124, Policy on Good Clinical Practice for Investigators, Section 4.1.4).

3.1.13. Terminates participation in an investigation that is determined to present an unreasonable or significant risk to participants, or for an inability to comply with the investigational plan (Reference GA 124, Policy on Good Clinical Practice for Investigators, Section 4.14 Premature or suspension of a trial; Policy RR 405, Study Completion, Administrative Hold, Suspension or Termination of IRB Approval).

3.1.15. Ensures that each participant signs the current version of the Thomas Jefferson University IRB-approved informed consent form and continues the process of informing participants about their ongoing participation throughout the duration of the study (References: Policy IC 701, Informed Consent and HIPAA Authorization: General Requirements; Policy IC 702, Informed Consent and HIPAA Authorization: Documentation).

3.1.16. Safeguards the scientific, ethical and regulatory validity of the clinical study by requiring strict adherence to participant enrollment criteria, participant identification methods (protection of confidentiality), management of participant medical care while enrolled, and biological specimen collection and handling requirements (Reference Policy GA 126, Participant Screening and Enrollment).

3.1.17. Ensures the management of participants' medical care while enrolled and that adverse events are recorded and, if serious, are promptly investigated and reported to the Sponsor and relevant institutional and regulatory authorities (Reference: Policy GA 120, Policy and procedure for Reporting and Reviewing Adverse Events and Unanticipated Problems Involving Risks to Subjects and Others).

3.1.18. Maintains a system for recording and managing data and observations from clinical studies, including required safeguards for electronic data collection systems.

3.1.19. Employs quality assurance practices that ensure scientific, ethical and regulatory compliance by permitting the independent review and assessment of policies, procedures and records for quality improvement purposes (Reference: Policy QA 302, QA/QC Program; QA 303, Audits by Regulatory Agencies).

3.1.20. Cooperates with regulatory authorities (e.g., FDA, OHR) in their assessment of the clinical research program's compliance with applicable regulations (Reference Guidance G 611, FDA Inspection of Clinical Investigators).
3.2. General Responsibilities of the Study Team

3.2.1. Communicate effectively with participants, other study team members, IRB and the Sponsor.

3.2.2. Support required training activities through their own professional development in relevant content areas.

3.2.3. Communicate all adverse events and abnormal laboratory results to the Investigator for an assessment of severity and report non-serious adverse events or serious adverse events to the IRB and Sponsor appropriately.

3.2.4. Meet regularly with the Investigator and other study team members to discuss participant participation and protocol progress.

3.2.5. Prepare for and attend Investigator and study start-up meetings.

3.2.6. Participate in monitoring visits and audits as appropriate.

3.2.7. Make available to Monitors, Auditors, IRB and regulatory authorities all requested study-related records.

3.2.8. Ensure accuracy, completeness, legibility and timeliness of case report forms (CRF).

3.2.9. Ensure that CRF accurately reflect source documents, explain any discrepancies between source documents and CRFs and endorse changes or corrections to a CRF.

3.2.10. Ensure documentation of study-related procedures, processes and events.

3.2.11. Comply with written procedures to document changes to data and/or CRF.

3.2.12. Maintain study documents as required by the regulations and Sponsor for the appropriate time frame and under secure conditions.

3.3. Delegation of Responsibility and Signature Authority

3.3.1. The Investigator has the authority to delegate any study-related task and responsibility to any member of the study team who has been properly trained to carry out the designated function.
3.3.2. The Investigator or his/her designee must identify the individual by name and/or by title, to whom significant study-related functions have been assigned.

3.3.3. Designated personnel may sign various documents as approved by the Investigator.

3.3.4. The Investigator may sign any document in the absence of designated personnel.

3.3.5. If a designated individual signs in place of another whose name is typed or printed near the space for signature, the signatory shall sign his or her name followed by the word "for" indicating they are signing for that person.

3.3.6. For instances in which the signatory is signing a totally blank space, that person shall simply sign his or her name and provide a date.

3.4. Transfer of Responsibility to Contractors

3.4.1. The Investigator has the authority to delegate any study-related task and duty to a qualified contractor (e.g., consulting firm, independent consultant) that has been properly trained to carry out the designated function.

3.4.2. The Investigator or his/her designee must identify the individual(s) by name and/or by title, to which significant study-related functions have been assigned in a properly executed vendor agreement.

3.4.3. The Investigator will maintain a file documenting the qualifications of such contractors as part of the study file.

4. References

Responsibilities of Sponsors and Investigators (21 CFR 312 Subpart D)
Responsibilities of Investigators (21 CFR 812 Subpart E)
Transfer of Obligations to a Contract Research Organization (21 CFR 312.52)
The Principles of ICH GCP (ICH E6, section 2.8)
Investigator (ICH E6, section 4.0)
Policy GA 124, Good Clinical Practice for Investigators
Policy QA 304, Study Team Training
1. **Purpose**
   To describe the requirements that must be included in written agreements with sponsors to ensure: (a) the human research protection program is applied to all sponsored research; (b) timely communication of information with sponsors that might affect the ongoing oversight of a protocol by the IRB is arranged; and (c) the benefits of knowledge obtained through research are realized and that the interests of the current and future research participants are protected.

2. **Responsibility for Executing the Policy**
   Director/Associate Director, OHR
   OHR Administrative Staff
   IRB Chairs/Vice Chairs
   Director, Office of Research Administration
   Associate Provost for Research Support Services

3. **Policy Statement**
   The OHR and the Office of Research Administration (ORA) shall require the written agreements with sponsors to include necessary provisions to evidence the protection of human research participants.

4. **Procedure**
   4.1. The Associate Provost for Research Support Services, who oversees the OHR and the ORA, shall ensure that the OHR and the ORA communicate regarding the inclusion of necessary provisions in sponsor agreements.

   4.2. ORA shall be responsible to ensure that a written agreement is entered into with each sponsor and each agreement includes, but is not limited to, the following:

   a) A provision obligating Thomas Jefferson University (“TJU”) to conduct the research according to the protocol and obligating the parties to comply with all applicable laws and regulations, including but not limited to, DHHS and FDA regulations and ethical obligations and expectations related to the research to protect human subjects. Contracts and funding agreements will specify that Thomas Jefferson University follows ICH-GCP (E-6) as embodied in 21 CFR 56.
b) A provision, if applicable, addressing the medical care for research participants with a research-related injury to include who is responsible to provide care and who is responsible to pay for the care.

c) In studies where the sponsor bears responsibility for monitoring of the research, reporting obligations to include the obligation of the sponsor to promptly report any findings of study monitors that could: (a) affect the safety of participants; (b) affect the willingness of study participants to continue participation in the study; (c) influence the conduct of the study; or (d) alter the IRBs’ approval to continue the study.

d) Plans for disseminating findings from the research and the roles that investigators and sponsors will play in publication or disclosures of results, including but not limited to, provisions: (a) obligating the sponsor to abide by TJU’s policies and procedures regarding the publication of findings from sponsored research; and (b) addressing the communication of results from a research study from the sponsor to TJU, then, as appropriate, from TJU to participants, when those results directly affected the participants’ safety or medical care.

4.3. The Office of University Counsel shall coordinate with the ORA and OHR on an ongoing basis to provide standard form agreement provisions to be included in all sponsor agreements including provisions addressing the items in Section 4.2 above. These provisions may be amended from time to time.
1. **Purpose**
   This policy describes the process to be followed for confirming the eligibility of subjects to enroll in human subjects research.

2. **Responsibility for Executing the Policy**
   Principal Investigator (Sponsor-Investigator)
   Participating Investigators
   Co-Investigators
   Designated Study Personnel

3. **Policy Statement**
   Every subject who is considered for enrollment in human subjects research must have his/her eligibility to participate confirmed according to this procedure.

4. **Procedures**
   4.1. **General Instructions and Responsibilities**
       The Principal Investigator and participating investigators or designees are responsible for ensuring written confirmation of a subject's eligibility to be enrolled in a clinical study prior to the subject's enrollment in the clinical study.

   4.2. **Preparing Subject Eligibility Documentation**
       After the protocol is finalized and approved, the Principal Investigator/designee should prepare a screening and enrollment log and a subject eligibility checklist including all of the inclusion and exclusion criteria for the study. These forms may be obtained from the sponsor. For retrospective studies, it is not necessary to keep a list of subjects screened, but an enrollment log is required. For studies with few (e.g. 1 or 2) eligibility criteria, an eligibility checklist is not required, but documentation of each subject’s eligibility must be maintained.

   4.3. **Conducting Screening Activities**
       As a general rule, consent must be obtained before any protocol specific screening procedures are performed on potential subjects. Proposed deviations from the rule must be brought to the attention of the IRB in the initial IRB submission.

       4.3.1. When conducting screening activities, the Principal Investigator/designee should use the screening and enrollment log as a running list of all potential subjects screened and enrolled for the study.
4.3.2. When a potential subject is identified, the Investigator/designee should obtain all protocol-relevant medical records and information regarding the subject. This must be done in compliance with institutional requirements and HIPAA regulations.

4.3.3. The Investigator/designee should record the status (e.g. screen failure, enrolled, etc.) of all potential subjects on the screening and enrollment log.

4.3.4. Based on discussions with the subject and review of the medical records, the Investigator/designee should complete a subject eligibility checklist for each potential subject.

4.3.5. All logs and checklists and originals or copies of appropriate supporting documentation will be maintained in each site's study file or specific subject file, as appropriate. For studies with only one or two eligibility criteria, such as blood or tissue banking studies, eligibility checklists are not required and when patients decline participation, this should be recorded on the screening and enrollment log or other list.

4.4. Subject Numbering

4.4.1. The Investigator will ensure that all participating investigators maintain a key to identify all screened and enrolled subjects. Each subject screened should be given a unique identifier. This identifier may change if the subject is enrolled. The subject code should include a site number if applicable, and sequential subject number. This procedure should be defined in the protocol.

4.4.2. Any other protocol-specific subject cohort assignment provided by the Sponsor-Investigator needs to be included. The protocol should be referenced for these instructions.

4.4.3. Once a subject's eligibility to participate in the clinical study has been confirmed, the subject will be assigned the unique subject number according to the protocol.

4.4.4. All study records that are maintained on each subject will use the unique subject number where possible to protect the subject's confidentiality.
5. Applicable Regulations and Guidelines
   General Responsibilities of Investigators (21 CFR 321.60)
   Specific Responsibilities of Investigators (21 CFR 812.110)
   Compliance with Protocol (ICH E6, Section 4.5)
   Randomization Procedures and Unblinding (ICH E6, Section 4.7)
   Trial Management, Data Handling, and Record Keeping (ICH E6, Section 5.5)
1. **Purpose**
   Designation of the Associate Provost for Research Support Services (APRSS) as the Institutional Official (IO) with overall responsibility for the Human Research Protection Program.

2. **Responsibility for Executing the Policy**
   The Provost of Thomas Jefferson University

3. **Policy Statement**
   This Policy designates the APRSS as the Senior Officer charged with responsibility for research, research integrity and science policy. The APRSS will be responsible for general oversight of the University’s Human Research Protection Program. The APRSS, in the role of IO, reports directly to the Provost of the University.

   The Director, Office of Human Research reports directly to the APRSS, and functions as the Director of the Office of Human Research and is responsible for the day to day operation of the Human Research Protection Program.
1. Purpose
To state the policy and outline the procedures regarding the protection of privacy interests of research subjects and confidentiality of subject data.

2. Responsibility for Executing the Policy
Director/Associate Director, OHR
IRB Chairs/Vice Chairs
IRB Members
OHR Administrative Staff
Investigators

3. Policy Statement
For the purposes of this policy, “privacy” will be defined as an individual’s desire to control the ways in which s/he is approached and/or the ways in which his/her private information is shared with others. Privacy may or may not be linked to confidentiality of personal information collected or generated during a research study. “Confidentiality” pertains to the handling, storage, collection and use of an individual’s personal information.

Privacy and confidentiality are supported by “Respect for Persons” and “Beneficence”, two of the principles of research ethics identified in the Belmont Report. Both 45 CFR §46.111 and 21 CFR §56.111 require the IRB to determine, as part of its review of research, that privacy is protected when appropriate.

HIPAA, The Health Insurance Portability and Accountability Act of 1996 became effective on April 14, 2003 with the publication of the Privacy Rule and its regulations for Protected Health Information (PHI).
3.1. The Privacy Rule promulgated regulations that:
- Established a requirement for a Privacy Notice to be provided to all patients and/or research subjects;
- The Privacy Notice must inform the patient/research subject how their PHI may be used or disclosed;
- The Privacy Notice will inform the patient/research subject their right to inspect, amend, and request an accounting of their PHI.
3.2. Disclosures of PHI:
Disclosures of PHI are permitted for treatment, payment, and healthcare operations without the need for authorization, however, an acknowledgement by the individual of receipt of a provider’s Privacy Notice explaining how PHI will be used is required. If disclosure is required, it must contain no more than the minimum information necessary to accomplish the intended purpose of the use or disclosure. The Privacy Rule restricts disclosure of PHI for specific purposes and establishes civil and criminal penalties for improper disclosure and/or use.

4. Procedures
4.1. Investigators Conducting Human Subjects Research:
Thomas Jefferson University must provide all patients and research subjects with a Privacy Notice that as a minimum:
- Limits the use and disclosure of the PHI taken;
- Gives the subject the right to access his/her records and to receive an accounting of who accessed their health information;
- Allows the subject to request amendment to his/her record and places limits on the use and disclosure;
- Limits the disclosure of the PHI taken to the minimum necessary to accomplish the goals of the study, unless a written authorization is obtained from the individual.

An investigator conducting human subjects research must provide the subject with an IRB- approved copy of the University consent form document that contains the HIPAA- compliant Privacy Notice approved by the University’s Legal Department.

Under the Privacy Rule, an investigator may:
- Conduct chart or record reviews;
- Acquire clinical data;
- Analyze data;
- Disclose /communicate data to co-investigator(s);
- Report data to a multi-site data center;
- Publish PHI.
The investigator is permitted to access, use and disclose PHI for research purposes under one of the following six conditions, and using the appropriate OHR Internal Authorization Form:

- An authorization is obtained from the subject (HIPAA authorization section in the generic consent form template);
- The IRB has waived the authorization requirement (OHR-3);
- Information is only collected in preparation for planning a research study;
- Only a limited data set is collected and accompanied by a data use agreement (OHR-6A or OHR-6B);
- Only Decedent PHI will be collected (OHR-17);
- The information to be collected will be de-identified (OHR-5).

The Principal Investigator is urged to consult the OHR forms listed above, and the Policy and Procedures Manual concerning the details of these authorizations, and to discuss his/her use of an authorization with the Associate Director, OHR, before going ahead.

4.2. Approval of a Waiver of Authorization under the Policy Rule
An investigator must satisfy the following criteria in order for IRB approval of a waiver of authorization:

a) The use/disclosure of the PHI involves no more than minimum risk to the privacy of the subject based on, at least, the following elements:
   - An adequate plan presented in the OHR-3 to protect identifiers from improper use/disclosure;
   - An adequate plan to destroy the identifiers at the earliest opportunity consistent with the conduct of the research, unless the law requires retention;
   - Adequate written assurances 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 project, or for research for which the use or disclosure of PHI would be permitted by the subject;
   - The research cannot practicably be conducted without the waiver;
The research cannot practicably be conducted without access to and use of PHI.

b) An investigator may use/disclose PHI for research purposes pursuant to a waiver of authorization from the IRB only if s/he has an approval letter signed by the Director/Associate Director, OHR that documents all of the following:

- Identification of the particular IRB, and the date of approval of the waiver;
- A statement that the IRB has determined that the waiver of authorization satisfies the criteria in the Privacy Rule as stated above;
- A brief description of the PHI for which use or access has been determined by the IRB to be necessary;
- A statement that the waiver of authorization has been approved by the convened IRB or by expedited review.

4.3. PHI and Recruitment for Research

The criteria for waiver of authorization for recruiting purposes under the Privacy Rule are essentially the same as for a waiver of informed consent under 45 CFR Part 46.116 (i.e., minimal risk to privacy compared to minimal risk to the subject).

If a treating physician wishes to share PHI with an investigator for enrollment purposes, the Investigator must obtain an authorization from the patient or a waiver of authorization from the IRB.

If an investigator wishes to review medical records to identify potential research subjects, s/he must include a plan for doing so in the protocol submission or provide the IRB with a Request for Waiver of Authorization to Collect PHI (OHR-3).

If an investigator wishes to view potential subjects’ PHI in the course of preparing for research, s/he must provide the IRB with a Review Preparatory to Research Request Form (OHR-29).

4.4. Accessing PHI through Limited Data Sets/Data Use Agreement:

A limited data set represents PHI that does not contain any direct identifiers. An investigator planning to use a limited data set should consult the OHR Form (OHR-6) as to what constitutes the specific direct identifiers. The use of a limited data set requires the investigator to complete a Data Use Agreement (OHR-6A or -6B) as required which will establish how the data can be used.
4.5. Accessing PHI through De-identification:
An investigator may use or disclose PHI without authorization if the PHI has been de-identified by the removal of specific identifiers so that the individual cannot be identified. Release or use of de-identified PHI is exempt from HIPAA requirements. IRB review is required for human subjects research even when the protocol uses de-identified PHI. The investigator must submit a De-identification certification form (OHR-5) to the IRB for review and approval.

4.6. Research on PHI of Decedents:
An investigator planning to use or disclose PHI of a decedent for research purposes must certify in the proposal that:
- The use or disclosure of the PHI is being sought solely for research;
- The research cannot be carried out without the PHI.

The IRB may request documentation from the investigator in the form a copy of the decedent’s death certificate. Under 45 CFR Part 46, the IRB is not required to review research to be carried out based on decedent’s PHI. PHI to be collected during research that falls under those regulations should be sent to the University Privacy officer for review.

4.7. Collection of PHI from Specimens and Tissue Samples
An investigator planning to obtain, use or store specimens or tissue samples that contain PHI for research purposes must consider the PHI identifiable if any of the elements designated as identifiers by HIPAA are maintained with the specimen or tissue sample.

4.8. Accounting of Research Disclosures
The Privacy Rule gives the subject the right to receive an accounting of all disclosures of PHI made by the investigator that occurred during the six years prior to the individual request for an accounting. The investigator must provide the accounting of research disclosures to the University Privacy Officer and not the IRB.

4.9. Multi-site Research:
If PHI for a study is to be shared by the investigator with other sites conducting the same research, the investigator must assure that:
- The consent document/authorization form lists the sites and sponsor (if any) that will be involved in the research and to whom the subjects PHI will be disclosed and for what purpose(s);
- Cooperative procedures are available so that PHI may be obtained from one or another of the sites in order to respond to a subjects request to inspect or copy his/her research information;
• The sites are informed of any amendment(s) to the subject’s PHI;

• In the case of studies operating under a waiver of authorization any request(s) from a subject to receive an accounting of disclosures are available to all the sites.

If research is being conducted in states other than Pennsylvania, the principal investigator must provide information on any state specific regulations on privacy requirements and genetic research. The principal investigator may consult with the Office of University Counsel for advice or direction.

5. Privacy and Confidentiality Issues
The IRB members must consider privacy and confidentiality as part of their regulatory and ethical duty to protect the rights and welfare of human subjects. During their review of a study, they must evaluate 1) the degree of sensitivity of the information being collected and the measures that have been established for protecting the confidentiality of the information obtained, and 2) the ways in which the subject is accessed and contacted throughout the duration of the study The IRB will require the investigator to provide such information in the OHR-2, the protocol and the confidentiality section of the consent document.

5.1. Confidentiality Issues
The IRB will require the investigator to indicate how long and where the study records will be retained, and whether they will be destroyed when the research is completed (Policy GA 123). Research data can, however, be retained indefinitely if reasonable justification can be provided.

The IRB is responsible for ensuring that the consent document adequately provides the subject with information concerning the extent to which confidentiality of the research and medical records will be maintained. Both 45 CFR § 46.116 and 21 CFR § 50.52 require that the consent document contain a statement describing the extent, if any, to which confidentiality of research records identifying subjects will be maintained. FDA regulations require, in addition, that subjects are informed of the possibility that the FDA may inspect the records for the study.

The IRB is also responsible for ensuring that the HIPAA section of the consent document is properly completed and contains information required to protect the subject’s PHI.
5.2. Privacy Issues
The IRB must also consider the protection of privacy during the subject’s total participation in the study. This extends from the recruitment process until the subject has completed the last study visit or has been contacted for the last time for final follow-up data collection. Issues of privacy that may be considered include:

- Appropriateness and privacy of location for recruitment and consent interview;
- The manner in which subject is contacted for recruitment, if by mail, email, or phone;
- The manner in which subjects are approached for participation in a study, if in person;
- The manner in which the subject is approached and/or contacted for the duration of the study;
- Setting of the research;
- Who obtains consent;
- Provision to address any privacy requests and/or complaints made by the subject during the study;
- Provisions to limit non-study personnel’s knowledge of subject’s participation in research study.

Researchers should respect an individual’s desire not to be approached, or to be approached in alternate ways, if so expressed. Research staff must not search medical records to which they ordinarily would not have clinical access; this constitutes a breach of privacy as well as confidentiality of the patient’s medical record. Similar concerns arise with any search of a database conducted to identify potential participants.

The IRB will also consider how screening data is handled by the investigator. Retention of this data without consent of the subject represents a potential breach of privacy that may be particularly egregious if the potential subject declines to participate in the study or does not qualify for the research. The FDA has addressed the issue of privacy and confidentiality during the screening process (FDA Information Sheet, Recruiting Study Subjects).
Furthermore, the IRB must be cognizant of the potential for sponsors and contract research organizations to create databases of potential subjects based on recruitment procedure(s), and provide, where possible, regulatory oversight of the process.

If relevant, the IRB also may consider the following privacy issues:

- What happens to the personal information obtained by phone if the caller ends the interview or hangs up?
- Are the data being gathered by a marketing company; if so are identifiers etc. being sold?
- Are names of non-eligible individuals being maintained in case they qualify for another study?
- Are paper copies of the records shredded or are readable copies put out as trash?

The acceptability of the procedures would depend on the sensitivity of the data gathered. For particularly sensitive information the IRB may require the investigator to obtain a Federal Certificate of Confidentiality (OHR Guidance Document, G 607).

5.3. The IRB and the Sponsor:

The FDA requires sponsors, or research monitors hired by the sponsor, to monitor the study for accuracy of data submitted to the FDA in accordance with regulatory requirements. Sponsors and monitors will only be provided with records directly pertaining to the study specific data and its verification, as determined by the Principal Investigator. These records will be printed and the PHI redacted before the records are provided. Sponsors and monitors may not have access to or view the electronic medical record (eMR). It is important that the investigator and/or the research coordinator inform the subject during the consent interview of the extent to which confidential records and PHI identifying the subject will be maintained and that, under law, the FDA may inspect the records.

The IRB must ensure that the information required in the HIPAA Privacy Statement has been completed in the investigator-submitted OHR generic consent form (OHR-8).
5.3.1. Privacy and Confidentiality Issues During Waiver of Documentation of Informed Consent:
The IRB must consider privacy and confidentiality in its analysis of the criteria to be met in order to allow research without the consent of the subjects. The IRB must determine whether the research represents minimal risk to the subjects and does not adversely affect the privacy of the subjects and/or confidentiality of subject data. Some research that represents no physical risk may still represent risk because of potential breaches of confidentiality as in the case of genetic research. This type of risk of harm is more likely if the research records are kept with the medical records, where employers or insurers could accidentally or intentionally have access.

5.3.2. Confidentiality of Information During IRB Review:
IRB members must be sensitive to the actions taken by the Board as well as the deliberations conducted during the review of protocols at each meeting. Although many of the issues discussed are not considered confidential, all members should exercise a degree of discretion (Policy GA 123).

5.3.3. Confidentiality Issues Within OHR:
OHR personnel should be sensitive to all information submitted to OHR, in particular, proprietary information submitted as part of a commercially sponsored clinical trial or a grant submitted to a federal or other agency, and PHI that might, of necessity, be included in the IRB file for the study.
1. **Purpose**
   To provide guidance to investigators regarding ordering, receipt, use, storage, securing and return or disposal of devices used in IRB approved human research conducted on TJUH premises.

2. **Application**
   This policy applies to all medical research devices used or implanted on TJUH premises as part of an IRB-approved research study.

3. **Definitions**
   3.1. **Investigational New Device**: A device permitted by the FDA to be tested in humans but not yet determined to be safe and effective for a specified use in humans and not yet licensed for marketing. This includes devices already approved for indications other than the one(s) under investigation. Even a device subject to 510(k) remains "investigational" until the 510(k) is cleared by FDA and the investigational use is subject to the requirements of the IDE regulation, informed consent and IRB review (21 CFR 812, 50 and 56, respectively).

   3.2. **Investigational Device Exemption (IDE)**: Exemptions from certain regulations found in the Federal Food Drug and Cosmetic Act that allows shipment of unapproved devices for use in clinical investigations. These investigations collect safety and efficacy data required to support a Premarket Approval application or a Premarket Notification [501(k)] submission to the FDA. All clinical evaluations of investigational devices must be approved by the IRB and, unless determined by the IRB to be “nonsignificant risk,” have an approved IDE before study is initiated.

   3.3. **Sponsor-investigator**: An investigator who has been granted an IDE# by the FDA.

   3.4. **TJUH Premises**: TJUH Premises means any facility owned, operated, or controlled by TJUH as defined by Medicare.

4. **Introduction**
   Medical devices used in human research are classified into one of two categories, significant risk devices and non-significant risk devices (see OHR Policy SC 501: “Policy and Procedure to Determine Whether a Device Study Involves a Significant Risk or Nonsignificant Risk Device”).

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Significant Risk (SR) Devices are defined in, and their use in human subjects research is governed by, regulations at 21 CFR 812.

The majority of significant risk devices involves an invasive procedure for implantation or use, and, as such, is managed by the administration of the TJUH operating room where these procedures are performed.

Non-significant risk (NSR) devices do not require invasive procedures for use, so it is appropriate that device accountability may be managed by the clinical research principal investigator (PI). The PI is responsible for maintaining a tracking record of device use by completing the device tracking form (OHR-21 found at http://www.jefferson.edu/ohr/irb/forms/) and incorporating the form into the study file. NSR device use is governed by abbreviated requirements at 21 CFR 812.2(b).

5. Review, Approval and Ordering Process
All device research involving humans, whether the device is deemed SR or NSR, must be approved by a TJU IRB prior to study initiation. IRB approval will not be granted if Part C, questions 11-21, of the OHR-2 is not satisfactorily completed. The OHR-2 must include information on and documentation of any required training of the PI or Co-Is in the use of the device and what individual or entity will certify competency of the investigators in device use and adherence to applicable regulations.

In addition, approval of all devices, equipment and supplies ordered through Supply Chain Management and used on TJU premises must be requested using the Value Analysis process defined in TJUH Policy 108.11, “Value Analysis Committee - Product Request Process”. Use of these research devices is not permitted until such approval is granted, regardless of the status of the trial within or outside of Jefferson.

Once approvals have been obtained, a Request to Purchase (RTP) is submitted to Supply Chain Management. The Purchase order, completed by the research coordinator/PI in conjunction with Perioperative Materials Management Services, should either reflect cost of $00.00 if the device is being supplied by the manufacturer/sponsor or a specific cost (per patient or aggregate).

Devices that are delivered directly to the PI by the manufacturer must be labeled as indicated below (Section 6.) and tracked using the OHR-21 form.

6. Receipt, Storage and Return of Devices
Research devices delivered to the OR, relevant satellite unit (such as the GI endoscopy suite, CVIR, etc.), or, when appropriate, directly to the investigator by the manufacturer must be clearly labeled “For Research Use Only” and placed in secure storage. Secure storage access must be restricted to members of the research team.
In addition to the “For Research Use Only” designation on the device package, the following information must appear on the device package label:

- Device Manufacturer
- Catalog or Part Number
- Description of the device
- IRB Control number and study title
- Name of the intended patient (if known)

At the end of the study, any unused/unopened devices should be returned, according to manufacturer instructions, to the manufacturer by the research coordinator.

7. Tracking
Manufacturers are responsible for device tracking in clinical trials where the manufacturer holds the IDE. Locally, tracking should be done using the device tracking website accessed through a link on the OHR home page, http://www.jefferson.edu/human_research/irb/index.cfm.

8. References
21 CFR 812
TJUH Policy 108.11, “Value Analysis Committee - Product Request Process”
1. **Purpose**
   To define the Thomas Jefferson University (TJU) Human Research Protection Program (HRPP).

2. **Application**
   This policy applies to all human subjects research conducted at TJU.

3. **Thomas Jefferson University’s Human Research Protection Program (HRPP)**
   The TJU Human Research Protection Program (HRPP) is the network of Offices and personnel at Thomas Jefferson University and Thomas Jefferson University Hospital, Inc., that work together to uphold the protection of human subjects in research at these institutions. Each stakeholder in the HRPP contributes its own area of expertise to the overall goal of protection.

The major stakeholders are as follows:

3.1. **The Office of Human Research (OHR)** is the core of Jefferson’s HRPP. The OHR provides administrative support for the three TJU Institutional Review Boards (IRBs). The OHR accepts submissions for IRB review, creates IRB meeting agendas, distributes submitted materials to reviewers and maintains the clinical trials repository. The OHR ensures that the IRBs review clinical research activities in compliance with all applicable regulations and policies. The OHR Quality Assurance and Improvement team conducts for cause and not-for-cause audits, performs consent observation and audits OHR/IRB functions on a regular basis.

The OHR is in the Jefferson corporate structure. The Associate Provost for Research Support Services (APRSS) has general oversight responsibilities for the OHR. The Director of OHR reports to the APRSS at weekly meetings or on an *ad hoc* basis. The APRSS reports directly to the University Provost.

3.2. **The Office of Research Administration (ORA)** assists researchers in applying for and managing sponsored funding. The ORA serves as the official point of contact for the various sponsors of scientific and scholarly activity including human subjects research and manages all sponsored projects in accordance with sponsor regulations and Jefferson policies. ORA consults with OHR regularly concerning subcontracts involving human subjects research, compensation to research participants in case of research-related injury, Medicare coverage analysis for clinical trials and other human research-related issues. The ORA also provides education and other resources to support the management of sponsored programs.
ORA coordinates and collaborates with the OHR during and after contract negotiation and execution to ensure that the study will be conducted in a manner consistent with good clinical practices, the Statement of Investigator Form 1572 signed by the Principal Investigator and on file with the sponsor; and all other applicable local, state and federal rules, laws and regulations, including without limitation privacy regulations promulgated pursuant to the Health Insurance Portability and Accountability Act or 1996 (HIPAA). While both OHR and ORA recommend commencement of the IRB and ORA processes simultaneously, a sponsored study may not be initiated and study drug/device will not be shipped prior to final IRB approval.

3.3. The Office of University Counsel maintains all TJU policies including those on Conflicts of Interest (COI) for employees, COI for the Board of Trustees, HIPAA, and Noncompliance with human subjects regulations. Counsel is a voting member of the three TJU IRBs and provides information regarding COI and local and federal law, when applicable, to the convened boards. Counsel is also involved in the review of existing IRB policies and procedures and in the writing of new Policies and Procedures.

3.4. The Investigational Drug Service (IDS) in the Department of Pharmacy, Thomas Jefferson University Hospital, reviews all in-patient clinical research protocols involving drugs and dispenses all research-related drugs used in in-patient clinical trials and in numerous out-patient clinical trials. Members of the IDS serve as voting members on all Jefferson IRBs.

3.5. The Office of Animal Resources (OAR) oversees animal protocols, including those that use tissue from living human beings, and does not permit initiation of such research without documentation of IRB approval.

3.6. The Office of Radiation Safety (ORS) through the Radiation Safety Committee reviews all protocols in which radiation greater than that used in usual clinical practice is employed. The Director of the ORS communicates all Radiation Safety Committee decisions that involve human subjects in research to the OHR.

3.7. The Conflict of Interest Committee (COIC) reviews all financial conflicts of interest for TJU faculty, including those pertaining to investigators involved in the conduct of human subjects research. The COIC works with the IRB to determine the best route to managing conflicts of interest for these investigators.

3.8. Other Offices and individuals including:
   - The Provost of Thomas Jefferson University ensures that there are adequate resources to support the goals of the HRPP
The Associate Provost for Research Support Services (APRSS) is the Senior Officer with oversight responsibility for research, research integrity and science policy. The APRSS is the Institutional Official (IO) for the HRPP and in that role answers directly to the Provost who in turn answers to the President.

The Clinical Trials Office (CTO) provides administrative and research coordinator support for oncology studies conducted by the Kimmel Cancer Center.

The Kimmel Cancer Center Protocol Review Committee (PRC) reviews all oncology studies for science and merit prior to IRB review.

The Jefferson Clinical Research Institute (JCRI) provides administrative and research, regulatory and clinical coordinator support for investigators on an as needed basis and conducts educational activities for researchers and research staff. The JCRI supports the Jefferson Clinical Research Forum (JCRF) and the Leadership Counsel of Clinical Coordinators (LCCC).

All of the personnel and entities involved in the HRPP make a valuable contribution towards the goal of ensuring that the protection of human subjects is held to the highest ethical standards at Thomas Jefferson University and Thomas Jefferson University Hospital, Inc.

4. Responsibility of the Offices and Personnel involved in the HRPP
The Director of OHR, the APRSS and the Director of Research Planning meet yearly, or as needed, to evaluate resources including but not limited to:

- Space requirements
- Personnel
- HRPP education program
- Legal counsel needs
- Conflict of interest
- Quality improvement plan
- Community outreach
- IRB functions and needs
All offices and personnel that are part of the HRPP are mandated by the TJU Code of Conduct to uphold and abide by all relevant federal and local regulations and laws and to conduct their activities in accordance with the highest ethical standards.

5. References
TJU Policy 107.02: Code of Conduct
1. **Purpose**
   The purpose of this policy is to explain training requirements for new IRB members and for investigators and key personnel involved in the conduct of human subjects research.

2. **Responsibility for Executing the Policy**
   Director/Associate Director, OHR
   OHR Staff

3. **Policy Statement**
   All IRB members are required to be trained in human subjects research and have an understanding of the federal and local regulations governing such research.

   All investigators and key personnel must complete required human research training that is administered by OHR prior to their involvement in the conduct of human research. Training status will be checked for all study personnel upon receipt of new study and continuing review submissions. If training is not complete for all personnel named on study, PI will be notified, and study will be held in suspension and will not be distributed for IRB review until training requirements are satisfied.

   Training is on-line and is accessible from the OHR homepage.

   Training requirements outlined below apply whether TJU personnel are engaged in research reviewed by a TJU IRB or a designated non-TJU IRB.

   For non-Jefferson personnel, OHR has the option of accepting certification of training that is comparable to that which is described in this policy.

4. **Policy Specifics**
   TJU uses the Collaborative Institutional Training Initiative (CITI), hosted by the University of Miami. CITI allows institutions to design training courses to their own specifications. The TJU OHR requires that all research personnel must complete human subjects research training in either the Biomedical or Sociobehavioral research track prior to their involvement in the conduct of human subjects research.
   
   - Biomedical Research Certification training modules and the separate set of modules on Good Clinical Practice are to be completed one time only.
   
   - Sociobehavioral Research Certification training modules are to be completed one time only
• To maintain either Biomedical or Sociobehavioral research certification, research personnel must complete a refresher course of selected training modules in the appropriate field every 2 years.

• For new personnel, documented CITI or other training in human subjects research will be accepted by the TJU IRB at the discretion of the Director or Associate Director, Office of Human Research. For those individuals, refresher course requirements will begin 2 years from date of their having completed the initial training requirements.

• New IRB members are required to complete the CITI modules for IRB Members even if they have completed the required Biomedical or Sociobehavioral initial training modules required in their research role(s). Refresher courses are not required for IRB members. IRB members who are involved in human subjects research must maintain their certification as noted above.

Jefferson personnel who took CITI training elsewhere should log on to www.citiprogram.org and change their registration to Jefferson in order to receive automated e-mail notifications of training due.
1. **Purpose**
   To establish a policy and procedure that will ensure that the membership of the University’s IRBs conforms to the requirements of 45 CFR Part 46.107(c) and 21 CFR 56.107(c).

2. **Responsibility for Executing the Policy**
   Director/Associate Director, OHR

3. **Policy Statement**
   The membership of the IRB will meet or exceed the requirements of [45 CFR Part 46.107(c)]. Each IRB will be comprised, at a minimum, of one or more non-scientist member(s) of varying backgrounds and experience, one or more unaffiliated non-scientist community member(s), and one or more faculty with expertise in medicine, basic science, and behavioral science.
   
   Appointments to each of the IRBs will be made in a way to ensure an appropriate mix of gender, race and cultural backgrounds to allow for appropriate and fair review of research activities commonly conducted at the University.

4. **Procedures**
   Scientist/physician members of the IRB usually have formal appointments in one of the colleges of the University. Each IRB shall also have as a voting member one or more PharmDs and/or clinical pharmacologists. For PharmDs and clinical pharmacologists preparing and dispensing a study drug does not constitute a COI. Nurses may serve as scientific members depending on their expertise and experience.
   
   Non-scientist members may or may not be affiliated with TJU or TJUH. Unaffiliated members may be non-scientists or scientists. TJU Board Secretaries are appointed as non-scientist voting members.
   
   Unaffiliated members by definition may not be affiliated with the University nor have a family member (1st degree relative) who is affiliated with TJU. These members are tasked with representing the views and attitudes of the community at large. Such members may be assigned as primary reviewers depending on the nature of the protocol and their experience or training. Unaffiliated members are expected to attend at least 50% of meetings yearly. If that expectation is not met, the Director, OHR or the Chair will meet with the individual to discuss ways to improve attendance.
Each IRB shall have access to a legal representative from the TJU Office of University Counsel who is knowledgeable about University commitments, federal and state regulations, standards of professional conduct and conflict of interest on the part of investigators, key personnel and IRB members. Counsel may be appointed as a voting or alternate member and attend the meetings as situations dictate. Counsel may count as either a scientist or non-scientist as per training or degrees.

The Director and Associate Director of the OHR shall be voting members of all IRBs. In the absence of the Chair of an IRB, the Vice Chair, or the Director/Associate Director, OHR will chair the meeting.

5. **Needs Assessments**
   Immediate needs regarding IRB membership or a requirement for a consultant are addressed at the bi-weekly reviewer assignment meetings of the Chair(s), Vice Chairs(s), Director, and Associate Director. The number of protocols to be reviewed, distribution of work load for the IRBs, the adequacy of the rosters and the time available to perform adequate reviews is also discussed at these meetings.
1. **Purpose**
   To establish an IRB that conforms to federal regulations for IRB membership as stated in 45 CFR Part 46.107, IRB membership, and 21 CFR Part 56.107.

2. **Responsibility for Executing the Policy**
   - Director/Associate Director
   - IRB Chair(s)
   - Associate Provost for Research Support Services

3. **Policy Statement**
   This policy stipulates the requirements for an IRB Chair and the following categories of IRB members for membership on one of the University's IRBs: Affiliated scientist/non-scientist members; unaffiliated community members; and alternate members. The Policy delineates the procedures by which such members are recruited, appointed and evaluated in their duties on the IRB.

   Appointment to each of the IRBs will be made on the basis of expertise and experience with an aim to maintain an appropriate balance of gender, race and ethnicity to allow for complete and adequate review of research activities commonly conducted at the University. Qualifications for IRB membership are outlined in OHR Policy OP 201.

4. **Procedures**
   4.1. Recruitment and Appointment of IRB Members
      4.1.1. **TJU/TJUH Scientist/Non-Scientist Members**: Potential IRB members in this category will be solicited by the Director and/or, Associate Director, OHR and/or the IRB Chairs. The appointment will be made, as appropriate, by the Director, OHR.

      The expertise and experience of a prospective candidate for IRB membership will be reviewed by the Director, OHR, and the Chair of the IRB to which the individual will be appointed. The individual will meet with the Director, OHR to discuss the responsibilities of IRB membership. New appointees are required to complete the Collaborative Institutional Training Initiative (CITI) training or equivalent on-line course for IRB members even if they have previously completed CITI training for investigators.

      Potential Board members who are TJU/TJUH employees are expected to inform their Department chairs or directors of the pending appointment.
4.1.2. Unaffiliated Community Members: Every effort will be made by the Director and/or Associate Director of OHR and the IRB Chairs to recruit individuals from the community who are not affiliated with the University or Hospital and whose family members are not affiliated. The same procedures will be followed in reviewing qualifications and training the community member.

4.1.3. Alternate Members: Alternate members may be recruited and their qualifications reviewed as described above for primary IRB members. The alternate member will have comparable qualifications to those of the primary member for whom s/he serves as alternate. The alternate member is formally appointed to the Board and is listed on the roster as a substitute for the primary IRB member with voting privilege. The IRB roster will present the required information about the alternate member in the same way as for the primary member. The IRB minutes shall document when an alternate member replaces a primary member. The alternate member shall receive and review the same material that is given to the primary member.

Maintaining OHRP approval of rosters: A designated OHR/OHR staff member will report all changes in IRB rosters to OHRP. As required by OHRP, scientist/non-scientist designation and affiliation status are indicated for each member. Changes in IRB membership will be reported to OHRP as they occur.

4.2. Recruitment and Appointment of an IRB Chair
The IRB Chair will be selected from those current or past members of an IRB who have had significant experience in IRB issues and in the operation of a convened IRB meeting. The IRB chairs will be selected and appointed by the Director of the OHR in consultation with the Associate Director, OHR and the Associate Provost for Research Support Services.

4.2.1. Responsibilities of an IRB Chair: The Chair is expected to have an in-depth understanding of the ethical principles of the Belmont Report, the Declaration of Helsinki, and the policies and procedures employed by the TJU IRB. S/he is expected to have a working knowledge of the federal rules and regulations that govern human subjects research. These are found in the Code of Federal Regulations (45 CFR 46, 21 CFR 50, and 21 CFR 56).

4.2.2. The IRB Chair will:

- Direct the full committee meetings and strive to keep the discussion of protocols focused on substantive issues.
- Vote on protocols unless a conflict of interest exists.

- Work with the Director and Associate Director, OHR in establishing, implementing and monitoring compliance with IRB policy.

- Will assign, in conjunction with the Director and Associate Director, OHR, two IRB members as principal reviewers for new protocols and one primary reviewer for continuing review and amendments that require full board attention. The assignments are based on the expertise of the reviewers.

- Review all protocols submitted and is expected to contribute to the evaluation of a study with respect to risk, scientific and statistical merit, and standards of medical or surgical practice.

- Evaluate the performance of each member, including the vice chair, on an ongoing basis.

- Communicate with members to resolve important issues prior to meetings of the convened committee.

- Assist OHR administrative personnel in the drafting of IRB correspondence to researchers regarding IRB decisions.

- If so delegated by the Director, OHR, review and sign IRB correspondence in a timely fashion.

- Serve as a reviewer for research that qualifies for an expedited process. The Director and Associate Director, and other designated IRB voting members may also conduct expedited reviews as appropriate.

- Represent the IRB in defending or discussing IRB decisions with researchers. In consultation with the Director or Associate Director, OHR, be empowered to suspend the conduct of a research project or clinical trial, pending IRB review, if he/she deems that subjects are placed at unacceptable risk or if he/she determines that an investigator is not following the IRBs policies or procedures.

4.2.3. At the discretion of the Director, OHR, the Chair:

- May be asked to represent the IRB in discussions with other offices at Thomas Jefferson University / Thomas Jefferson University Hospital including the Methodist Hospital Division.
• May be asked to represent the IRB in discussions with federal authorities.

4.3. Recruitment and Appointment of an IRB Vice Chair

The IRB Vice Chair will be selected from those current or past members of an IRB who have had significant experience in IRB issues. The IRB Vice Chairs will be selected and appointed by the Director of the OHR in consultation with the Associate Director, OHR, IRB Chair and the Associate Provost for Research Support Services.

4.3.1. The Vice Chair’s duties are as follows:

• Chair the Board meeting in the absence of the Chair

• At the discretion of the Director/Associate Director, assume additional duties of the Chair in the absence of the Chair

• Serve as a 4th reviewer for all new protocols (two Board members, Chair and Vice Chair)

• Attend protocol review assignment meetings

• Review Final and Expedited transactions as assigned

• Evaluate the performance of each member on an ongoing basis.

4.4. Evaluation of Member Performance

IRB Member performance and membership needs are assessed on an ongoing basis at the IRB reviewer assignment meetings of the Chairs, Vice Chairs and Director/Associate Director. The Director, Associate Director, or Chair/Vice Chair will meet with any member upon request who wants to discuss their own performance, the performance of a Chair or Vice Chair or any IRB related issue.

Individual IRB member performance is also formally assessed once a year on a rotating basis at the reviewer assignment meetings (one or two members at each meeting) by the following criteria:

• Meeting attendance record

• Quality of reviews

• Meeting Participation

Feedback to the member is provided by the Director/Associate Director, OHR or Chair/Vice Chair of the relevant Board and the evaluation form is kept on file in the office of the Director, OHR.
The Chairs and Vice Chairs are also evaluated on an on-going basis at the IRB reviewer assignment meetings with the Director and Associate Director. There is ample time at these meetings to discuss any general Board issues or specific issues related to the conduct of Board meetings. Chairs and Vice Chairs are also evaluated by the Director and Associate Director through observation of how full Board meetings are conducted. The Director and Associate Director are voting members of all TJU Boards and attend meetings regularly.

To monitor effectiveness, evaluations will be periodically re-visited to assess whether IRB members have taken steps to improve performance as necessary. Lack of improvement may warrant a follow-up evaluation.

5. References
   IRB Member Evaluation Form
1. **Purpose**
   To establish a procedure under 45 CFR, Part 46 107(f) to allow the OHR to invite individuals with competence in special areas to serve as consultants for the review of a particular study or issue(s) which require expertise beyond that available on the reviewing IRB.

2. **Responsibility for Executing the Policy**
   Director and Associate Director, OHR and IRB Chair: Selection of consultant.  
   Director and Associate Director, OHR and IRB Chairs: Assignment of reviewers and assessment of appropriate expertise for review of research protocols.  
   IRB Chairs: Communication of the use of a consultant(s) to the IRB members.  
   Consultant: Review of research protocol and submission of a written report to the IRB at or prior to the meeting.

3. **Policy Statement**
   In accordance with 45 CFR Part 46.107 (f), the Director or Associate Director, OHR, in their discretion, and in consultation with the IRB Chair, may invite an individual with expertise in the area of special need to serve as a consultant for the particular study.

4. **Procedures**
   At the time of the assignment of reviewers, the Director, Associate Director, OHR and the Chair of the IRB will evaluate each research proposal to decide whether there will be appropriate expertise available from the IRB members who will be in attendance. If that is not the case, the Director will invite a consultant with expertise in the appropriate research area to be a reviewer.

   The Associate Director, and/or Director, OHR, in consultation with the IRB Chair will determine the individual to be invited as consulting reviewer. The Administrative Secretary of the IRB will provide the appropriate study-related material to the consultant. The consultant will provide an in-depth written review of the study that may be delivered by the consultant at the convened meeting of the IRB or read in the consultant’s absence by the IRB Chair. Pertinent comments/information will be incorporated into the minutes. The consultant cannot vote on the study but if attending the meeting may participate in the discussion.

   A consultant may be drawn from the membership of any of the IRBs, from Thomas Jefferson University faculty or from individuals outside of the institution who have appropriate expertise.
Consultants who are TJU faculty but not IRB members must sign a confidentiality agreement and provide the IRB with a conflict of interest disclosure as per TJU Policy 107.03, “Conflicts of Interest Policy for Employees” (see COI Disclosure for IRB Consultants from the forms section of the OHR website), and such disclosure must indicate that they have no conflict of interest pertaining to the study they have been asked to review. Consultants who are not TJU faculty will be asked to sign a confidentiality agreement, and provide a COI Disclosure and their Curriculum Vitae. Any prospective consultant with a conflict of interest will not be engaged for such reviews.

IRB consultants with a conflict of interest:

- Are excluded from discussion except to provide information requested by the IRB.
- Leave the meeting room for discussion and voting.
- Are not counted toward quorum.

The IRB Chair will inform the IRB members at the convened meeting of the Board that a consultant has reviewed the study and either the consultant or the IRB Chair will present the review.

5. **Tools**

COI Disclosure Form for IRB Consultants (See Forms section of OHR website)
1. **Purpose**
   To establish the authority and composition of the IRB, and to describe the procedure for review and approval of an IRB submission.

2. **Responsibility for Executing the Policy**
   Director/Associate Director, OHR

3. **Policy Statement**
   The IRB is a University standing committee empowered to protect the rights and welfare of human research subjects recruited to participate in research activities conducted under the auspices of the Institution. The IRB has full authority to approve, require modifications in, disapprove, terminate or suspend all research activities that fall within its jurisdiction as specified by both the federal regulations and local institutional policy.

   As specified in 45 CFR, Part 46.107(c) and 21CFR 56.107(c), IRB membership, each IRB shall consist of one or more nonscientist members, one or more unaffiliated lay members, and one or more faculty in each of the areas of medicine/basic science/behavioral science where it is anticipated that protocols will be submitted such that the IRB will qualify for an unrestricted reviewing status from OHRP. Each IRB shall have as a member one or more PharmD's. Generally, appointment to the IRB is for a three-year term. A member may be re-appointed. All appointed members of TJU IRBs are voting members.

4. **Procedures**
   A week prior to the IRB meeting, the Director, Associate Director, OHR, and the Chair and Vice Chair will meet and assign reviewers to all new studies, amendments and continuing reviews requiring full board review. Two primary reviewers are assigned for new studies, and one primary reviewer is assigned to each continuing review and amendment. Reviewers are chosen based on scholarly or scientific expertise and IRB experience. Reviewers are expected to conduct an in-depth review of the study based on completion of a reviewer questionnaire.

   If appropriate expertise is not available on the Board, the study may be assigned to a primary reviewer with appropriate expertise from one of the other on-campus IRBs, or to an appropriate consultant as stipulated in Policy OP 203, *Use of Consultants for Review of Studies*. 
Documents pertaining to studies (initial review, continuing review and modification to approved studies) requiring review by the convened IRB are available on the IRB electronic submission portal one week prior to the relevant convened meeting. Members who are not able to access the materials electronically are sent the relevant documents by overnight express one week prior to the IRB meeting. Documents for studies that qualify for expedited review are also available on the electronic submission portal one week prior to the relevant IRB meeting.

5. Tools
   Policy OP 203, *Use of Consultants for Review of Studies*
1. Purpose
This policy defines the duties required of the IRB member

2. Responsibility for Executing the Policy
Associate Provost for Research Support Services
Director/Associate Director, OHR
IRB Chair/Vice Chair

3. Policy Statement
The primary duty of each IRB member is to review human subjects research applications with the purpose of assessing whether they are ethically and scientifically sound with regard to the participation of human subjects. The IRB member is expected to be knowledgeable about regulations governing human subjects protection, biomedical and behavioral research ethics and the Thomas Jefferson University policies governing human subjects research. The individual IRB member, as well as the convened IRB, must be, and must be perceived to be, fair and impartial in its deliberations, and immune from pressure either by the University’s administration, the investigator whose study is being reviewed or from other professional and nonprofessional sources.

4. Policy Specifics
4.1. Duty to the University
The IRBs are appointed as University Committees. As such, the IRB members serve the University as a whole. Therefore, members must not allow their own interests or that of their departments to supersede their duty to protect the rights and welfare of research subjects.

4.2. Term of Duty
In so far as possible, IRB members and chairpersons are expected to commit to a 3-year-term and during that time, fulfill certain duties. These duties will be described prior to appointment. Each IRB member is expected to fully understand the duties of an IRB member prior to accepting appointment as an IRB member.

4.3. Specific Duties
4.3.1. Regular Members:
4.3.1.1. **Unaffiliated Members:** Unaffiliated members provide input regarding their knowledge about the local community and discuss issues and research from that perspective. They also review the informed consent document from a nonscientist point of view.

4.3.1.2. **Non-Scientist Members:** Nonscientist members are expected to provide input on areas germane to their knowledge, expertise and experience, professional and otherwise. For example, the Assistant University Counsel member of the IRB should present the legal view of specific areas that may be discussed, such as exculpatory language or state requirements regarding consent. Nonscientist members should advise the Board when additional expertise in a nonscientific area is required to assess whether the protocol adequately protects the rights and welfare of subject, and to comment on whether the consent document is understandable.

4.3.1.3. **Scientist Members:** Scientist members are expected to contribute to the evaluation of a study on its scientific and statistical merits and standards of practice. These members should also be able to advise the Board whether additional expertise in a scientific or nonscientific area is required to determine whether the protocol adequately protects the rights and welfare of subjects.

4.3.1.4. **Chairperson:** In addition to the above responsibilities, germane to the member’s status, the chairpersons chair the meetings of the IRB. The Chairpersons perform, or delegate to an appropriate voting Board member, authority to perform expedited review when appropriate. The chairperson is empowered to suspend the conduct of a research project or clinical trial deemed to place individuals at unacceptable risk pending IRB review. The chairperson is also empowered, pending IRB review, to suspend the conduct of a study if he/she determines that an investigator is not following the IRBs policies or procedures.

If the Chair cannot attend, or must leave a convened meeting, the Vice Chair, or the Associate Director of the Office of Human Research or another qualified individual will be appointed as the interim chair.
4.3.2. **Primary Reviewers:** In addition to the duties described in section 4.3.1, each regular member will be expected to act as a primary reviewer for assigned studies at convened meetings. The primary reviewer presents his or her findings resulting from review of the application materials and provides an assessment of the soundness and safety of the protocol and recommends specific actions to the Board. He or she leads the discussion of the study by the convened IRB. The primary reviewer is required to review the entire protocol submission, and to provide a written report in the form of a completed questionnaire for reviewers entitled, *RQ-1 IRB Reviewer Questionnaire* (Version 4/2008).
1. Purpose
The policy herein provides the framework to ensure that IRB meetings are conducted and documented in a manner consistent with federal and institutional policies.

2. Responsibility for Executing the Policy
Director/Associate Director, OHR
IRB Chair/Vice Chair

3. Policy Statement
Except when an expedited or exempt review procedure is used, the IRB will review proposed research at a convened meeting at which a quorum is present. Each IRB will meet biweekly except when the month contains a fifth week (45 CFR.103 (b) (4); 46.108).

4. Policy Specifics
4.1. Applications for review will be checked by OHR staff for inclusion of all relevant forms and IRB and HIPAA training status for all participating personnel listed on the proposal transmittal form. Incomplete applications or those with personnel who are not current regarding training will not be accepted or distributed for review.

4.2. IRB meetings and Materials Sent to Members Prior to the Board Meeting: Each IRB will meet biweekly except when the month contains a fifth week. Yearly schedules for each IRB will be published and distributed to all IRB members and will be posted on the IRB website. All materials for review are available on the IRB electronic submission portal one week prior to the relevant convened meeting. Members who are not able to access the materials electronically are sent the relevant documents by express mail one week prior to the convened meeting. It is expected that all IRB members will review all provided materials in enough depth to be able to discuss the information at the convened meeting. A member wishing to obtain additional materials provided to the primary reviewer(s) may request that information from the administrative secretary of that IRB.

Documents provided to all IRB members include:
- Meeting agenda,
- The OHR-1 Transmittal form,
- The OHR-2 Protocol Summary,
• Proposed informed consent document,

• Continuing review/renewal material,

• Any amendments,

• Other pertinent documents such as questionnaires and recruiting advertisements.

Primary reviewers will receive the above items plus:

• The complete protocol (new and renewal applications),

• A copy of the NCI generic consent document for CIRB oncology studies,

• The Investigator Brochure for studies involving an investigational drug or biologic and/or any information pertaining to an investigational device,

• Copy of any federal or other grant application including DHHS approved sample consent form and DHHS-approved protocol.

For review using the expedited procedure, the primary reviewer will receive all of the information that a primary reviewer receives for a protocol reviewed at a convened meeting.

4.3. Primary Reviewers:
Primary reviewer(s) are assigned to provide in-depth review of new studies, continuing reviews, and amendments by completing the appropriate reviewer questionnaire and presenting the study to the committee. In general, two IRB members are assigned to each new study, one to each continuing review, and one to each amendment. This number may be increased as necessary to add additional expertise to the review (Policy OP 204).

4.4. Quorum:
A meeting cannot be convened until a quorum has been achieved. A quorum is defined as the presence of greater than half of the total voting members of a Board. For example, if the Board’s voting membership is 14, the quorum necessary to convene a meeting would be 8. If that same Board’s voting membership is 15, the quorum would still be 8. The Board Secretary determines that quorum is met and the quorum number is documented in the meeting minutes.

Furthermore:
A quorum consists of regular and/or alternate members and must include at least one member whose primary concerns are in scientific areas and one non-scientist voting member who represents the general perspective of research subjects. The non-scientist contributes to quorum and may be either an affiliated or non-affiliated member. Also see Policy OP 201, IRB Membership.

When FDA-regulated research is reviewed, one member who is a physician must be present.

An alternate member may attend in place of an absent regular member in order to fulfill the quorum requirements. The alternate member must be listed on the OHRP- approved roster as the alternate for that member.

The presence of a consultant may not be added towards a quorum.

If a quorum is temporarily lost during a meeting, no further votes can be taken until it is regained.

If a quorum is permanently lost during a meeting, the meeting will be adjourned.

When the convened IRB reviews research involving prisoners, the prisoner advocate/representative is present.

If the IRB reviews research that involves categories of participants vulnerable to coercion or undue influence, one or more individuals who are knowledgeable about or experienced in working with such participants is present.

4.5. Meeting Minutes:
The OHR administrative staff assigned to the Board, or a designee, will take the minutes of each meeting. The minutes will document the following items:

- The order in which the submissions were reviewed;
- Actions taken by the IRB with;
- Separate deliberations for each action;
- Meeting attendance, including status of any attendee who is not a regular member (alternate, consultant), and any conflicts of interest. When an alternate member replaces a primary member;
- Status of members (scientist, non-scientist, non-affiliated);
• Votes for each protocol as numbers for, against, and abstaining;

• Who is absent during the vote, and explanation of any conflicts that require the absence;

• The basis for requiring changes in the research;

• The basis for disapproving the research;

• Summary of the discussion of controverted issues and their resolution;

• For initial and continuing review, the approval period if it is not one year;

• References to federal regulations that justify the determinations for:
  o Waiver or alteration of the consent process (not required for exempt studies);
  o Research involving pregnant women, human fetuses and neonates;
  o Research involving prisoners;
  o Research involving children;

• Information regarding the risk determination for research involving devices;

• References to the rationale for the determination that a device poses significant or non-significant risk;

• If the research involves persons with impaired decision-making and/or adults unable to consent, the appropriate regulatory criteria have been met;

• Names of members who leave the meeting because of a conflict of interest including conflict of interest as the reason for the absence.

An electronic copy of the final minutes will be retained on a secure server. In addition, the final minutes will be made available to Board members upon request. The minutes will be retained as described in Section 4.2 of Policy GA 121.

4.6. Voting

4.6.1. Conducting a Vote
Members of the IRB vote upon the recommendation of the primary reviewers according to the established criteria for approval stated above. Members will also determine the level of risk (minimal or greater than minimal), the length of the approval period (no greater than one year), and the necessity of monitoring of the investigative site. Unless otherwise determined by the members, the approval period will be one year. Approval periods less than one year will be noted in the minutes.

A majority greater than half of the voting members present must vote in favor of a motion in order for that motion to carry. Only regular members or alternate members attending the meeting in place of their assigned regular member may vote. Any member with a conflict of interest with the study must absent themselves from the room during deliberation and voting on the study and this absence must be indicated in the minutes. This would include any member who will be involved in the conduct of the study.

4.6.2. Motions for Voting

The IRB evaluates each proposal to determine if the criteria at 45 CFR 46.111 and other applicable regulatory requirements have been met. The IRB makes the decision to approve or not approved based on the “Guidance for IRB Voting Criteria” document. The IRB makes the following recommendations:

4.6.2.1 Approved

The IRB will recommend that a proposal is approved if no changes are requested or if the changes requested are consistent with those described in the “Motion to Approve” category of the “Guidance for IRB Voting Criteria” document. When this occurs, the requested changes will be reviewed by designated IRB personnel.

4.6.2.2 Not Approved

The IRB will recommend that a proposal is not approved if the changes requested are consistent with those described in the “Motion to Not Approve” category of the “Guidance for IRB Voting Criteria” document. When this occurs, the proposal must be revised, re-submitted in full, and reviewed by a convened IRB.

If the IRB does not have enough information to deliberate, the IRB may defer a vote. Once the necessary information is obtained, the study must be reviewed by a convened IRB.

In either case, the original reviewer(s) will be invited to provide comments as consultants if the study is subsequently reviewed by a different Board.
4.6.3. Reporting IRB Decisions to Researchers
See OHR Policy GA 113, section 4.

4.7. Telephone Use

4.7.1. Convened Meeting Using a Speakerphone:
If a member is unable to be physically present during a convened meeting, but is available by telephone, the meeting may be convened using a speakerphone where the absent member is in direct contact with the members present at the meeting. This will allow the member participating by speakerphone to participate in the discussion of the protocol and to cast a vote providing that this member has had an opportunity to review the materials reviewed by the members present at the meeting (OHRP Notice, March 28, 2000; FDA Information Sheets).

4.7.2. Meeting Conducted Via Telephone Conference Call:
On occasion, a meeting may be convened by telephone conference call, provided that quorum of members, as defined above, participates. All members must be connected simultaneously for a conference call to take place.

Members that do not participate in the conference call may not vote by proxy on the issues discussed.

4.8. Changes in IRB Membership
Changes in the membership of an IRB will be communicated to OHRP by the Director, OHR as described in Policy OP 202.
1. **Purpose**
   
   To establish a program of oversight of human research activities that is linked to the Continuing Review (CR) process.

   To develop a collegial relationship with clinical investigators and study coordinators to assist them in developing effective procedures to conduct and monitor all aspects of human subjects research and Good Clinical Practice.

   To create a culture within the University of a partnership between investigators and clinical coordinators and the Office of Human Research that embraces the principles of responsible conduct of clinical research.

2. **Responsibility for Executing the Policy**

   Director/Associate Director, OHR
   QA/QI Team

3. **Policy Statement**

   The program is structured as a quality assurance, education and improvement program coupled with CR rather than one of a strict audit and compliance program.

   Investigators and their staffs will be supported through consultation and education in order to: (1) augment and facilitate continuing reviews of ongoing clinical research with human subjects; (2) enhance protection for human subjects enrolled in that research; (3) insure compliance on the part of the investigators and their staffs with the ethical principles and regulations pertaining to human subjects research.

   The Quality Assurance Evaluation Form completed by both the Quality Assurance Team and the Principal Investigator/Study Coordinator will serve as the audit report, a format for the corrective action plan and as one of the OHR education/training initiatives.

   To this end, the activities of the Program will:
   
   - Provide the opportunity via site audits to evaluate the Human Research Protection Program as a whole.
   
   - Conduct routine quality assurance site visits, including, if appropriate, observation of the informed consent process, often but not always arranged around the time of CR for any given study.
   
   - Assist investigators and coordinators in conducting self-evaluation of their studies.
• Assist investigators in preparing their study sites for external audits.

• Provide consultation and educational materials for investigators and study coordinators.

• Provide a means to make improvements in good clinical practice and adherence to human subjects regulations by periodic review of quality assurance evaluations with Principal Investigators and research staff.

• Provide a means to assess and educate, when appropriate, community outreach activities at the time of annual review, if requested by the IRB or at any time if requested by the research staff or the steering committee.

• Conduct inspections and audits in response to allegations of non-compliance with human subjects regulation and/or inquiries or complaints received from research subjects, regulatory agencies or industrial sponsors.

4. Procedures

4.1. Not-For-Cause Audits

The Quality Assurance/Improvement Specialist or designee(s) will make random site visits of investigators conducting a diverse sampling of federally-sponsored, commercially-sponsored and internally-funded studies of greater than minimal risk, some of minimal risk and some that enroll vulnerable subjects. Particular attention will be paid to periodic review of internally-funded studies for which no external review is carried out.

Studies in the above categories will be selected and, after review of the study files the QA/QI Specialist will make an appointment with the Principal Investigator and Study Coordinator to review and discuss the study file and study operations.

The QA/QI form will serve as a basic guideline to determine whether:

• Study personnel have been submitted to the IRB;

• The information contained in the investigator study file is consistent with the information in the IRB study file;

• There are current and valid signed consent forms for all subjects;

• All CRs were submitted and approved in a timely manner;

• All changes to the protocol or consent form were IRB-approved amendment before implementation;
• Adverse event and unanticipated problem reports were submitted in a timely manner, and;

• Documentation of eligibility criteria has been maintained;

• Proper procedures for data confidentiality and security have been followed.

All completed QA/QI reports will be reviewed with the Director/Associate Director, OHR.

The report, which will contain descriptions of any noncompliance issues will be delivered to the investigator for his/her signature. If any compliance issues that are not serious or continuing have been identified, a written corrective action plan will be required.

4.2. For-Cause Audits

For cause audits may be requested by a convened Board, a Board Chair or Vice Chair, or the Director/Associate Director, OHR. For cause audits may be ordered as a result of audit reports from the OHRP, FDA, other governmental funding agency, as part of a noncompliance investigation, or as a result of complaint registered by a study participant or his/her family member. For cause audits will take precedence over not-for-cause audits.

4.3. Observation of the Consent Process

Studies can be chosen for observation of the consent process at random by the QIT for general quality assessment and improvement, or for the specific purpose of ensuring protection of participants. The latter type can be requested by a convened Board, a Board Chair or Vice Chair, or the Director/Associate Director, OHR. Studies for which observation of the consent process might be chosen as a method to protect participants include those involving:

• Vulnerable populations, including children, individuals who are decisionally impaired, terminally ill or very sick, low income, low education, and drug users;

• Narrow time windows for recruitment and consent, for example, a study in which pregnant women are approached shortly prior to delivery;

• Individuals in high stress situations, for example, a study in which individuals with shortness of breath are approached in the ER;

• Large payments to a parent (in particular, a low income parent) for a child’s participation;
• Foreign language speakers where a translator is present for the consent process;

• Surrogate consent where the surrogate is or is not a family member.

In these observations, the QIT specialist will pay particular attention to any biases in the presentation of information to the participant, the reactions of the participant, whether all of the participant’s questions are adequately answered, and whether the person conducting the consent process is appropriately respectful of the special vulnerabilities of the participant and/or the stresses of the specific situation. This process is also designed to increase participant understanding.

4.4. Assessment of Compliance with Audit Findings
The determination may be made to re-audit 6 months after the initial audit to assess the success of the investigator’s proposed corrective action plan. Studies found to be in continuing noncompliance will be reported to the relevant convened IRB and suspended to enrollment pending actions or recommendations of the Board. Board decisions may include but not be limited to:

• Additional training for study personnel;

• Structured oversight of the study by an independent monitor appointed by the Department Chair in conjunction with the IRB;

• Temporary or permanent suspension of the PI or other research personnel from involvement in research depending on the nature of the noncompliance.

4.5. IRB Announcements:
As OHR policies and forms are updated, email announcements are sent to the researchers and research staff. The announcements include a list of the updated policies and forms, as well as a description of the changes. The announcements are also available on the OHR website. These announcements are intended to keep research personnel informed of new requirements related to their human subjects research. Feedback from research personnel is solicited and is considered when making future policy and form revisions.

5. Internal Review of QA/QI Reports
The intent of the review process is one of quality improvement and education rather than audit and compliance. However, if serious or continuing noncompliance is revealed an IRB subcommittee to investigate the finding(s) will be convened as per TJU Policy 110.15 “Institutional Review Board Review of Noncompliance Issues” and all investigatory and reporting procedures outlined in that policy will be followed.
The QA reports will also be used to assess the efficacy of the Human Research Protection Program as a whole. Violations and deviations may be indicative not of isolated non-compliance on the part of investigators, but of a systemic problem resulting from a gap in the HRPP where this particular issue is inadequately or not addressed. If this is the case, OHR will make appropriate modifications to the HRPP, in our educational literature, website information, training programs, etc. Subsequently, OHR will conduct another audit on the same or other investigators to assess whether the HRPP modifications have permeated the research community and resolved the original systemic problems.

6. Tools
   OHR Internal Quality Assurance Evaluation Form
1. **Purpose**
   This policy will explain quality assurance measures used to continually assess the effectiveness of OHR operations.

2. **Responsibility for Executing the Policy**
   Director/Associate Director, OHR
   OHR Administrative Staff
   IRB Chair/Vice Chair

3. **Policy Statement**
   Quality assurance and control of the daily operations of the IRBs and the OHR staff ensure that they actively support the mandate of the IRBs as defined in the OHR and IRB policies and procedures. This policy pertains to all research submitted to the OHR for IRB review.

4. **Procedures**
   The QA/QC program consists of the following components to ensure QA/QC for all personnel involved in the daily operations of the human subjects protection program:
   - Training and continuous education for the OHR administrative staff;
   - IRB member education;
   - Review or oversight of interactions of the administrative staff with the IRBs and the research community;
   - Regular review and assessment of policies and procedures;
   - Training on Human Subjects in Research (Certification exam every 3 years);
   - Annual Human Subjects Training;
   - HIPAA in Research training;
   - OHR staff meetings;
   - Other timely meetings to discuss OHR issues;
   - Encouragement to qualify as a Certified IRB Professional (CIP).
   - Assessing audit reports on a continual basis to determine if the Human Subjects Protection Program requires modification.
5. **IRB Member Education**
   All non-scientist IRB members are required to complete the on-line CITI course for IRB members. Members who are scientists who have completed the CITI modules required in order to perform human subjects research are not required to take the CITI IRB member modules but are encouraged to do so.

   On a regular basis, OHR staff, selected members from other research support offices (Office of Research Administration, Office of University Counsel, Environmental Safety, etc.), selected Jefferson faculty or IRB members make a short continuing education presentation on topics intended to increase IRB member understanding of clinical research and applicable regulations.

6. **Internal QA/QI Program**
   Not less than once yearly, the QA/QI Program will audit the following for completeness, accuracy, content, and/or effectiveness:
   - TJUs FWA and OHRP-approved IRB rosters;
   - Three sets of minutes from each of the 3 IRBs with one set of minutes describing review of a study involving children and at least one in which a phase 1 trial is reviewed;
   - Twelve current IRB files including:
     - Exempt review (3 files)
     - Expedited review (3 files)
     - Full Board review (4 files including at least 1 significant risk device study)
   - Any other policies and procedures as necessary;
   - Review for completeness of IRB files for all studies that involved for-cause terminations or suspensions, noncompliance, or unanticipated problems requiring reporting to federal agencies.
   - Community outreach activities. The goals and activities undertaken by the stakeholders will be evaluated to determine if they are being met and are effective. Relevant stakeholders will be consulted as necessary to re-evaluate the goals and activities.

   The Director, OHR, has the authority to implement and/or modify existing policies or procedures to ensure efficient, transparent operations that adhere to federal and University regulations or recommend new policies and procedures to the Associate Provost for Research Support Services for implementation.
1. **Purpose**
   This policy states the necessary preparations required for regulatory audits of the IRB and the appropriate actions of those individuals who might interact with the auditors.

2. **Responsibility for Executing the Policy**
   - Director/Associate Director, OHR
   - OHR Administrative Staff
   - IRB Chair/Vice Chair
   - Principal Investigators

3. **Policy Statement**
   The policy pertains to all research submitted to the IRB. Quality assurance and quality control of the daily operations of the OHR and the IRBs are necessary to ensure that they support the IRB’s mandates under federal and institutional regulations. Consequently, this policy and procedures provides a means for dealing with external auditing and accrediting agencies.

4. **Procedures**
   4.1. **Preparing for an Audit**
   Certain regulatory and/or accrediting agencies have authority to audit the operations of IRBs. Such agencies include: FDA, OHRP, the Joint Council on Accreditation of Health Care Organizations (JCAHO), sponsors or funding agencies of research, and others who may be authorized by regulations or agreement with the University to audit specific documents and procedures.

   For external audits involving the FDA or OHRP, the following individuals must be immediately notified:
   - Associate Provost for Research Support Services
   - Director, OHR
   - University Senior Counsel and Corporate Compliance Officer
   - Hospital Administration, if applicable
   - Department Chair

   The Director, OHR, and the OHR administrative staff designated to participate in the audit are required to follow the following steps in preparing the site for an audit.
4.2. Participating in an Audit
The OHR Administrative staff is expected to know and follow the procedures for the conduct of external and internal audit of specific studies or study sites. Prior to being granted access to OHR or IRB documentation, inspectors or auditors should be asked to provide identification and proof of their authority or authorization to conduct the audit and have access to OHR and/or IRB documents. No entity other than those listed on the consent for the study may have access to any document that includes subject identifiers. OHR shall be responsible for redaction of such information from files prior to the audit, if required.

Auditors will be provided with an adequate working area to conduct the audit and the OHR staff shall make every reasonable effort to be available and to accommodate and expedite any auditor’s request.

Documents may be copied and taken off-site only by individuals authorized in writing by the Director, OHR, the University Senior Counsel and Corporate Compliance Officer, or the Associate Provost for Research Support Services to do so.

4.3. Follow-up after an audit
Reports resulting from the audit requiring official response, either verbal or written, should be addressed by the Principal Investigator, the Director, OHR, or other appropriate individuals, as soon as possible after a site specific audit. Reports of the audit, either verbal or written and directed to the operations of the IRBs should be addressed to the Director, OHR, as soon as possible.

For an FDA audit the Director, OHR, should request a FDA Form 483 from the auditor at the completion of the exit interview.

The OHR will review the results of the audit to determine if any further action is required. If a PI was audited, OHR may determine it necessary to implement a corrective action plan based on the audit results. If the audit showed continued deviation from protocol and/or IRB regulations, OHR may find it necessary to initiate a non-compliance investigation. OHR will also use the audit results to evaluate the human research protection program to determine if any modifications are necessary.
1. **Purpose**  
This policy and procedure describes the process for conducting and documenting training of the Principal Investigator, Co-Investigators and other designated individuals who participate in the conduct of human subjects research.

2. **Responsibility for Executing the Policy**  
Director/Associate Director, OHR  
Principal Investigator

3. **Policy Statement**  
This policy pertains to all investigators, research coordinators, research nurses and other designated individuals who are involved in supervising, managing or conducting FDA-regulated and all other human subjects research within Thomas Jefferson University.

The Principal Investigator at each site assumes the responsibility for the conduct of a clinical study and the protection of human subjects and has the authority to delegate portions of that responsibility to other key personnel. S/he is responsible for ensuring that key personnel to whom those responsibilities are delegated also are qualified by training and experience to perform their study-related duties.

All personnel are responsible for taking the appropriate training to conduct study-related duties, to document training, and to demonstrate they can apply training in the conduct of their duties.

4. **Procedures**  
4.1. **Principal Investigator’s Employee Training Plan**  
Thomas Jefferson University complies with federal directives to educate key research personnel by requiring those personnel to complete a formal program of training on federal and University policies and procedures pertaining to the conduct of human subjects research.

The Principal Investigator will ensure that all study personnel on human subjects research studies complete mandatory initial and on-going University training programs regarding the ethically and scientifically sound conduct of human subject research as provided by the OHR.
Training of key personnel concerning a specific research study will be scheduled and supervised by the Principal Investigator and/or his/her designee. The initial training program should familiarize key personnel with the development and specifications of the investigational products, including preclinical safety information, and pertinent regulatory requirements on conducting clinical studies in accordance with Good Clinical Practice (GCP).

Designated training staff on site or commercially sponsored courses may be used to provide this training. This training is to be distinguished from the human subjects training provided by OHR. The training should consist of at least the following elements:

- Standard Operating Procedures (SOP);
- Investigational Product Development and Specifications;
- Drug Chemistry and Mechanism of Action (or, Device Design and Development);
- Pre-clinical Testing and Results;
- Safety Profile and Expected Adverse Events;
- Manufacturing/Quality Assurance Process;
- Investigational New Drug (or, Investigational Device Exemption) Process;
- Applicable Regulatory Requirements (Investigational Product Accountability, Reporting Requirements);
- Investigator Brochure Development (if applicable);
- Monitoring Guidelines and Procedures
- Protection of Human Subjects (IRB, Informed Consent, Other Internal or External Regulatory Groups);
- Study Documentation and Files;
- Study Design and Conduct;
- Protocol and Case Report Form (CRF) Development;
- Entering information on the CRF;
- Data Collection, Analysis, Interpretation, and Reporting.
TJU/TJUH Staff who are responsible for assessing sites and Investigators for inclusion in a clinical study, and for study monitoring, should receive training in the following areas:

- Investigator Qualification and Interviewing
- Facility and Resources Assessment
- Site Initiation and Training
- Investigational Product Accountability Procedures
- Monitoring Visit Preparation
- Records Inspection
- Monitoring Report Preparation
- Study Closeout Procedures

The Principal Investigator should provide an appropriate period of time for new employees to cover the topics in this curriculum. New employee training must be completed before individuals participate in the conduct of a clinical study or engage in contacts with study subjects.

For continuing education purposes, the Principal Investigator's designee should schedule ongoing in-house GCP and human subject protection updates, to be provided by the Principal Investigator's staff or OHR as appropriate.

4.2. Site Team Training

Participating Investigators and all key personnel who are working on or overseeing research on human subjects should receive initial and ongoing training regarding the responsible conduct of research and SOPs.

All personnel will support required training activities by taking an active part in their own professional development in relevant content areas.

The Investigator must ensure that all key personnel are knowledgeable about all protocol-specific regulatory requirements for ongoing study protocols, study procedures and investigational products.

Investigators and other key personnel should attend periodic workshops and seminars to acquire timely information about topics germane to the field of human subject investigations.
4.3. Documentation of Training
The Principal Investigator will maintain copies of training program certificates of completion and all updated Staff Training records for all his/her employees in their appropriate personnel training files.

5. Applicable Regulations
General Responsibilities of Sponsors (21 CFR 312.50)
Selecting Investigators and Monitors (21 CFR 312.53)
General Responsibilities of Investigators (21 CFR 312.60)
General Responsibilities of Sponsors (21 CFR 812.40)
Selecting Investigators and Monitors (21 CFR 812.43)
General Responsibilities of Investigators (21 CFR 812.100)
Specific Responsibilities of Investigators (21 CFR 812.110)
The Principles of ICH GCP (ICH E6, section 2.8)
Investigator's Qualifications and Agreement (ICH E6, section 4.1)
Adequate Resources (ICH E6, section 4.2)
Trial Management, Data Handling, and Record Keeping (ICH E6, section 5.5)
Selection and Qualification of Monitors (ICH E6, section 5.18)
NIH Notice OD-00-029 Required Education in the Protection of Human Research Participants (June 5, 2000)
Clarification on June 5, 2000 Notice, OD-00-039 (Sept 12, 2000)
1. **Purpose**
   To define a policy and procedure as to how the IRB will make a determination whether outside verification is required to ascertain that no material changes have been made to an IRB-approved protocol without IRB notification.

2. **Responsibility for Executing the Policy**
   - Director/Associate Director, OHR
   - Investigators
   - Research Coordinators
   - IRB Members

3. **Policy Statement**
   The need for outside verification could arise when a principal investigator (PI) is under special oversight by the IRB or a federal agency or has specific conflicts of interest that require an increased amount of monitoring by the IRB and/or other institutional offices. There may be other situations to which this policy will apply.

4. **Procedures**
   The Director or Associate Director, OHR, will make a determination as to when outside verification will be required that no material changes have been made to an IRB-approved protocol.

   For many situations, the OHR’s Quality Assurance Team (QAT) will be dispatched to the study site to conduct an audit of the file for the study in question. A member of the QAT will create a report for presentation to the Director or Associate Director, OHR.

   In some situations, it may be more appropriate or expeditious for the IRB to determine an institutional or extra-institutional individual(s) who can provide verification of the status of a particular study. The IRB may invite these individuals to a meeting to present a report or simply discuss the submitted report at a meeting. The IRB will also determine whether or not the PI will be notified of these reports.
The findings of the QAT, institutional or extra-institutional status reports will be shared with the PI who will be asked to provide to the IRB a written explanation of the discrepancies. If the discrepancies are systematic and/or substantial, the IRB may determine that a non-compliance hearing or other educational or penal action is required. Also, if the discrepancies reveal a significant increase in risk to the subjects, the IRB may require that the study be suspended or terminated.
1. Purpose
This policy elaborates the criteria that the IRB must evaluate and approve before any study-related procedure involving human subjects can be initiated. The criteria are based on the ethical principles of the Belmont report and Food and Drug Administration (FDA) and Department of Health and Human Services (DHHS) regulations pertaining to human subjects research.

2. Responsibility for Executing the Policy
Associate Director, OHR
IRB Chair/Vice Chair
IRB Members
IRB Reviewer(s)

3. Policy Specifics
3.1. Review of Studies by TJU IRBs
The IRB chair is responsible for providing on-going guidance during the meeting concerning the review and deliberative processes leading up to the vote on the proposal.

Primary reviewers must have scientific or scholarly expertise, or other knowledge that allows an in-depth initial review of the protocol submission and for making all appropriate approval recommendations for consideration by the convened IRB. They should also ascertain whether any special considerations exist that may influence the review of the proposal such as conflicts of interest and/or financial disclosures, and whether third party verification of the submitted information is necessary. Primary Reviewers must have the appropriate scientific or scholarly expertise, or other knowledge, that enables thorough review.

At the time of assignment of reviewers, if there is not at least one person on the IRB with appropriate expertise or knowledge to conduct an in-depth review, the IRB defers protocol review to another meeting, another TJU IRB or obtains consultation.

The approval date is the date the IRB voted to approve with or without conditions. The expiration date of an approved protocol is one (1) day less than a year from the date of IRB approval. For approved protocols, the expiration date is the last date that the protocol is approved.
3.2. Review of Studies Involving Vulnerable Populations
When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects (Note: 21 CFR 56.111 also includes “handicapped” as a vulnerable population category). If research involves vulnerable participants, the IRB chair, the Director, and Associate Director, OHR, will ensure that at least one reviewer (or consultant if necessary) has the knowledge and scientific expertise to perform in-depth review of the protocol. The protocol may be reassigned to another Board in order to ensure such expertise. If consultants are employed, even if from another Jefferson Board, their comments and concerns will be duly noted in the minutes, but they may not vote on the protocol.

3.3. Review of Studies by Outside IRBs
1) If it is determined that the University has a significant financial or other interest in the commercial sponsor a research study (Policy GA 106), no University IRB may review the study.

In this case the study will be submitted to an IRB with which the University has an IRB Authorization Agreement. The external IRB will be the IRB of record for the study, and the OHR will maintain a file for the study.

2) When TJU relies on an independent or other IRB, a formal agreement either via an IRB Authorization Agreement (IAA), a memo of understanding (MOU) or a formal contract between Jefferson and an independent IRB is executed that specifies how regulatory activities such as non-compliance, education of investigators and staff, reporting responsibilities, conflict of interest determination, etc. are divided between the reliant and the reviewing IRBs.

3.4. When a researcher is the lead investigator of a multi-site study, the IRB evaluates whether the management of information that is relevant to the protection of participants is adequate.

3.5. For initial review of research by a convened IRB, any additional information provided to an individual reviewer will be available to any IRB member who wishes to review it.

The IRB will determine that researchers have the resources necessary to protect participants:
- Adequate time for the researchers 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 participants.

• Availability of medical or psychosocial resources that participants might need as a consequence of the research.

3.6.1. For initial review the IRB determines:
• That the researcher will obtain the legally effective consent of the participant or the participant’s legally authorized representative.

• That the circumstances of the consent process provide the prospective participant or the legally authorized representative sufficient opportunity to consider whether to participate.

• That the circumstances of the consent process minimize the possibility of coercion or undue influence.

• That individuals communicating information to the participant or the legally authorized representative during the consent process will provide information in language understandable to the participant or the representative.

• That information being communicated to the participant or the representative during the consent process will not include exculpatory language through which the participant or the legally authorized representative is made to waive or appear to waive any of the participant’s legal rights.

• That information being communicated to the participant or the legally authorized representative during the consent process will not include exculpatory language through which the participant or the legally authorized representative releases or appears to release the researcher, the sponsor, the organization or its agents from liability for negligence.

• That required disclosures will be provided to each participant or a legally authorized representative in accordance with legal and regulatory requirements.

• Whether additional disclosures are required for inclusion in the consent process.
• That the consent process will be documented according to legal and regulatory requirements.

3.6.2. When following DHHS regulations:
• The IRB determines that the required and appropriate additional elements of disclosure are included in the consent process.

To allow use of the long form of consent documentation, the IRB determines:
  o The consent document embodies the basic and required additional elements of disclosure.
  o The participant or the participant’s legally authorized representative will sign the consent document.
  o A copy of the consent document will be given to the person signing the consent document.
  o The researcher will give either the participant or the representative adequate opportunity to read the consent document before it is signed.

To allow the use of the short form of consent documentation, the IRB determines:
  o The short form document states that the elements of disclosure required by regulations have been presented orally to the participant or the participant’s legally authorized representative.
  o A written summary embodies the basic and required additional elements of disclosure.
  o There will be a witness to the oral presentation.
  o For participants who do not speak English, the witness is conversant in both English and the language of the participant.
  o The participant or the participant’s legally authorized representative will sign the short form.
  o The witness will sign both the short form and a copy of the summary.
  o The person actually obtaining consent will sign a copy of the summary.
  o A copy of the signed short form will be given to the participant or the legally authorized representative.
  o A copy of the signed summary will be given to the participant or the legally authorized representative.

3.6.3. When following the FDA regulations the IRB determines:
• The required and appropriate additional elements of disclosure are included in the consent process.

• There is a statement noting the possibility that the FDA may inspect the records that will be provided to each participant.
• There is a statement that the results of the research will be posted on clinicaltrials.gov.
  o “A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.”

• The participant or the participant’s legally authorized representative will sign and date the consent document.

• The researcher will give either the participant or the legally authorized representative adequate opportunity to read the consent document before it is signed.

3.6.4. When following the FDA regulations to allow the use of the short form of consent documentation, the IRB determines:
• The short form document states that the elements of disclosure required by regulations have been presented orally to the participant or the participant’s legally authorized representative.

• A written summary embodies the basic and required additional elements of disclosure.

• There will be a witness to the oral presentation.

• For participants who do not speak English, the witness is conversant in both English and the language of the participant.

• The participant or the participant’s legally authorized representative will sign the short form document.

• The witness will sign both the short form and a copy of the summary.

• The person actually obtaining consent will sign a copy of the summary.

• A copy of the signed short form will be given to the participant or the legally authorized representative.

• A copy of the signed summary will be given to the participant or the legally authorized representative.

3.6.5. When following the FDA regulations the IRB determines:
• When a participant withdraws from a study, the data collected on the participant to the point of withdrawal remains part of the study database and may not be removed. The consent document cannot give the participant the option of having data removed.

• A researcher may ask a participant who is withdrawing whether the participant wishes to provide continued follow-up and further data collection subsequent to their withdrawal from the interventional portion of the study. Under this circumstance, the discussion with the participant distinguishes between study-related interventions and continued follow-up of associated clinical outcome information, such as medical course or laboratory results obtained through non-invasive chart review, and addresses the maintenance of privacy and confidentiality of the participant's information.

• The researcher must obtain the participant’s consent for this limited participation in the study (assuming such a situation was not described in the original consent document). The IRB must approve the consent document.

• If a participant withdraws from the interventional portion of a study and does not consent to continued follow-up of associated clinical outcome information, the researcher must not access for purposes related to the study the participant's medical record or other confidential records requiring the participant's consent. However, a researcher may review study data related to the participant collected prior to the participant's withdrawal from the study, and may consult public records, such as those establishing survival status.

3.6.6. Waiver or alteration of the consent process/parental permission:
• The IRB is allowed to waive or alter the consent process by determining that the criteria for waivers or alterations are met.

• The IRB is allowed to waive parental permission by determining that the criteria for waivers or alterations are met (see Reviewer Form RQD1, questionnaire for research involving children).

• The IRB is allowed to waive the requirement for written documentation of the consent process by determining that the criteria for waivers are met.

• The IRB documents its findings justifying the waiver or alteration.

3.6.7. When following DHHS regulations:
The IRB is allowed to waive or alter the consent process by determining that the regulatory criteria for waivers or alterations of the consent process are met and that the research is not regulated by the FDA.

The IRB is allowed to waive the requirement to document the consent process by determining that the regulatory criteria for waivers are met.
- When the IRB considers waiving the requirement to obtain written documentation of the consent process, the IRB reviews a written description of the information that will be provided to participants.
- When granting waivers of the requirement to obtain written documentation of the consent process, the IRB considers requiring the researcher to provide participants with a written statement regarding the research.

3.7. Review of Community Based Research
For review of research in which community members may be involved in research design, implementation, and dissemination of results, the IRB will:
- Include member(s) or a consultant with expertise in community based research.

- Require a description of the steering committee or other mechanism whereby community input is solicited and implemented.

- Assess the quality and effectiveness of the steering committee at the time of continuing review and, if IRB, investigator/staff or member of the steering committee requests, review by the Quality Improvement team will be initiated and feedback will be provided.

3.8. Review of Department of Defense Supported Research

Additionally, in order to approve research covered by this policy the IRB shall determine that all of the following requirements are satisfied:
- Risks to subjects are minimized: (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.
• 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 subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

• Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons. (Note: 21 CFR 56.111 also includes “handicapped” as a vulnerable population category).

• 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 45 CFR 46.116 and 21 CFR 50.20.

• Informed consent will be appropriately documented, in accordance with, and to the extent required by 45 CFR 46.117 and 21 CFR 50.20.

• When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

• When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

4. Tools/References

OHR OHR-8 Internal Form
Policy and Procedure for the Determination of Conflicts of Interest
45 CFR 46.111 (a)
45 CFR 46.111 (a) 2
21 CFR 56.111 (a)
21 CFR 56.111 (a) 2
OHRP Compliance Activities: Common Findings and Guidance #3, #14, #15, #72
FDA Information Sheets: Frequently Asked Questions
Guidance G-620, Department of Defense (DoD) Requirements for the Conduct of Human Subjects Research
1. Purpose
To elucidate the policy, procedures, and criteria for renewal of an approved human subjects study, and for the review of changes that may occur during the approved period of the study.

2. Responsibility for Executing the Policy
Director/Associate Director, OHR
OHR Administrative Secretaries involved with Continuing Review
IRB Chair/Vice Chair
IRB Members

3. Policy Statement
The IRB will conduct continuing review (renewal) of a current approved study being conducted within its jurisdiction at intervals appropriate to the degree of risk, but not less than once per year. Depending on risk assessment, the IRB may determine that continuing review is required at an interval less than one year. The IRB has the authority to observe or have a third party observe the consent process and the research. The IRB delegates this activity to the administrative secretaries responsible for administration of the continuing review process and the quality assurance/quality improvement program that is conducted in conjunction with the continuing review process.

4. Specific Policies
4.1. IRB Approval Period and the Requirements for Renewal
A study must have active IRB approval as long as the following procedures are being conducted at the approved research site:

- Any research-related interventions
- Follow-up of participants, including long-term follow-up for survivorship
- Collection or analysis of private identifiable information or tissue

Once all of the above procedures have been completed, continuing review for a study is no longer required, and the study may be closed with the IRB. Researchers must report premature completion of a study to the IRB. If no further research activity will occur, and OHR-9 final report must be submitted to close the study.

For research meeting the above criteria, the IRB(s) must conduct continuing review at intervals appropriate to the degree of risk, but not less than once per year. Research must be reviewed and approved by the IRB on or before the expiration date of the current IRB approval.
Investigators are required to submit an OHR-9 Continuing Review form and Progress Report 6 weeks prior to the expiration date of the study. If the investigator fails to submit a continuing review and progress report to the IRB prior to the expiration date, the research activities must cease. If the investigator, in conjunction with the IRB, determines that the subjects on the study would suffer a hardship if medical care were discontinued, appropriate medical care may continue beyond the expiration date for a reasonable amount of time provided that the investigator is in the process of submission of a renewal of the study to the IRB. However, the data collected during this period of lapsed IRB approval may not be used for research purposes.

Under federal regulations a study that is not renewed by the expiration date automatically expires. If a study expires, new subject enrollment and study-related activities that are NOT critical to subject well-being must cease. To re-open a lapsed study to enrollment and study-related activities, an OHR-9 Continuing Review application along with the documents specified on the OHR-9 must be submitted for IRB review. If a Continuing Review is not received within 60 calendar days of the expiration date, a study will be administratively terminated. If an expired study has been completed, an OHR-9 Final Report must be submitted.

If a protocol expiration date occurs during the process of continuing review (e.g., it expires following the IRB’s review and while the IRB is awaiting requested changes), all research activities must cease except those deemed medically necessary for the subjects’ health or well-being and no new enrollment may occur. The protocol need not be re-submitted as a “new full review” protocol since the continuing review is, by regulation, equivalent to a new full board review. The investigator must certify in the submission that no subjects were enrolled during the expired time period.

4.2. Extension of IRB Approval Period
There is no grace period extending the conduct of the research beyond the expiration date of IRB approval. Extensions beyond the expiration date will not be granted.

4.3. Withdrawal of IRB Approval of a Study
IRB approval for the conduct of a study may be withdrawn at any time if warranted by the conduct of the research and if the risks to the subjects are determined by the IRB to have increased to a point where they are determined to be unreasonably high. This might come about by a more than expected number of adverse events, unexpected serious adverse events or unanticipated problems, or evidence that the investigator is not conducting the research in compliance with IRB or University guidelines. Such findings may result in more frequent review of the study to determine if approval should be withdrawn or enrollment stopped until corrective measures can be taken or the study terminated.
4.4. Continuing Review
Continuing review includes, but may not be limited to the following activities:

4.4.1. Site Visits and Third Party Verification (see also OHR policies GA 101 and QA 301).

The IRB has the authority to observe, or have a third party observe, the consent process of research it has approved, and to verify that the study is being conducted as required by the IRB and within University Policies and site-specific procedures as appropriate. OHR personnel or IRB members may conduct a site visit. Generally, site visits are delegated by the Director, OHR, to the administrative secretaries whose responsibility it is to conduct the administration of the continuing review process and the QA/QI program.

4.4.2. Review of Serious and Unexpected Adverse Events and Unanticipated Problems That Pose a Risk to Subjects and Others

Subject safety is of the greatest importance for the individual subjects and the clinical study. A serious adverse event or unanticipated problem must be promptly reported to the sponsor and the IRB. At the time of continuing review, the IRB should ensure that the criteria for the original IRB approval under 45 CFR 46.111 continue to be satisfied. Information regarding unanticipated problems that have occurred since the previous IRB review, in most cases, will be pertinent to the IRB’s determination at the time of continuing review. It may also be appropriate for the IRB at the time of continuing review to confirm that any provisions under the previously approved protocol for monitoring study data to insure safety of subjects have been implemented and are working.

A brief summary of any adverse events and/or unanticipated problems is to be included with the continuing review. The summary should address whether there have been unanticipated problems and that adverse events have or have not occurred at the expected frequency and level of severity as documented in the research protocol, consent form and/or any investigator brochure.

Researchers are obligated to report to participants any new findings that arise from the IRB review process that may affect their willingness to continue in the study.

4.4.3. Amendments
Changes in a study during the period for which the study has IRB approval may not be initiated without prior IRB convened Board or expedited review and approval (see OHR Policy RR 408) except when necessary to eliminate apparent immediate hazards to subjects.
If the change was initiated to eliminate apparent immediate hazards to a subject, it must be reported promptly (within 3 working days) to the OHR using form OHR-12 for determination of whether the change was consistent with ensuring the subjects’ welfare. If consistent, the amendment will be reviewed by a convened Board or expedited review. If not, then the PI will meet with the Director/Associate Director and a physician with expertise in the relevant discipline to review the decision making process. Based on this meeting, the changes may be considered as an amendment, a deviation, or a violation. The Board will be notified of the outcome.

The IRB uses required criteria for approval for all reviews of research including reviews of modifications to previously approved research when the modification affects a criterion for approval.

All other changes requiring an amendment to the protocol and/or consent form must be submitted to the IRB by completion of OHR form OHR-12 and approved prior to their implementation.

Unless an amendment qualifies for expedited review, all Board members including alternate members will receive all modified materials for review at a convened meeting.

The IRB may request a quality assurance audit if concerns about safety or implementation of study modifications arise.

4.4.4. Significant New Findings

During the course of an approved study, the IRB may be required to review reports generated from data safety monitoring boards, adverse events, current literature and other sources to determine if: The status of the research has changed; the risk/benefit balance is still acceptable; new information needs to be conveyed to the subjects; if a segment of the population may be bearing an undue burden of research risk. Such significant new findings will be reviewed by the convened IRB or by expedited review by the Director/Associate Director, OHR, where appropriate.

4.4.5. Reports from Employees, Staff and Faculty

It is the responsibility of the investigative team, medical and nursing staffs or any other employees of TJU/TJUH to promptly report to the IRB through the OHR, any findings, results, occurrence or new information about an active study involving human subjects research that could affect the rights and welfare of the subjects. It is the responsibility of the Director, OHR, and/or the IRB staff and members to act on any such information in order to protect the research subjects.
4.4.6. Reports of Alleged Non-Compliance With Federal Regulations at 45 CFR Part 46 or the Requirements of the IRB.

All reports of inappropriate involvement of human subjects in research from any source must be received and reviewed by the Director, OHR. All reports of alleged non-compliance with federal regulations involving human subjects deemed to be credible must be handled according to the University’s Policy entitled: IRBs-Investigating Allegations of Non-Compliance With Human Subjects Regulations (TJU Policy #107.13).

The IRB has the authority to suspend or terminate approval of research that is not being conducted in accordance with IRB policies, is not in compliance with federal regulations, or has been associated with serious harm to subjects or others. All such suspensions or terminations shall be reported by the Director, OHR, to the Office of Human Research Protections and/or the FDA as appropriate.

4.4.7. Verification from an external source that no material changes have occurred since the previous IRB approval.

If the IRB determines that it needs verification from sources other than the Principal Investigator, that no material changes have occurred since the previous IRB review, the IRB may request an independent assessment of information or data provided in the renewal application. Sources for such outside information could include copies of FDA or sponsor audits, site visits conducted by authorized personnel, reports from subjects or study staff, or an audit requested by the IRB. If the necessity arises, the scope and extent of such an independent assessment will be determined on a case-by-case basis.


The purpose of the continuing review is to review the progress of the entire study, as well as the changes that occurred during the progression of the research. It may be only after the research has begun that the real risk can be determined and the preliminary results used to compute the stated (IRB approved) risk/benefit balance can be evaluated. The IRB can, at this point, determine whether the study can be renewed with the same risk profile or if new information has changed that profile.

Continuing review of a study at the time of expiration may not be conducted through an expedited review procedure unless: 1) the study is eligible for, and was initially reviewed by expedited review, or 2) the study has changed such that the only activities remaining are eligible for expedited review.
Continuing reviews are approved according to all applicable regulatory criteria. (See IRB reviewer questionnaire RQ-1, and OHR Policy RR 401)

Proper completion of the OHR OHR-9 Continuing Review Form and the reviewer questionnaire checklist will provide an appropriate review of the above issues.

4.6. Expedited Review
Generally, if a research study did not qualify for expedited review at the time of initial review, it does not qualify for expedited review at the time of continuing review except in limited circumstances. It is also possible that research activities that initially qualified for expedited review may have changed or will change such that expedited review would no longer be permitted for continuing review.

Continuing reviews will be designated as expedited according to the Expedited Checklist- Continuing Review.

Continuing review submissions will be available to all IRB members on the IRB electronic submission portal one week prior to a meeting date. A reviewer who initially reviewed the study, if still on the IRB, or a reviewer who has expertise in the area of the research, will be designated the primary reviewer. In addition, the Quality Improvement Specialist shall review the complete IRB study file in preparation for a possible QA visit.

5. Procedure for Reviewers- Continuing Review
Continuing reviews requiring full board review will be assigned, at the reviewer assignment meeting, to one or more Board members with appropriate expertise as primary reviewers for review and presentation to a convened Board. If the consent form has expired by the time of submission to the IRB, this information will be entered into the database and the Principal Investigator will be notified that the study expired and has been administratively terminated.

All materials and documents submitted for review are posted on the electronic submission portal one week prior to the IRB meeting. The assigned reviewers and all Board members have access to:

- The full protocol, application, or a protocol summary containing the relevant information necessary to determine whether the proposed research continues to fulfill the criteria for approval.
- The current consent document.
- Any newly proposed consent document.
- A status report on the progress of the research (OHR-9).
Primary reviewer(s) will:

- Check that the OHR 9 form is completed,
- Check the date of the initial IRB approval and compare it to the date when the first subject was enrolled,
- Check the total number of subjects enrolled and compare the original OHR-2 form for total number of subjects approved by IRB,
- Review the IRB study file (Quality Improvement Specialist),
- Check the certification section to ensure all subjects signed and received a consent form, if appropriate,
- Check for an updated OHR-2,
- Check demographics of subjects enrolled and compare to demographics of recruitment intended as stated on the OHR-2,
- Check for conflict of interest certification,
- Complete, sign, and date the OHR reviewer questionnaire.

The IRB will determine:

- Whether the protocol needs verification from sources other than the researchers that no material changes had occurred since previous IRB review (see 4.4.7 above).
- That the current consent document is still accurate and complete.
- Whether any significant new findings that arise from the review process and that might relate to participants’ willingness to continue participation should be provided to participants.

The reviewer(s) will present the full continuing review for discussion and vote at a convened Board meeting. The IRB will make the recommendation to approve or not approve as described in Policy OP 206.

6. Expiration Date

The expiration date for studies appears on first and last pages of a stamped consent form and on the IRB approval letters. Except as noted above in section 4.1, all trial activity must cease by midnight on the date of expiration.
7. References
   45 CFR 46.109
   21 §56.109
   45 §46.110
   21 §312.32(a)
   21 CFR§314.80
   21 CFR§600.80
   45 §46.103(b)(5)(iii)
   45 CFR§46.116(b)(5)
   21 §50.25(b)(5)
   21 CFR§56.108(b)(1)
   FDA Information Sheets: Continuing Review After Study Approval

8. Tools
   OHR OSA-9 Continuing Review Form OHR Policy QA 301
   OHR OHR-12 Amendment to a Research Protocol Form
   Thomas Jefferson University Policy on IRBs: Investigating Allegations of Non-
     Compliance with Human Subjects Regulations (Policy #1074.3)
   OHR Checklist for Continuing Review
1. **Purpose**
   To delineate the requirements for classifying a study as exempt from IRB review, and the procedure for making the determination and conducting the review.

2. **Responsibility for Executing the Policy**
   Director/Associate Director, OHR
   IRB Chairs/Vice Chairs
   Designated OHR Staff

3. **Policy Statement**
   A new study may be designated as exempt from IRB review provided it meets one of the criteria cited in 45 CFR 46.101 (b).

4. **Procedures**
   Exemption determinations are not made by investigators. The Director, Associate Director, designated OHR staff or IRB Chair or Vice Chair who has no conflict of interest with the research will review all studies that potentially qualify for exempt status according to §46.101(b) and determine which of the six listed exemption categories is appropriate. These individuals will review all pertinent study-related information and notate the appropriate criterion for exemption on the OHR New Submission Checklist. OHR staff can obtain an authoritative decision about whether a research study is exempt and which category it falls under by asking the Director or Associate Director. The title and the appropriate citation from §46.101(b) will also be entered onto the agenda for a convened Board meeting, and, subsequently, into the minutes for audit and record-keeping purposes.

The six exempt categories from 45 CFR 46.101 are as follows:

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

2) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless:
   (i) information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and
   (ii) 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, or reputation.
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 paragraph (b)(2) of this section, if:
i) the human subjects are elected or appointed public officials or candidates for public office; or (ii) federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

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

5) Research and demonstration projects which are conducted by or subject to the approval of department or agency heads, and which are 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.

6) Taste and food quality evaluation and consumer acceptance studies, (i) if wholesome foods without additives are consumed or (ii) if a 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 Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

Exempt studies, while not within the purview of federal human subjects regulations, are held to ethical standards of Thomas Jefferson University and Thomas Jefferson University Hospital. The following standards are evaluated based on review of information provided in the OHR-18 Application for Exemption from IRB Review:

- The research holds out no more than minimal risk to participants.
- Selection of subjects is equitable
- Privacy of subjects is maintained
- The activity involves research
• Adequate provisions are in place to maintain confidentiality of identifiable information

• If there are interactions with participants, the IRB will determine whether or not there should be a consent process and that:
  o Participation is voluntary.
  o Name and contact information for the researcher is provided.
  o There is a description of procedures.
  o The consent process is adequate and based on IRB consent form templates (as directed in OHR-18)

The Associate Director and/or designated OHR staff will conduct this evaluation as part of their review of the exemption application. The Director or an IRB Chair may also fulfill this task as appropriate.

An exemption letter may be immediately released to the Principal Investigator for a study that is determined to be exempt and has no conditions for approval. However, any amendments to the study must be submitted to the IRB. When the study is completed, the principal investigator should notify the IRB.

Exempt studies will be maintained in the OHR file system and database until OHR is notified by the Principal Investigator that the study has been completed.
1. Purpose
To delineate the requirements for classifying the review of new studies, and continuing reviews as expedited and the procedure for conducting the review.

2. Responsibility for Executing Policy
Director/Associate Director, OHR
IRB Chair/Vice Chair
OHR Data Coordinator

3. Policy Statement
As cited in 45 CFR 46.110, an IRB may use the expedited review procedure to review certain types of research involving no more than minimal risk and for minor changes in previously approved research during the period for which approval is authorized.

The reviewer will make the recommendation to approved or not approve as described in Policy OP 206. Recommended changes may be reviewed using the expedited procedure unless:

1. The reviewer determines that the proposal does not meet the criteria for expedited review and should be reviewed by a convened Board.

2. In the opinion of the reviewer, the proposal should be disapproved as the term is used at 45 CRF 46.110(b). In this case the proposal must be revised, re-submitted in full, and reviewed by a convened Board.

The convened IRB will be notified, for informational purposes, of all research proposals that have been approved by the expedited procedure.

4. Procedures
4.1. Determination and Processing of Expedited Review
All new studies will be received by the data coordinator, who will enter each proposal into the computer-generated agenda for the next IRB meeting, review the submission for required documents, attach a OHR New Submission Checklist to the study and pass it on to the Associate Director, OHR, who will triage the study for the type of review required.

The Associate Director or designee will preview each new study in relation to the federal criteria for expedited studies as stated in 45 CFR 46.110, 21 CFR 56.11, and as outlined in the OPRR Document, “Categories of Research That May Be Reviewed by the Institutional Review Board Through an Expedited Review Procedure” (1998) to determine if any of the categories are applicable. If so, the
Associate Director will notate on the OHR Internal New Submission Checklist the appropriate criterion. The study will then be given expedited review by the Director, Associate Director, Chair, Vice Chair and/or designated IRB members as appropriate.

All expedited studies are entered into the minutes of the appropriate meeting. However, per federal regulations, the Board is not required to vote on these items. They are documented for information, auditing and record-keeping purposes only. As soon as the expedited study is approved, an approval letter and stamped materials may be released to the Principal Investigator, and the study may begin.

For expedited studies, the reviewers will receive the same materials that a primary reviewer receives. (See Policy OP 206).

4.2. Expedited Reviewers
   The chair and Director/Associate Director will determine when IRB members are ready to act as expedited reviewers. Board secretaries assigned as expedited reviewers will have received training by a senior IRB staff member.

4.3. Expedited Criteria
   The expedited review criteria as outlined in the OPRR Document, “Categories of Research That May Be Reviewed by the Institutional Review Board Through an Expedited Review Procedure” are as follows:

4.3.1. Research activities that (1) present no more than minimal risk to human subjects, and (2) involve only procedures listed in one or more of the following categories, may be reviewed by the IRB through the expedited review procedure authorized by 45 CFR 46.110 and 21 CFR 56.110. The activities listed should not be deemed to be of minimal risk simply because they are included on this list. Inclusion on this list merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects.

4.3.2. The categories in this list apply regardless of the age of subjects, except as noted.

4.3.3. The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects’ 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.
4.3.4. The expedited review procedure may not be used for classified research involving human subjects.

4.3.5. IRBs are reminded that the standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review-expedited or convened--utilized by the IRB.

4.3.6. Categories one (1) through seven (7) pertain to both initial and continuing IRB review.

Research Categories:
4.3.6.1. Clinical studies of drugs and medical devices only when condition (a) or (b) is met.

(a) Research on drugs for which an investigational new drug application (21 CFR Part 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.)

(b) Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

4.3.6.2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:

(a) from healthy, non-pregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or

(b) from other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

4.3.6.3. Prospective collection of biological specimens for research purposes by noninvasive means.

Examples: (a) hair and nail clippings in a non-disfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care
indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncanulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) 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; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.

4.3.6.4. 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: (a) 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; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electoretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

4.3.6.5. Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for non-research purposes (such as medical treatment or diagnosis). (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b) (4). This listing refers only to research that is not exempt.)

4.3.6.6. Collection of data from voice, video, digital, or image recordings made for research purposes.

4.3.6.7. 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: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(2) and (b)(3). This listing refers only to research that is not exempt."

4.3.6.8. Continuing review of research previously approved by the convened IRB as follows:

(a) 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

(b) where no subjects have been enrolled and no additional risks have been identified; or

(c) where the remaining research activities are limited to data analysis.

4.3.6.9. Continuing review 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.

5. Tools

OHR New Submission Check List
1. **Purpose**
   To provide information to the individuals conducting human subjects research as to how the OHR and the IRB may take action to suspend or terminate previously approved research.

2. **Responsibility for Executing the Policy**
   Director/Associate Director, OHR
   Convened IRBs
   IRB Chairs/Vice Chairs

3. **Definitions**
   3.1. **Suspension of IRB Approval**: An action that temporarily stops some or all research activities of an approved protocol.

   3.2. **Termination of IRB Approval**: An action initiated by the convened IRB to permanently close a research study.

4. **Policy Statement**
   Federal Regulations require that the IRB have the authority to suspend or terminate approval of research that is not being conducted in accordance with IRB requirements or that has been associated with unexpected serious harm to research participants. Suspensions and terminations are actions that may be temporary or permanent and that may affect some or all research procedures. Suspensions and terminations may be ordered by a convened IRB, the Director or Associate Director, OHR, or an IRB Chair or Vice Chair in consultation with the Director or Associate Director. If suspension or termination is not ordered by a convened IRB, the action will be reported for review to a convened IRB.

4.1. **Suspension or Termination of IRB approval**:
   Examples of situations that may result in suspension or termination include but are not limited to:
   - Research not being conducted in accordance with IRB requirements;
   - Unexpected serious harm to research subjects;
   - Non-compliance with federal or local regulations;
   - Research misconduct issues.
Before deliberating on issuing a suspension or termination, the IRB may require additional information about the study. At this point, the IRB may initiate a fact-gathering review by the Quality Improvement Team or a third party not involved with the research study and who has expertise in the type of research being conducted or expertise in the specific area of concern.

The findings of this fact-gathering review will be reported to the IRB, and the IRB will make its deliberations based on this information.

The IRB will notify the Investigator in writing of its decision to suspend or terminate a study and provide a rationale for its actions. This letter will include an opportunity for the PI to respond to the IRB’s determination and to attend an IRB meeting to discuss the suspension or termination and provide clarification of issues.

4.2. Procedures to Follow Regarding Subjects Participating in Suspended or Terminated Trials:
When a study is suspended or terminated the PI must devise a corrective action plan that is submitted to the IRB for approval. The plan must address the following issues:
- PI Notification of current subjects and the means by which and the timeframe in which they must be notified

- Consideration of actions the PI will take to protect the rights and welfare of currently enrolled subjects by:
  - Transferring subjects to another investigator;
  - Making arrangements for clinical care outside of the research setting;
  - Allowing continuation of some research activities under the supervision of an independent monitor;
  - Requiring or permitting follow-up of participants for safety reasons;
  - Withdrawal from the trial in an orderly fashion including any appropriate clinical testing related to safety;
  - Notifying (if appropriate) subjects of adverse events or outcomes.

5. Reporting Suspensions and Terminations
All terminations or suspensions of human subjects research will be reported as mandated in University Policy #110.15 and OHR Policy GA 114 to University Officials within 5 working days and to federal or other agencies, as applicable, within 10 working days of the IRB determination.
6. Supporting Documents

45 CFR 46.113  Suspension or termination of IRB approved research
21 CFR 56.113  Suspension or termination of IRB approved research
TJU Policy 110.15  IRB Review of Noncompliance Issues
OHR Policy GA 114  Reporting of Unanticipated Problems, Terminations, Suspensions and Non-Compliance
1. **Purpose**
   This policy elaborates the process of IRB review of amendments to IRB-approved human subjects research.

2. **Responsibility for Executing the Policy**
   - Director/Associate Director, OHR
   - OHR Administrative Secretary for Amendments
   - IRB Chairs/Vice Chairs
   - IRB Members
   - Investigators

3. **Policy Statement**
   Changes in a study during the period for which the study has IRB approval may not be initiated without prior IRB approval of an amendment to the protocol and/or consent form except where necessary to eliminate immediate apparent hazards to subjects. If such an exception to the rule is utilized, an amendment must be submitted to the IRB as soon as possible (see Policy RR402).

4. **Procedures**
   **4.1. Submission of Amendments**
   An amendment to a study protocol and/or the informed consent document is to be submitted to the OHR as a completed OHR-12, Amendment to Research Protocol Form, containing a summary of the changes to the protocol and/or consent form. The required protocol and/or consent form changes, if any, must be clearly indicated in a manner that is reproducible (i.e., a hi-lighter pen is NOT reproducible). Clean copies of the revised protocol and/or OHR-2, consent form, and other amended materials must also be included for IRB stamping.
   **4.1.1. Amendments include, but are not limited to, changes in:**
   - Aims that affect the design of the study or a sub-study
   - Study design
   - Randomization methods
   - Recruitment sample size
   - Recruitment practices
   - Eligibility/exclusion criteria
   - Data collection methods or instruments
• Data collection or visit schedule

• Interventions or treatments

• Risk or Benefit to the subject

4.2. Receipt of Amendments
Amendments for on-campus studies are received by the OHR Data Coordinator and logged into the computerized agenda for the appropriate IRB meeting. The Associate Director, OHR, will preview the amendment and make a determination as to category of review.

4.3. Review of Amendments
Amendments requiring on-campus convened Board review will be assigned a primary reviewer at the time the reviewer assignment committee assigns reviewers for the studies to be reviewed at the next Board meeting. In so far as possible, the chosen reviewer will be one of the original reviewers of the study. If both of the original reviewers are no longer IRB members, the reviewer chosen for the amendment will be a current Board member who has expertise in the area of the study.

All members of the reviewing Board, including alternate members, will receive the OHR-12 and all modified materials. All materials and documents submitted for review are posted on the electronic submission portal one week prior to the IRB meeting. The assigned reviewers and all Board members have access to all materials posted.

The Primary Reviewer(s) will be present and discuss the amendment at the convened meeting of the Board. The amendment will be handled by the Board as is done for new studies (Policy RR 401) and continuing reviews (Policy RR 402).

4.4. Approval of Amendments
The recommendation to approve or not approve will be made as described in Policy OP 206. A formal approval letter for the amendment will be released to the Investigator along with an IRB-approved revised consent form, if consent form changes were required.
4.5. Full and Expedited Review of Amendments

As cited in 45 CFR 46.110, and IRB may use the expedited review procedure to review certain types of research involving no more than minimal risk and for minor changes in previously approved research during the period for which approval is authorized. In conducting the review, the reviewer(s) may exercise all of the authorities of the IRB except that the reviewer(s) may not disapprove an expedited amendment as the term is used at 45 CFR 46.110(b). In this case the proposal must be revised, re-submitted in full, and reviewed by a convened Board. The IRB uses required criteria for approval for all reviews of research including reviews of modifications to previously approved research when the modification affects a criterion for approval.

The Associate Director, or Director, OHR, will preview each amendment to determine the level of IRB review required.

The following categories of amendment must receive convened IRB review:

- Amendment changes risk/benefit ratio of study
- Amendment substantially alters science of study
- Amendment requires special expertise for review
- Amendment provides new information that may affect a subject’s decision to continue participation

Also to be considered when making determination:

- Is enrollment open or closed?
- Are subjects currently receiving treatment?
- Is the amendment to be implemented at TJU, or is it being submitted for administrative purposes only?

Modifications that are minor exclude procedures that involve more than minimal risk or do not fall into categories (1)-(7) of research that can be reviewed using the expedited procedure. Consequently, minor amendments can be reviewed using an expedited review procedure. Examples of minor amendments include but are not limited to:

- The addition of research activities that qualify for exemption or fall under an expedited review category
- Advertising
- A minor increase or decrease in the number of participants
• Narrowing the inclusion criteria

• Broadening the exclusion criteria

• Changes to the dosage form (e.g., tablet to capsule or liquid) of an administered drug when the dose and route of administration remain constant

• An increase in the number of safety visits for the purpose of increase safety monitoring

• A decrease in the number of study visits, provided the decrease does not affect the collection of information related to safety evaluations

• Changes in remuneration

• Changes to improve the clarity of statements or to correct typographical errors, provided that the change does not significantly alter the content or intent of the statement

• The addition or deletion of qualified investigators

• The addition or deletion of study sites

• Minor changes specifically requested by other university committees with jurisdiction over research

The amendment will be given expedited review by the Director, Associate Director, Chair, and/or designated IRB members as appropriate.

All expedited amendments will be entered onto the agenda and minutes of the appropriate Board meeting for information, auditing and record-keeping purposes only. As soon as an expedited amendment is approved and approval letter and stamped materials may be released to the Principal Investigator, and the amendment may be implemented.

5. Tools
OHR-12 Amendment to Research Protocol Form
1. **Purpose**
   To provide information to individuals conducting human subjects research regarding how to close out a study after completion of all aspects of the study.

2. **Responsibility for Executing the Policy**
   - Principal Investigator
   - Study Team Members
   - OHR Administrative Staff for Continuing/Final Review

3. **Policy Statement**
   This policy describes the procedure whereby an investigator must notify the IRB when a human subjects research project has been completed.

4. **Procedures**
   4.1. **Studies Involving Subjects**
   Study completion means that all activities involving subject follow-up and/or analysis of identifiable patient information, including any access to patient records for data confirmation, have been completed. Upon study completion the Principal Investigator must submit, in a timely manner, a final report to the IRB using the OHR OHR-9 *Continuing Review/Final Report Form*. The investigator must complete the progress report section (Section C or D, as relevant) covering the entire period of the study so that the IRB will be able to determine the success of the study relative to the initial IRB approval. The final progress report should include a brief summary of the success/outcomes of the trial, success or failure of enrollment, retention problems, unanticipated problems, impact of the research on standard of care, and potential future directions for the research.

   If all requested documentation has been submitted, the OHR administrative staff will review the IRB file for completeness, and place the Final Report on the agenda for the next appropriate meeting of the convened IRB. The Final Report will be assigned to the Chair of that IRB and be given expedited review. If the Final Report is considered to be complete and approved by the Chair, the IRB will be so informed for information only at its meeting and the information recorded in the minutes of the meeting.

   4.2. **Studies Involving Chart or Film Reviews**
   For a completed chart or film review, the IRB requires a Final Report within 30 days of completion of the study.
4.3. Studies Declared Exempt
   For completed exempt studies, a Final Report is required in the form of a letter to the IRB rather than the submission of the OHR-9 form simply stating that the study has been completed as originally approved by the IRB.

5. Tools
   OHR OHR-9 Continuing Review/Final Form
1. **Purpose**
   Provide direction for the review and approval of advertisements.

2. **Responsibility for Executing the Policy**
   Associate Director, OHR
   IRB Chair/Vice Chair
   IRB Members

3. **Procedures**
   The IRB will review advertising that is intended to be seen or heard by a prospective subject to solicit their participation in the study, or to solicit interest from other healthcare workers in referring participants to the study.

   The IRB need not review and approve listing of clinical trials on a web site or in a booklet when the system format limits the information presented to basic trial information such as: Title; Purpose of the Study; Protocol Summary; Basic Eligibility Criteria; Study Site Location; and How to Contact the Site for Further Information.

   The IRB or primary reviewer must review the information contained in the advertisement, and the mode of communication. No advertising may be used until the IRB or primary reviewer has approved it.

   Any review of an advertisement should assure that the advertisement does not:
   - State or imply a favorable outcome or other benefit beyond what is stated in the consent form and the protocol;
   - Make claims, either explicitly or implicitly, that the drug, biologic or device is safe or effective for the purposes under investigation;
   - Make claims, either explicitly or implicitly, that the drug, biologic or device is known to be equivalent or superior to any other drug, biologic or device;
   - Use terms such as “new treatment”, “new medication” or “new drug”;
   - Promise “free medical treatment” when the intent is only to say that the subjects will not be charged for taking part in the investigation.
   - Inappropriately emphasize payment for participation (e.g., no money amounts, inappropriate wording)
   - Include any exculpatory language.
These criteria apply to initial review, continuing review and review of modifications.

Advertisements to recruit subjects should be limited to the information necessary for potential subjects to determine their interest or eligibility. When appropriately worded, the following items may be included in the advertisement:

- The name and address of the investigator and/or the research facility;
- The condition under study and/or the purpose of the research;
- A summary of the criteria that will be used to determine eligibility for the study;
- A brief list of benefits, if any, and any significant risks;
- The time or other commitment required of the subject;
- The location of study and the person or office to contact to volunteer or for further information.

Final copies of all advertising materials including printed advertisements or audio or videotaped advertisements must be reviewed by the OHR before they are implemented at THU/TJUH.
1. **Purpose**
   The Policy will define the criteria to be used by a reviewer and the IRB when reviewing proposed payments, and the procedures to be followed.

2. **Responsibility for Executing the Policy**
   - Director/Associate Director, OHR
   - IRB Chair/Vice Chair
   - Principal Investigator

3. **Procedures**
   The IRB should assure that payment is appropriately presented for what it is, recruitment incentive and compensation for participation, by assigning it to the Payment section of the consent form. No reference to payments should be made in the Benefits section. All information about the amount and schedule of payments for participation should be included in the consent form.

   The IRB must assure that the amount and schedule of payments are neither coercive nor present undue influence. The payment amount should be neither excessive, thereby potentially presenting undue influence on the subject to participate, or exceedingly small, thereby undervaluing the subject’s commitment of time and effort to the study.

   Furthermore, the payment schedule should not be structured in such a way that the subject’s voluntariness in participating might be coerced by the desire to obtain the payment. Payment for participation should not be contingent upon completion of the entire study, but prorated to include payment for each visit or test, as appropriate. Payment of a small portion as an incentive to complete the study is acceptable provided that the amount is not coercive or so large as to unduly induce subjects to remain in the study when they would otherwise have withdrawn. Payment to participants who have withdrawn from the study may be made at the time they would have completed the study.

   Compensation for participation in a trial offered by a commercial sponsor may not include a coupon good for a discount on the purchase price of the product once it has been approved for marketing, because this unduly implies that market approval of the test article is guaranteed.
Special attention should be paid to payments in pediatric studies, as in many cases, the payment goes to the parent and not the child. In these situations, the IRB needs to assure that the parent is not being unduly influenced by the payment to enroll the child, especially since the child is subservient to the parent’s decision. Children are federally designated as a vulnerable subject population, but they also can be vulnerable to coerced decision-making on the part of their parents.
1. **Purpose**
   To delineate the criteria by which the recruitment of subjects will be evaluated.

2. **Responsibility for Executing the Policy**
   Associate Director, OHR
   IRB Chair/Vice Chair
   IRB Members
   Principal Investigator

3. **Procedures**
   Recruiting methods, including advertising and payment arrangements to subjects, the University or Investigators, can affect the equitable selection of subjects and an appropriate informed consent process. Consequently, the IRB will systematically review proposed recruitment processes to judge whether they fulfill the regulatory requirements of informed consent.

   Certain payment arrangements (Policy RR 411) between sponsors, organizations, investigators, and those referring potential subjects ultimately may place participants at risk of coercion, undue influence or may cause inequitable selection of subjects. These arrangements should receive careful review by the IRB to determine whether they are ethical and approvable.

3.1. **Procedures Applicable to the Research Subject**
   When assessing whether recruitment of subjects is both ethical and equitable and follows federal regulations and IRB policy, the IRB must take the following criteria into consideration:
   - The inclusion/exclusion criteria
   - Venues in which advertising about the study will appear
   - The setting in which the potential subject is approached for recruitment
   - The intended populations of potential subjects to be approached for recruitment
   - Whether potential subjects are vulnerable to coercion or undue influence, by nature of their situation, social status, level of education, health status, cognitive ability, etc.
   - Whether any payment or non-monetary incentive to subject seems disproportionate to the procedures the subject will undergo
• That a sponsor compensating participants by offering a coupon good for a discount on the purchase price of the product once it receives marketing approval is prohibited

• Whether information concerning the amount and schedule of payments is clearly set forth in the consent document and the amount is reasonable and not excessive

The IRB may decide that certain recruitment procedures need to be eliminated or modified to avoid the possibility of the subject feeling coerced into participating in the research. The IRB may also require changes to the recruitment process to make the recruitment of potential subjects more equitable.

3.2. Procedures Applicable to the University, Investigators and Key Personnel

In order for the University and its investigators and key personnel to remain unbiased in the conduct of human subjects research and protect against undue influence or inequitable selection of subjects, the following payments to researchers or the University are not permitted under this policy:

• Entering into a human subjects research agreement that contains an enrollment incentive provision.

• Acceptance of or a request for an enrollment incentive by the University, its investigators, or subcontractors.

• Fees paid to the researcher or University that exceed the actual costs for recruiting human subjects.

• Bonuses, milestones, or similar forms of additional payments to the researcher or University for timely, early, or over-enrollment of human subjects, for retention of human subjects, or for timely or early IRB approval.

• Use by the sponsor of per subject payment rates that vary based only upon the number of human subjects enrolled, including increased per subject rates paid for over-enrollment of subjects.

• Extra-contractual benefits acquired by the researcher or University such as unrestricted research gifts, medical or office equipment, authorship rights, journal subscriptions, educational stipends, payment of conference fees, software, personal gifts, favors, or similar inducements provided in exchange for enrolling human subjects.

• Payment of referral or finder’s fees in exchange for the referral by a professional of the professional’s patients or clients as potential subjects in human subjects research.
• Obtaining human subjects through recruitment firms or persons whose practices are not consistent with this policy.

3.3. Recruitment of subjects through Private Medical Information (Recruiting from a practice for another investigators research).

The health care provider (personal physician or physician director of a practice) must 1) approve contacting his/her or the practice’s patients for research purposes, 2) introduce the study to the patient, and 3) obtain the patient’s permission to be contacted by the study staff.

The health care provider may introduce the study either verbally during the course of medical care delivery, or through a recruitment letter.

The recruitment letter must be signed by the practitioner, or the practitioner and the investigator. In some cases, the letter may be signed by a physician representative on behalf of the entire practice (Department or Division head or clinical practice director).

The recruitment letter must contain the following:
  • Introduction of the researcher and the topic of the research
  • Purpose of the research
  • Brief description of what the subject’s involvement (may be simply a telephone interview to determine if inclusion criteria are met)
  • An “opt in” or “opt out” mechanism such as a number to call or a postcard to return within a specified time period (e.g., 10 days)
  • A statement that if there is no response indicating “opt out” within the specified time period, a research staff person may call.

Researchers may not contact potential subjects unless an “opt in” response has been received or an “opt out” decision has not been received within the specified time period.

All recruitment letters must be approved by the IRB.

3.4. IRB Review of Advertisements

The IRB will consider the following when reviewing advertisements:
  • The information contained in the advertisement.
  • The mode of its communication.
  • The final copy of printed advertisements.
The final audio or video taped advertisements.

The IRB will also ensure that advertisements do not:

- State or imply a certainty of favorable outcome or other benefits beyond what is outlined in the consent document and the protocol.

- Include exculpatory language.

- Emphasize the payment or the amount to be paid, by such means as larger or bold type.

- Promise “free treatment” when the intent is only to say subjects will not be charged for taking part in the investigation.

- Make claims, either explicitly or implicitly, about the drug, biologic, or device under investigation that are inconsistent with FDA labeling (When following FDA regulations).

- Use terms, such as “new treatment,” “new medication,” or “new drug,” without explaining that the test article is investigational (When following FDA regulations).

The IRB will review advertisements to ensure they are limited to the information prospective subjects need to determine their eligibility and interest, such as:

- The name and address of the investigator or research facility.

- The purpose of the research or the condition under study.

- In summary form, the criteria that will be used to determine eligibility for the study.

- A brief list of benefits to subjects, if any.

- The time or other commitment required of the subjects.

- The location of the research and the person or office to contact for further information.
1. Purpose
To delineate the criteria by which the IRB determines that research employing drugs or devices meets all FDA requirements.

2. Responsibility for Executing the Policy
Director/Associate Director, OHR
IRB Chair/Vice Chair
IRB Members
Principal Investigators

3. Procedures
If research involves an investigational drug or device the Principal Investigator (PI) will confirm that the IND or IDE numbers are valid by providing the IRB with one of the following:

- The sponsor protocol imprinted with the IND or IDE number
- A written communication from the sponsor documenting the IND or IDE number
- A written communication from the FDA documenting the IND or IDE number (required if an investigator listed on the protocol holds the IND or IDE)

If a study involves an FDA-regulated product, but no IND or IDE number is provided by the sponsor, the PI must confirm that the research meets one of the following IND or IDE exemptions:

3.1. IND Exemptions
3.1.1. Exemption 1
- The drug product is lawfully marketed in the United States.
- The investigation is not intended to be reported to FDA as a well-controlled study in support of a new indication for use nor intended to be used to support any other significant change in the labeling for the drug.
- If the drug that is undergoing investigation is lawfully marketed as a prescription drug product, the investigation is not intended to support a significant change in the advertising for the product.
• The investigation does not involve a route of administration or dosage level or use in a patient population or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product.

• The investigation is conducted in compliance with 21 CFR 50 and 56.

• The investigation is conducted in compliance with the requirements of 21 CFR 312.7.

3.1.2. Exemption 2
• The clinical investigation is for an in vitro diagnostic biological product that involves one or more of the following:
  o Blood grouping serum.
  o Reagent red blood cells.
  o Anti-human globulin.

• The diagnostic test is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established, diagnostic product or procedure.

• The diagnostic test is shipped in compliance with 21 CFR 312.160.

3.1.3. Exemption 3
• A clinical investigation involving use of a placebo if the investigation does not otherwise require submission of an IND.

If none of these exceptions are met then the sponsor must obtain an IND#.

3.2. IDE Exemptions (also see OHR Policy SC 501 regarding significant and non-significant risk devices)
• A diagnostic device, if the sponsor complies with applicable requirements in 21 CFR 809.10(c) and if the testing:
  o Is noninvasive.
  o Does not require an invasive sampling procedure that presents significant risk.
  o Does not by design or intention introduce energy into a subject.

• Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure.
• A device undergoing consumer preference testing, testing of a modification, or testing of a combination of two or more devices in commercial distribution, if the testing is not for the purpose of determining safety or effectiveness and does not put subjects at risk.

• A custom device as defined in 21 CFR 812.3 (b), unless the device is being used to determine safety or effectiveness for commercial distribution.

If the IDE exceptions are not met, the sponsor must obtain an IDE# from the FDA.

If the sponsor determines that a device involves non-significant risk and does not meet the above requirements, then the investigator will ensure that the research will be conducted in accordance with the following abbreviated IDE requirements:

• Consent will be obtained from each subject under the investigator’s care in accordance with 21 CFR 50

• The PI will document the consent accordingly, unless documentation is waived.

• The device is not a banned device.

• The sponsor labels the device in accordance with 21 CFR 812.5.

• The sponsor obtains IRB approval of the investigation after presenting the reviewing IRB with a brief explanation of why the device was not a significant risk device, and maintains such approval.

• The sponsor ensures that each investigator participating in an investigation of the device obtains from each subject under the investigator’s care, consent under 21 CFR 50 and documents it, unless documentation was waived.

• The sponsor complies with the requirements of 21 CFR 812.46 with respect to monitoring investigations.

• The sponsor maintains the records required under 21 CFR 812.140(b) (4) and (5) and makes the reports required under 21 CFR 812.150(b) (1) through (3) and (5) through (10).
• The sponsor ensures that participating investigators maintain the records required by 21 CFR 812.140(a)(3)(i) and make the reports required under 812.150(a) (1), (2), (5), and (7).

• The sponsor complies with the prohibitions in 21 CFR 812.7 against promotion and other practices.

3.3. Submission to the IRB
Complete all required information regarding investigational drugs or devices in the OHR-2, Part C.

Attach any FDA correspondence regarding IND or IDE applications to the submission.
1. **Purpose**
   To distinguish between a significant risk (SR) device and a non-significant risk (NSR) device and to indicate the procedure the IRB must follow when reviewing studies involving such devices.

2. **Responsibility for Executing the Policy**
   - IRB Members
   - Principal Investigators
   - OHR Administrative Staff

3. **Policy Statement**
   The Investigational Device Exemption (IDE) regulations (21 CFR part 812) describe two types of investigational devices, SR and NSR. An “investigational device” is defined here as a device whose safety and/or effectiveness is being evaluated in a clinical trial and which therefore falls under the IDE regulations. Other devices being used in a clinical trial whose safety and/or effectiveness are not being evaluated do not fall under IDE regulations. Investigational devices that are determined to be SR devices are governed by IDE regulations at 21 CFR 812.3. Investigational devices that are determined to be NSR devices are governed by the abbreviated requirements at 21 CFR 812.2(b).

   The major differences regarding research involving these devices are in the approval process and in record keeping and reporting requirements. NSR device studies do not require an IDE application to be submitted to and approved by the FDA. Furthermore, sponsors and IRBs do not have to report the IRB approval of a NSR device study to the FDA. In NSR device studies, the IRB serves an essential function for the FDA by acting as its surrogate with respect to the review, approval and continuing review.

   Investigators employing investigational devices will certify on the OHR-2 form that they will observe their responsibilities regarding such use (21 CFR 812 subpart E).

4. **Procedures**
   4.1. The IRB Decision Process for a Device Study
4.1.1. What is a Significant Risk (SR) Device?
Under 21 CFR 812.3 (m), a significant risk device means an investigational device that:

- Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject;
- 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;
- 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
- Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

4.1.2. What is a nonsignificant Risk Device?
An NSR device is one that does not meet the definition for a SR device.

4.2. IRB Review
4.2.1. Nonsignificant Risk Device Studies
If an investigator or sponsor proposes a study to the IRB that involves a NSR device, the IRB must review the study at a convened meeting.

The investigator or sponsor must provide the IRB with:

- An explanation of its determination of the device as NSR;
- The rationale used in making its risk determination [(21 CFR 812.150(b)(10)];
- A description of the device;
- Reports of prior investigations with the device;
- Information about other IRBs and their determinations;
- A risk assessment and the rationale for the determination of risk;
- Any other information that an IRB would need to review and approve the study.
The risk determination should be based on the proposed use of the device in the specific investigation and not on the device alone. The IRB must consider any potential harm that may result from the use of the device. The IRB may consult with the FDA for its opinion.

The IRB may agree or disagree with a sponsor’s or independent investigator’s initial NSR assessment. If the IRB agrees with the assessment that the study involves a NSR device and approves the study, the study may begin when the investigator receives the approval letter from the IRB. Submission of an IDE application to the FDA is not required.

If the IRB disagrees with the sponsor’s designation of the device as NSR, the sponsor must notify the FDA that the IRB has made a SR determination. In this case the study can be conducted as a SR study only after the FDA approves an IDE and an IRB approves the investigation.

Once the NSR/SR decision has been made by the IRB, the IRB must determine whether the study should be approved. The criteria for approval are the same as those for any other FDA regulated study (21 CFR 56.111). Generally, NSR studies require review at a convened meeting of the IRB. In some cases, a study involving a NSR device may qualify as minimal risk, in which case, the IRB may review the study under its expedited review procedure (21 CFR 56.110).

4.2.2. Significant Risk Device Studies
In deciding if a device to be employed in a study poses a significant risk, the IRB must consider the nature of the harm that may result from the use of the device. Studies where the potential harm to subjects could be life threatening, could result in permanent impairment of a bodily function or permanent damage to a body structure, or could necessitate medical or surgical intervention to preclude permanent damage to body structure should be considered a SR device. If the subject must undergo a procedure as part of the investigational study, e.g., surgery, the IRB must consider the potential harm that could be caused by the procedure in addition to the potential harm caused by the device.

The FDA considers studies of investigational SR devices to present more than minimal risk and requires IRB review at a convened meeting. The FDA has the ultimate decision in determining if a device is SR. If a sponsor files an IDE with the FDA because it believes the device to be a SR and the FDA disagrees (or does not accept SR designation), the FDA will return the IDE application to the sponsor and the IRB will be responsible for determining whether it represents a NSR device.
4.3. IRB Responsibilities following SR/NSR Determination

Following determination of SR/NSR status, the IRB will:

- Notify the sponsor and investigator of an SR decision

- Review the study according to the requisite criteria (21 CFR 56.111). If study received SR designation, review will occur only after the sponsor obtains the IDE.

- Document the SR/NSR determination in the minutes of the convened IRB by referencing the OHR-25.

The IDE status for the study is documented with a copy of the IDE approval letter from the FDA.
1. **Purpose**
   To describe the procedures by which TJU participates in the National Cancer Institute (NCI) Central IRB (CIRB) review of multicenter oncology trials conducted by NCI-established cooperative groups.

2. **Responsibility for Executing the Policy**
   - Director/Associate Director, OHR
   - IRB Chair/Vice Chairs
   - KCC Clinical Trials Office (CTO), Regulatory Division
   - KCC Network Regulatory Personnel
   - Principal Investigators

3. **Policy Statement**
   The OHR and its IRBs have agreed to participate in the NCI CIRB independent review model by acceptance of oncology studies given prior approval by the CIRB. In participating in the NCI model, the TJU IRB, pursuant to a fully executed IRB Authorization Agreement (IAA), agrees to the division of responsibilities as outlined in the IAA that covers the "independent model." In that model, the signatory institution (TJU) agrees to provide the CIRB with local context considerations including but not limited to the following:
   - State and local laws
   - Conflict of Interest policies
   - Boilerplate language for inclusion in the consent document

4. **Procedures**
   Prior to TJU IRB acceptance of an NCI CIRB-approved study, the study must be reviewed by the Kimmel Cancer Center Protocol Review Committee (PRC) for competing trials and scientific merit.

   Once reviewed by PRC, the CIRB Acknowledgement Memo is uploaded to the TJU IRB electronic submission Portal and an IRB control number will be assigned.

   **JeffTrial:** Submission materials uploaded to JeffTrial include the following:
   - CIRB Materials: upload the CIRB Acknowledgement Memo
   - Protocol
   - Subject materials
• Consent form
• Investigator Brochure
• CIRB Approval letter

NO PAPER COPY will be submitted to the TJU IRB.

The IRB will be notified of this transaction through its inclusion in the meeting minutes of the next convened Board.

Responsibilities of the signatory institution include but are not limited to the following:

• Report to the CIRB potential unanticipated problems or serious or continuing noncompliance.

• Merge the CIRB-approved local boilerplate text into the CIRB-approved consent document.

• Insure the conduct of research at Affiliate Institutions is monitored by the same office as the Signatory Institution.

• Insure that the boilerplate language and Institutional requirements are consistent with those of the Signatory Institution.

TJU reserves the right to independently audit and conduct investigations into alleged noncompliance in accordance with TJU Policy and to review and act upon reports of unanticipated problems in accordance with TJU OHR policy.

If there is a decision to send a CIRB-approved study to a convened IRB for review, the IRB will follow the usual procedures for review and approval of a new study, and will assume oversight for the study. The IRB may choose to use the CIRB documents in its consideration of the protocol and consent form.

The responsibilities of the NCI CIRB and the Signatory Institution are provided in detail in the attachment to the fully executed IAA which is kept on file in the OHR office.

5. References
CTO Policy 120 “Policy for CIRB Process for Cooperative Group Trials”
1. Purpose and Introduction
To delineate the policy and procedure for IRB review, approval, and supervision of a proposal involving a humanitarian device exemption (HDE).

Humanitarian Use Devices (HUDs) are devices that are intended to benefit patients by treating or diagnosing a disease or condition that affects fewer than 4000 individuals in the United States per year. Because of the high cost of conducting large-scale clinical trials for devices designed for small target populations, the FDA has determined that use of a HUD under an HDE is not considered research and thus there is no requirement for presenting the results of scientifically valid clinical investigations demonstrating effectiveness. However, sufficient information must be presented for the FDA to determine that the device does not pose an unreasonable or significant risk of illness or injury, and that the probable benefit to health outweighs the risk of illness or injury from its use.

Although use of a HUD under an approved HDE is considered clinical care and not research, FDA requires that the IRB review and regulate the clinical protocol, much as it would a research protocol.

2. Responsibility for Executing the Policy
Institutional Review Boards
Principal Investigators
Administrative Staff, OHR

3. Policy Statement
An approved HDE authorizes marketing of the HUD. However, an HUD may only be used in facilities where an IRB has approved the use of the device to treat or diagnose the specific disease and will supervise clinical testing of the device. The labeling for the HUD must state that the device is a HUD and that, although federal law authorizes the device, the effectiveness of the device for the specific indication has not been demonstrated.

HDE applications do not have to be renewed by the FDA and are valid as long as the use of the device continues to meet the conditions of the HDE application. An IRB approved HUD protocol does, however, require periodic continuing review for the duration of its use at the institution.

4. Procedures
4.1. Responsibilities of the IRB regarding HDEs
The IRB will consider the following items that are generally included in the HDE application:
• The generic and trade name of the device

• The FDA HDE number (6 digits)

• The date of the HUD designation

• Indications for the use of the device

• Description of the device

• Determination that the sponsor has determined the device does not pose an unreasonable or significant risk of illness or injury and that the probable benefit to health outweighs the risk of illness or injury from its use.

• Demonstration that no comparable devices are available for that purpose and that they could not otherwise bring the device to market without receiving HUD status.

• Any contraindications, warnings, and precautions for the use of the device

• Adverse effects of the device on health

• Alternative practices and procedures

• Marketing history

• Summary of studies using the device

The IRB must conduct both initial and continuing review of the HUD and monitor adverse events. Approval may be granted for a maximum one year or less depending on the perceived risk.

4.2. Initial Review

Initial IRB approval of the HDE application must be performed at a convened meeting of the IRB. The IRB need not approve individual uses of an HUD, but rather may approve the use of the device without any restrictions as long as the use remains within the scope of the FDA-approved indication. Determination of significant vs. non-significant risk by the IRB is not required since the device is being used for clinical care.
Regulations do not require the use of an IRB approved consent form for HUDs, but a consent form may be required by the IRB. The IRB can also require that both the investigator and the subject sign the Device Brochure to indicate that the subject and the investigator have had a discussion about the HUD and that the subject has understood the use of the device and its potential risks.

4.3. Continuing Review
Continuing review must follow the requirement found at 21 CFR 56. The FDA has determined that the IRB may elect to conduct the review using expedited review procedures since the initial review was performed by a convened IRB and the use of the HUD within its approved indication(s) does not constitute research.

The use of an HUD outside its FDA approved indication(s) (e.g. in a clinical research trial for another indication) requires an IRB submission as per FDA regulations for an Investigational Device Exemption (IDE) 21 CFR 812 and OHR Policy SC 501.

If an HUD is used in an emergency situation that is not within the FDA approved indication(s), the regulations at 21 CFR 814.124 and OHR Policy GA 112 apply.

4.4. Adverse Events
The IRB shall receive and review adverse event reports from the investigator.

5. Reference
See link below for FDA Guidance for HDE Holders, Institutional Review Boards (IRBs), Clinical Investigators, and FDA Staff - Humanitarian Device Exemption (HDE) Regulation: Questions and Answers.

http://www.fda.gov/RegulatoryInformation/Guidances/ucm110194.htm

OHR Policy SC 501, “Determining Whether a Device Study Involves a Significant Risk or Nonsignificant Risk”

OHR Policy GA 112, “Emergent Use of a Drug, Biologic, or Medical Device”
1. **Purpose**
   To describe the policy and procedures for IRB review of the enrollment of pregnant women and non-pregnant women of childbearing potential as subjects in clinical research.

2. **Responsibility for Executing the Policy**
   - Director/Associate Director, OHR
   - IRB Chair/Vice Chair
   - IRB Members
   - Principal Investigator
   - Research Coordinators

3. **Policy Statement**
   Research involving pregnant women raises multiple ethical and regulatory issues. The Department of Health and Human Service (DHHS) amendment to 45 CFR Part 46, Subpart B, 201-21, "Additional Protections for Pregnant Women and Human Fetuses involved in Research" became effective March 19, 2001. The rule supports all of the special protections for pregnant women and fetuses involved in research that have been in force since 1975.

   Pregnancy encompasses the period of time from implantation to delivery. A woman shall be assumed to be pregnant if she exhibits any of the presumptive signs of pregnancy such as missed menses, until the results of a pregnancy test are negative or until delivery. [45 CFR 46, Subpart B, 202(e)]

   A major distinction is that the original rule did not permit inclusion of a pregnant woman as a research subject unless the purpose was to attend to the health needs of the mother, and the fetus was placed at risk only to the degree necessary to treat the mother, and required the permission of both parents.

   The amended rule aims to promote a policy of presumed inclusion of pregnant women in clinical trials. This inclusion was accomplished by the removal of the previous requirement for paternal consent which led to the exclusion of many women from protocols that were expected to have direct benefit for pregnant women. Thus the pregnant woman became the sole decision maker as to participation.
Under Thomas Jefferson University’s FWA, Subpart B will be applied to all research that is funded by a federal agency. While Jefferson’s FWA does not apply to non-federally-funded human subjects research, Jefferson does extend the spirit, if not the letter, of the Common Rule to all human research at Jefferson. Except when deemed appropriate by the IRB, some flexibility in interpretation and application of the federal regulations at Subpart B is allowed.

3.1. Inclusion of Pregnant Women
Federal regulations concerning research on women who are pregnant specify that no pregnant woman can be involved as a subject unless the purpose of the research is to meet the health needs of the mother, the fetus will be placed at risk only to the minimum extent necessary to meet such needs, and the research presents minimal risk to the fetus.

3.2. Inclusion of Non-pregnant Women of Childbearing Potential
It must be assumed that pregnancies will occur as a result of the inclusion of non-pregnant women of childbearing potential as subjects in clinical trials. This presents problems for IRBs regardless of advice to use precautions. The IRB must evaluate the various safeguards that might be proposed that would afford some increase in subject safety such as frequent pregnancy tests, reliable means of contraception, and abstinence.

4. Procedures
The consent document should include a clear statement about risks to the subject and the embryo or fetus and the potential for birth defects if pregnancy were to occur.

Generally, women of childbearing potential should not be included in a trial if teratogenicity (malformations of development) is likely, since the risk of malformation of the fetus far outweighs any societal benefit. The IRB should also be aware that the risks of a teratogenic compound might be transferred between the sexes. A drug with the potential to affect an individual’s DNA may be given to a man who may impregnate a woman who is unaware of the risk.

4.1. Duties of IRB when research involves pregnant women, or fetuses, prior to delivery.
The Investigator Brochure should be carefully reviewed by a physician reviewer to ensure that appropriate animal studies have been completed that have not indicated fetal loss, birth deformities, low birth weight, and reduced survival as well as mutagenicity.

The protocol should be carefully reviewed for opportunities to reduce the risk benefit ratio for both the mother and the fetus, and the minutes of the convened IRB meeting should reflect the discussion regarding the protection of the mother and the fetus. The risks to the mother and the fetus should be considered separately. If the risk to the fetus is increased by enrollment of the mother in the
study, then the father, if available, should be a participant in the consent process. The protocol should have clear plans for follow-up of the pregnant woman up to and after delivery.

When the IRB considers such research, it must satisfy all of the conditions specified in 45 CFR, Subpart B, sec 203, 204, as cited below:

- Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses.

- The risk to the fetus in not greater than minimal, or any risk to the fetus that is greater than minimal is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or fetus.

- Any risk is the least possible for achieving the objectives of the research.

- The woman’s consent or the consent of her legally authorized representative is obtained in accord with the informed consent provisions of 45 CFR Part 46, subpart A, unless legally waived or altered.

- The woman or her legally authorized representative, as appropriate, is fully informed regarding the reasonably foreseeable impact of the research on the fetus or resultant child.

- For children, as defined in 45 CFR 46.402(a), assent and permission must be obtained in accord with the provisions of 45 CFR 46, subpart D.

- No inducements, monetary or otherwise, will be offered to terminate a pregnancy.

- Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy.

- Individuals involved in the research will have no part in determining the viability of fetus.

5. Reference
45 CFR 46, Part B, sec 202, 203
1. **Purpose**
   To define the requirements for the review of research involving prisoners as subjects in human research.

2. **Responsibility for Executing the Policy**
   Director/Associate Director, OHR
   Principal Investigator
   IRB Chair/Vice Chair
   IRB Members

3. **Policy**
   The IRB shall apply additional protection as necessary to protect research subjects that are potentially vulnerable to coercion in regard to autonomy, conditions that may affect risk/benefit determinations, or unequal burden in research (Belmont Report). When an IRB regularly reviews research involving a vulnerable population, at least one individual, whether a member or a consultant who is knowledgeable about and experienced in working with such subjects, should be present at the meeting when the study is discussed.

   If an investigator indicates to the IRB that prisoners will participate in his/her research, or if a subject(s) enrolled on a research protocol may reasonably be expected to be or is incarcerated at some time during his/her enrollment, additional requirements will apply to IRB review of the study (45 CFR 46 Subpart C) if funded by the Department of Health and Human Services (DHHS).

   The IRB may approve DHHS funded research only if it finds that the following conditions have been met:

   3.1. The IRB will certify to DHHS through the Office for Human Research Protections (OHRP) that the IRB has reviewed the research under the conditions required by the federal regulations and that the research falls within the permissible categories.

   The research will not begin until OHRP verifies that the research falls into one of the following permissible categories:

   - The projected research involves practices which have the intent and reasonable probability of improving the health and wellbeing of the prisoner subjects. The IRB may approve studies where some prisoners are assigned to a control group, and thus may not benefit from participation. The FDA has published notice in the Federal Register of its intent to permit such research.
• Research on conditions affecting prisoners as a class (e.g. vaccine trials on hepatitis or HIV) provided that the Secretary, DHHS, has published notice of its intent to approve such research.

3.2. Any possible advantages accruing to the prisoner through participation in the research, when compared to general living conditions, medical care, quality of food, amenities, and opportunities for earnings in prison, should not be of such a magnitude that the prisoner’s ability to weigh the risk(s) and potential benefit of the research in the limited-choice environment of the prison is unduly influenced.

3.3. The risks involved in the research are commensurate with the risks that would be accepted by non-prisoner volunteers.

3.4. Selection procedures within the prison or prison population are fair to all prisoners and not subject to arbitrary intervention by prison authorities or other prisoners. Prisoners selected as control subjects must be selected randomly from the group of eligible prisoners unless the Principal Investigator provides justification to the IRB in writing for employing some other procedure.

3.5. Information provided to prisoner subjects is presented in language that is appropriate for the subject population.

3.6. Adequate assurance has been obtained that the Parole Board(s) will not take into account the prisoner’s participation in the research when making decisions regarding parole. Each prisoner will be informed in advance that participation in the research study will have no effect on his/her parole.

3.7. At the end of the prisoner-subject’s participation in the research, adequate provision has been made for follow-up examination or care that takes into account the varying lengths of prisoner sentences, and of ways for informing participant of this fact.

If a subject in a DHHS funded research study becomes incarcerated after enrollment in an on-going study, the Principal Investigator must immediately inform the IRB in writing.

After receiving the Principal Investigator’s notification of prisoner status for one of the subjects, the IRB must review the protocol again at its earliest opportunity with a prisoner or prisoner advocate as a voting member of the convened Board.
The IRB can either approve the involvement of the prisoner–subject in the research in accordance with this policy, or determine that the subject be withdrawn from the study. In addition, the IRB should assure, when appropriate, that the consent document stipulates that any subsequent incarceration of a research subject may result in the termination of the subject’s participation by the investigator without the subject’s consent.

The OHRP has provided the following clarification regarding Part C definition of prisoners and parolees: (1) parolees who are detained in a residential treatment center as a condition of their parole are considered prisoners for purposes of research taking place within that facility; (2) prisoners living within the community and sentenced to court-supervised monitoring or treatment regardless of whether they are described as parolees or probationers are not considered prisoners; (3) prisoners wearing monitoring devices are generally not considered to be prisoners. However, situations of this type may require an analysis of the particular circumstances of the planned subject population.

4. Procedures
4.1. IRB Responsibilities for Review of DHHS funded Research Involving Prisoners
The IRB will take into consideration all applicable federal and University policies, as well as the additional requirements for prisoners to participate in research as described in 45 CFR 46, Subpart C. While the TJU IRB is not obligated under its FWA to apply Subpart C to non-DHHS funded research, Subpart C regulations will be followed as closely as is reasonably possible.

The IRB may not review or make determinations regarding studies involving prisoners as a target population unless the Board has a voting member who qualifies as a bona fide prisoner advocate. Documentation of the expertise of the prisoner advocate will be provided by a curriculum vita.

When a research participant becomes a prisoner, and the IRB has not previously reviewed the proposal for prisoner populations, the IRB will conduct a review of the research proposal in accordance with Subpart C and determine one of the following:

- IRB review and approval is not required if the research interactions and interventions or the obtaining of identifiable private information will not occur during the incarceration period;

- Withdrawal of the participant from the study is not necessary if the participant will not be placed at undue harm or risk;
• Approve research participation for non-prisoner participants, but approve participation of prisoner-participants as pending (if the seven required findings in 45 CFR 46.305(a) have been met) and the IRB is awaiting confirmation from OHRP that the proposed research falls within the categories of research permissible under 45 CFR 46.306(a)(2). All interactions and interventions with, including obtaining identifiable private information, must cease for these prisoner-participants until the requirements of Subpart C have been satisfied with respect to the relevant protocol.

• Approve research participation for non-prisoner participants but defer participation for prisoner-participants if the seven required findings in 45 CFR 46.305(a) have not been met to the satisfaction of the IRB. All interactions and interventions with, including obtaining identifiable private information, must cease for these prisoner-participants until the requirements of Subpart C have been satisfied with respect to the relevant protocol.

NOTE: OHRP has allowed one important exception. If the Principal Investigator asserts that it is in the best interests of the participant to remain in the research study while incarcerated, the IRB Chairperson may determine that the subject may continue to participate in the research until the requirements of Subpart C are satisfied.

For studies that were not intended to include prisoners, the IRB must determine which of the following situations applies:

• Non-prison study (not previously reviewed and certified under Subpart C) in which participant has become incarcerated (or otherwise fits the definition of prisoner in 45 CFR 46.303(c)) and the PI wishes to continue the individual's participation in the study.

• Non-prison study with at-risk population (i.e., probationers, substance abusers).

• Non-prison study, majority of study population are non-prisoners but PI seeks to enroll some prisoners (as defined in 45 CFR 46.303(c)).

• Minimal risk DHHS conducted or supported epidemiologic research, majority of study population are non-prisoners but PI seeks to enroll some prisoners (prisoners are not the focus of the study) and the sole purpose of the study is either:
  o To describe the prevalence or incidence of a disease by identifying all cases;
  o To study potential risk factor associations for a disease.
o Initial Subpart C review of study designed to be conducted in a prison or using prisoners as defined in 45 CFR 46.303(c), the PI seeks to enroll already incarcerated subjects.

For DHHS-supported research, the University must certify to the Secretary (through OHRP) that an IRB designated under its Federalwide Assurance has made the seven findings required under 45 CFR 46.305(a), and a statement indicating that the IRB chose one of the four permissible categories of research in 45 CFR 46.306(a)(2). OHRP does not require that the prisoner letter include a specific listing or rationale behind the IRB findings. The institution may wish to include a brief, protocol-specific explanation of the IRB’s rationale for each finding.

The institution must indicate in the certification letter which of the four categories of permissible research involving prisoners in 45 CFR 46.306(a)(2) is applicable to the proposed research. Research involving prisoners can proceed only if the research fits under a category of permitted research under 45 CFR 46.306(a)(2). OHRP will make its own determination, based on the information in the prisoner certification letter, the protocol materials and the grant application as to whether any of the four categories apply to the proposed research.

The University must include a statement that indicates that the IRB was constituted as per requirements in 45 CFR 46.304. OHRP does not require that the prisoner certification letter include information about the manner in which the IRB fulfills the requirements of 45 CFR 46.304. The institution may wish to provide the name of the prisoner representative.

The following information must also be sent to OHRP: the protocol application (which includes the protocol and any IRB submission material); the grant application (including any grant award updates); and the prisoner certification letter containing the following information:

- FWA number;
- IRB number for the designated reviewing IRB;
- Site(s) where research involving prisoners will be conducted;
- If prisoner research site is "engaged in research", provide FWA #;
- DHHS Grant Award number;
- DHHS Funding Agency Name;
- Funding Agency Grants/Program Officer Name and Telephone #;
• Title of DHHS Grant;

• Title of Protocol (if the same as the title of the grant, indicate as such);

• Version date of the informed consent document to be used with prisoners;

• Date(s) of IRB Meeting(s) in which the protocol was considered and provide a chronology of: Date of initial IRB review; and/or

• Date of Subpart C reviews including: type of IRB review (initial, amendment, addendum, continuing review); and special IRB review for prisoner issues.

• Principal Investigator.

• Justification for the use of prisoners in the study. If applicable, delineate the protocol to be conducted in the prison from the overall project described in the grant application;

• Study objectives or study aims;

• Brief summary of study procedures;

• Customary treatment or services at the prison (or alternative to incarceration) research site(s) for the condition being studied;

• Description of how risks specific to a prison (or alternative to incarceration) setting are minimized; Whether the prison site(s) are "engaged in research" and whether they have obtained an assurance with OHRP;

• Whether a Certificate of Confidentiality was obtained by the PI for the study;

• Description of recruitment procedures in the specific prison (or alternative to incarceration) setting; and/or Description of how the consent form was altered for use with a prison population or specific prisoner and whether the subsequently incarcerated participant will be re-consented.

All prisoner research certification letters will be mailed to:
OHRP Prisoner Research Coordinator
Office for Human Research Protections (OHRP)
Department of Health and Human Services
The Tower Building
1101 Wootton Parkway, Suite 200
Rockville, MD 20852
4.2. Non-prisoner Participants
The IRB may approve the research for non-prisoner participants only if all the criteria in Subpart C are satisfied.

The IRB must inform the Investigator in writing that no prisoner-subjects can be enrolled or involved until the IRB/institution receives a letter from OHRP that acknowledges receipt of the prisoner certification and indicates the Secretary's (through OHRP) determination that the proposed research falls within the categories of research permissible under 45 CFR 46.306(a) (2).

5. Reference
OHRP Guidance on the Involvement of Prisoners in Research, May 23, 2003
1. Purpose
This Policy presents the federal regulations governing the enrollment of children and neonates and in clinical research and the procedures that investigators must follow in proposing a protocol involving this class of subjects and the procedures that the IRB must adhere to in reviewing and approving such a protocol.

2. Responsibility for Executing the Policy
Investigators
Research Coordinators
IRB Members
OHR Administrative Staff

3. Policy Statement
The Children’s Health Act of 2000 requires that all research involving children that is supported or regulated by the Department of Health and Human Services be in compliance with Subpart D of 45 CFR Part 46. The FDA has also adopted the provisions of Subpart D except for 46.408 (c) that pertains to the waiver of the consent provisions of 45 CFR, Subpart A. Under Thomas Jefferson University’s FWA, Subpart D will be applied to all research that is funded by a federal agency. While Jefferson’s FWA does not apply to non-federally-funded human subjects research, Jefferson does extend the spirit, if not the letter, of the Common Rule to all human research at Jefferson. Except when deemed appropriate by the IRB, some flexibility in interpretation and application of the federal regulations at Subpart D is allowed.

The additional safeguards of Subpart D require the IRB to determine the level of risk and the prospect of direct benefit presented to the child by the proposed research. Although enrollment of children in clinical trials presents difficult considerations for IRBs, such enrollment is important to the children because children differ markedly from both animals and adults and thus research using these as models cannot substitute as alternatives for testing agents in children. The lack of appropriate testing of agents in children will potentially increase their risk of harm from exposure to practices or treatments untested in children. Furthermore, new therapies or useful general knowledge concerning diseases or conditions specifically affecting children could not be developed.

Research in children requires that the IRB carefully consider the degree of risk, and possible benefit to the child involved in the research for this is at the core of the concept of beneficence when considering research in a pediatric population, and must be considered before the Board can realize that it has the authority to approve the study.
This Policy is to be considered in connection with OHR Policy IC 703, Policy and Procedures for Parental Permission and Child Assent to Participate in a Research Protocol, and Policy SC 704, Child Assent.

4. Procedures

4.1. Minimization of Risks

The IRB must ascertain whether the risks to children can be minimized, and must consider the risks from the prospective subject's point of view. The IRB members should be familiar with the ways in which research can be modified to minimize risks to children in particular. The investigators conducting the study should be properly trained and experienced in conducting research with the pediatric population and in the evaluation and management of adverse events in this population.

In addition to fulfilling the criteria stated in 45 CFR 46.111, the IRB can approve research involving children only if the research proposed falls into one of the following categories:

- The research presents no more than minimal risk to the child (§46.404).

- Research involving an intervention or procedure presenting greater than minimal risk to children, but offers the prospect of direct benefit or may contribute to the well-being of the individual child (§46.405).

- Research involving an intervention or procedure that presents only a minor increase over minimal risk yet does not offer any prospect of direct benefit or contribute to the wellbeing of the individual child.

If the IRB cannot determine that the research falls into one of the above categories it must disapprove the study.

Under 45 CFR 46.407, if it is felt that the research, not otherwise approvable, presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children, the study may be referred to the Secretary of the DHHS for review.

4.2. Research Presenting Greater Than Minimal Risk

The IRB can approve research on children that presents greater than minimal risk only if the risk is justified by the anticipated benefit to the subject, or the risk is only a minor increase over minimal risk and there is anticipation that the study is likely to yield generalizable knowledge about the subjects’ disorder or disease. Such knowledge must be considered essential for the understanding or amelioration of the subjects’ disorder or condition.
For the IRB to approve research under 45 CFR 46.405, it must be able to justify that not only is there a balance of risk and anticipated benefit, but the relation of the anticipated benefit to the risk must be at least as favorable to the subjects as that presented by the available alternatives. There must be "research equipoise" between two or more arms of a concurrently controlled trial, where one arm represents currently accepted practice, or between a single arm study and the alternatives available off study.

"Research equipoise" is a conceptual state where there is honest professional disagreement among experts about whether the experimental or the control treatment should be considered the preferred treatment or practice; i.e. there is genuine uncertainty about which intervention is better. Research equipoise does not require numeric equality of intervention risks and benefits, but only approximate equality. For example, an experimental intervention may pose more risk to subjects than accepted practice as long as it also offers the prospect of greater direct benefit to the subjects and the risk to potential benefit is within generally accepted practice guidelines.

4.3. Child Assent (Also see Policy IC 704)

An important part of research on children is the provision for obtaining and documenting child assent. In determining whether children are capable of assenting, the IRB shall take into account the age maturity, and psychological state of the children in the study population. This may apply to all of the children or on a case by case basis as determined by the IRB. A child’s assent to participate in a clinical trial protocol implies that he/she has agreed to participate after being fully informed about the study in lay language geared to the level of the child’s comprehension of the procedures involved and the attendant risks and benefits. Mere failure to object should not be construed as assent. How the assent process will be carried out must be clearly stated in the protocol. It is the presumption in Pennsylvania that an individual 18 years of age is of legal age and can sign for him/herself. While there is no specific age where assent is required under Pennsylvania law, in concurrence with the practice of other institutions, the University’s IRBs require that children age 7 to 17 be asked to indicate their assent on the assent form, or, if a child’s level of understanding and maturity permit, understanding and signing the parental permission form.

It is important to note that a pregnant female under the age of 18 is considered emancipated and thus is permitted to make decisions independent of parents. The same applies to an individual under the age of 18 that is living on his/her own and financially supporting them.
In addition to the child’s assent, one or more parents must give permission for the child’s participation on the study depending on the risk involved and whether a benefit is expected. If the risk is minimal, or if the risk is greater than minimal with the prospect of a direct benefit, the assent of the child and the permission of one parent are sufficient. If the risk is greater than minimal, but there is no prospect of a benefit, the child’s assent as well as the permission of both parents is required unless this is not possible for reasons stated in OHR Policy IC 703.

5. NIH Policy on Children
The “NIH Policy and Guidelines on the Inclusion of Children as Participants in Research Involving Human Subjects” applies to all initial applications/proposals involving human subject research supported or conducted by the NIH that will be funded under a Type I investigator-initiated grant (RO-1, RFP, contract etc.).

The NIH Guidance was developed because medical treatments applied to children are often based upon testing of drugs/devices only in adults and scientifically evaluated treatments are often less available to children because of reasons against their inclusion in research studies. The American Academy of Pediatrics has reported that only a small fraction of all drugs and biological products marketed in the U.S. have had clinical trials performed in pediatric patients and a majority of marketed drugs are not labeled for use in pediatric patients. Consequently, the goal is to increase participation of children in clinical research protocols so adequate data will be obtained to support treatment for disorders and conditions affecting them.

Under the NIH Policy, children, who are defined as individuals under the age of 21, must be included in all clinical trial protocols unless there are scientific or ethical reasons to exclude them. If children are not excluded, proposals must have a section entitled, “Participation of Children” that must: 1) describe plans for inclusion of children; 2) justify the age range used; 3) indicate the expertise of the research team with regard to children; 4) describe the facilities for the children and, 5) and indicate the number of children to be included in order to have sufficient power for meaningful analysis. It is expected that children will be included in NIH Type 1 research involving human subjects unless there are scientific or ethical reasons why the study cannot enroll children. If the intent is to exclude children, you must justify your exclusion by defending one or more of the following exclusionary circumstances.

- The research topic is irrelevant for children
- Children are barred from participation by law because of the risk
- Study is redundant; knowledge is being obtained in another study or is already available.
- Separate age-specific children study is preferable
• Rarity of the disorder makes inclusion of children extremely difficult

• The limited number of available children is already enrolled in a nationwide pediatric disease network

• Study design precludes direct applicability to children

• Insufficient adult data to judge potential risk for children

• Study design is a follow-up of an adult study

These issues must be addressed in the OHR-2, *Summary of the Research Protocol*.

6. **Children as Wards of the State or Other Agency**
   Under §46.409, children who are wards of the State or other agency can be included in research approved under § 46.404 or § 46.405, and may also be included in research approved under § 46.406 or § 46.40. If such research is: 1) Related to their status as wards; 2) conducted in schools, camps, hospitals, institutions where the majority of the children involved as subjects are not wards. If the research is approved under such conditions, the IRB shall require the appointment of an advocate for each child who is a ward, in addition to any other individual acting as guardian or in loco parentis. One individual may serve as an advocate for more than one child. The advocate must be an individual who has the appropriate background and experience and who agrees to act in the best interests of the child. This individual must not be associated in any way with the research, the investigator, or the guardian organization.

7. **Research Involving Neonates (45 CFR 46.205)**
   7.1. Viable Neonates
   A neonate after delivery that has been determined to be viable may be included in research only if the extent permitted by and in accord with the requirements of 45 CFR 46 Subparts A and D.

   7.2. Neonates of Uncertain Viability and Nonviable Neonates
   Individuals engaged in research will have no part in determining the viability of a neonate.

   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.
7.3. Neonates of Uncertain Viability

Until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research covered by this Subpart B unless the following additional conditions have been met. The IRB determines that:

- 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

- The purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means, and there will be no added risk to the neonate resulting from the research.

- The IRB will accept the consent of either parent or her legally authorized representative.

7.4. Nonviable Neonates

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

- Vital functions of the neonate will not be artificially maintained;

- No research procedure will 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 biomedical knowledge that cannot be obtained by other means.

The IRB will require the consent of both parents unless one parent is unable to consent due to unavailability, incompetence or incapacity. The IRB will not permit consent by a legally authorized individual for research involving a nonviable neonate.

8. Tools

DHHS requirements in 45 CFR Part 46, Subpart D for Research involving Children, as illustrated in the “NIH Policy and Guidelines on the Inclusion of Children as Participants in Research”.

OHR Internal Form OHR-2, Summary of the Research Protocol

45 CFR 46.205, Research Involving Neonates
1. Purpose
This Policy will define the requirements for the inclusion of women and minorities in research involving human subjects based on the NIH Revitalization Act of 1993, PL 103-43, and the subsequent NIH Policy and Guidelines as amended in October 2001, and provide a procedure for the enrollment of such individuals in clinical trials conducted at the University.

2. Responsibility for Executing the Policy
   Investigators
   Research Coordinators
   IRB Members
   OHR Administrative Staff

3. Policy Statement
   It is the policy of the NIH that women and members of minority groups and their subpopulations must be included in all NIH clinical research, unless a clear and compelling rationale and justification establishes to the satisfaction of the relevant Institute/Center Director that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research.

   Cost is not an acceptable reason for exclusion except where the study would duplicate data from other sources. Furthermore, women of childbearing potential should not be routinely excluded from participation in clinical trials.

   This policy applies to research subjects of all ages in all NIH-supported clinical research studies.

4. Procedures
   TJU Investigators developing a grant (contract proposal) submission to the NIH for a clinical trial must construct a research plan that addresses the inclusion of women and minorities and their subpopulations appropriate to the scientific objective of the study. The research plan should describe the composition of the proposed study population in terms of sex/gender and racial/ethnic group, and provide a rationale for selection of such subjects. Outreach programs for the recruitment of such subjects must be included in the research plan.
4.1. Investigator-initiated NIH-defined Phase III Clinical Trials

When an NIH Phase III clinical trial is proposed, the investigator must review the evidence whether or not clinically important sex/gender and race/ethnicity differences in the intervention effect(s) are to be expected. This evidence may include, but is not limited to, data derived from prior animal studies, clinical observation, metabolic studies, genetic, observational, natural history, epidemiology, and other relative studies.

Based on prior studies, the investigator must consider which of the following three situations will apply when planning, conducting, analyzing and reporting an NIH-defined Phase III clinical trial:

4.1.1. Prior studies support the existence of significant differences. If the data from prior studies indicate significant differences in the response of men and women to an intervention, then the Phase III clinical trial must be designed to answer two primary questions, one for men and the other for women, with adequate sample size for each.

The research plan or proposal must include a description of plans to conduct analyses to detect significant differences in intervention effect by sex/gender, racial/ethnic groups and relevant subpopulations, if applicable.

The investigator must include in his/her annual Progress Report cumulative subject accrual and progress in conducting analyses for sex/gender and race/ethnicity differences. Inclusion of the results of the sex/gender, race/ethnicity analysis in any publication submission is strongly encouraged. If the analyses reveal no differences, a brief statement to that effect is adequate.

The IRB must approve the final plan for analysis.

4.1.2. Prior studies support no significant differences. If the data from prior studies do not support a significant difference(s) of clinical or public importance in the intervention effect, then sex/gender, race/ethnicity will not be required as subject selection criteria. However, DHHS strongly encourages the inclusion and analysis of sex/gender and racial/ethnic subgroups.
4.1.3. Prior studies neither support nor negate significant differences. If data from prior studies neither support or strongly negate the existence of significant differences of clinical or public health importance of the intervention effect based on sex/gender, or race/ethnicity and relevant subpopulation comparisons, then the investigator conducting the NIH–defined Phase III must include sufficient and appropriate entry of sex/gender and racial/ethnic participants so that a valid analysis of the interventions effects can be determined. The conditions to be followed in the research plan or proposal are the same as those described above.

For all three situations, cost is not an acceptable reason for exclusion of women and minorities from clinical trials.

The final protocol submitted to the IRB for review and approval must contain a plan for valid analysis. “Valid analysis” means an unbiased assessment that will, on average, yield the correct estimate of the difference in outcomes between two groups of subjects. The principal requirements for ensuring a valid analysis of the question of interest are: (1) Allocation of study participants of both sex/genders (male and females) and different racial/ethnic groups to the intervention and control groups by an unbiased process such as randomization; (2) unbiased evaluation of the outcomes of study participants; (3) use of unbiased statistical analysis and proper methods of inference to estimate and compare the intervention effects among sex/gender and racial/ethnic groups.
Policy SC 508: Differences in State and Federal Law and Reporting Requirements Affecting the Protection of Privacy Interests of Research Subjects

1. Purpose
Differences in state and federal law pertaining to research should be clarified.

2. Definitions
Policies set forth the Federal definitions applicable to research and the laws of the Commonwealth of Pennsylvania. Specific policies should be consulted to ensure legal compliance.

3. Applications
Consistent with specific IRB policies, if the principal investigator has questions concerning the application of Federal and state laws related to research, the principal investigator is responsible for securing clarification. Recognizing that state laws may differ with respect to the Federal laws and the laws of states other than the Commonwealth of Pennsylvania, the principal investigator and the IRB shall contact the Director or Associate Director, OHR, who will refer the question(s) regarding the laws to the Office of University Counsel for clarification to ensure appropriate application in research.

4. Special Considerations Concerning Confidentiality Related to Required Disease, Abuse and HIV Reporting
4.1. Confidentiality of Records (See 45 CFR 46.116 (a)(5); 21 CFR 50.25 (a)(5)) Consent forms must explain the extent to which information obtained in connection with the research and that could identify the subject will remain confidential and will not be disclosed without the subject’s permission. Limits on confidentiality, including the Commonwealth of Pennsylvania’s requirement for reporting of suspected child abuse or neglect, reportable communicable and infectious diseases including HIV/AIDS, must be clearly explained in the consent form, as applicable. For example, a phrase may be added to the appropriate section of the consent form as follows: “Because this study involves questions regarding [child abuse][a reportable disease], you should be aware that the laws of the Commonwealth of Pennsylvania require healthcare professionals learning of suspected [abuse or neglect][disease/condition] to report it to the proper authorities.” Note: Where a research study involves sensitive topics, researchers should consider applying for a Certificate of Confidentiality. (These certificates should not be used to attempt to avoid reporting of suspected abuse or neglect, however.)
4.2. Mandatory Reporting of Diseases, Infections, and Conditions
Researchers and subjects should be aware that the laws of the Commonwealth of Pennsylvania (See, 28 Pa. Code § 27 and 35 P.S. § 7607) require health care professionals and health care facilities to report to the Pennsylvania Department of Health (Department) all diseases, infections and conditions listed in the table below.

<table>
<thead>
<tr>
<th>WITHIN 24 HOURS</th>
<th>WITHIN 5 DAYS</th>
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<tr>
<td>Animal bite.</td>
<td>AIDS.</td>
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<tr>
<td>Anthrax.</td>
<td>Amebiasis.</td>
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<td>Arboviruses.</td>
<td>Brucellosis.</td>
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<tr>
<td>Botulism.</td>
<td>CD4 T-lymphocyte test result with a count of less than 200 cells/µL or a CD4 T-lymphocyte percentage of less than 14% of total lymphocytes (effective October 18, 2002).</td>
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<tr>
<td>Cholera.</td>
<td>Campylobacteriosis.</td>
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<tr>
<td>Diphtheria.</td>
<td>Cancer.</td>
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<tr>
<td>Enterohemorrhagic E. coli.</td>
<td>Chancroid.</td>
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<tr>
<td>Food poisoning outbreak.</td>
<td>Chickenpox (varicella) (effective January 26, 2005).</td>
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<tr>
<td>Haemophilus influenzae invasive disease.</td>
<td>Chlamydia trachomatis infections.</td>
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<tr>
<td>Hantavirus pulmonary syndrome.</td>
<td>Congenital adrenal hyperplasia (CAH) in children under 5 years of age.</td>
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<tr>
<td>Lead poisoning.</td>
<td>Cryptosporidiosis.</td>
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<tr>
<td>Legionellosis.</td>
<td>Encephalitis.</td>
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<tr>
<td>Measles (rubeola).</td>
<td>Galactosemia in children under 5 years of age.</td>
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<tr>
<td>Meningococcal invasive disease.</td>
<td>Giardiasis.</td>
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<td>Plague.</td>
<td>Gonococcal infections.</td>
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<td>Poliomyelitis.</td>
<td>Granuloma inguinale.</td>
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<tr>
<td>Rabies.</td>
<td>Guillain-Barre syndrome.</td>
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<tr>
<td>Smallpox.</td>
<td>HIV (Human Immunodeficiency Virus) (effective October 18, 2002).</td>
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<tr>
<td>Typhoid fever.</td>
<td>Hepatitis, viral, acute and chronic cases.</td>
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<td></td>
<td>Histoplasmosis.</td>
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<td></td>
<td>Influenza.</td>
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<td>Leprosy (Hansen’s disease).</td>
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<td>Leptospirosis.</td>
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<td>Listeriosis.</td>
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<td>Lyme disease.</td>
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<td>Lymphogranuloma venereum.</td>
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<td></td>
<td>Malaria.</td>
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<tr>
<td>Conditions</td>
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<td>-----------------------------------------</td>
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<tr>
<td>Maple syrup urine disease (MSUD) in children under 5 years of age.</td>
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<tr>
<td>Meningitis (All types not caused by invasive Haemophilus influenza or Neisseria meningitis).</td>
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<tr>
<td>Mumps.</td>
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<tr>
<td>Perinatal exposure of a newborn to HIV (effective October 18, 2002).</td>
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<tr>
<td>Pertussis (whooping cough).</td>
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<tr>
<td>Phenylketonuria (PKU) in children under 5 years of age.</td>
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<tr>
<td>Primary congenital hypothyroidism in children under 5 years of age.</td>
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<tr>
<td>Psittacosis (ornithosis).</td>
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<tr>
<td>Rickettsial diseases.</td>
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<tr>
<td>Rubella (German measles) and congenital rubella syndrome.</td>
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<td>Salmonellosis.</td>
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<td>Shigelllosis.</td>
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<tr>
<td>Sickle cell disease in children under 5 years of age.</td>
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<tr>
<td>Staphylococcus aureus, Vancomycin-resistant (or intermediate) invasive disease.</td>
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<tr>
<td>Streptococcal invasive disease (group A).</td>
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<tr>
<td>Streptococcus pneumoniae, drug-resistant invasive disease.</td>
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<tr>
<td>Syphilis (all stages).</td>
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<td>Tetanus.</td>
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<td>Toxic shock syndrome.</td>
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<td>Toxoplasmosis.</td>
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<tr>
<td>Trichinosis.</td>
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<tr>
<td>Tuberculosis, suspected or confirmed active disease (all sites).</td>
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<tr>
<td>Tularemia.</td>
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</table>

### 4.3. Other Reporting Requirements

Healthcare providers in Pennsylvania are also required to report:

- Serious or imminent plans to harm oneself or another
- Child neglect or abuse
- Child sexual abuse
Child abuse or suspected child abuse reporting requirements extend to abuse committed by a parent, a person responsible for the welfare of the child (i.e., anyone who provides care or supervises the child), an individual living in the same house, or a paramour of the child’s parent.

4.4. HIV/AIDS Related Considerations
No HIV-related test shall be performed without first obtaining the informed written consent of the subject or legally authorized representative. Any consent shall be preceded by an explanation of the test, including its purpose, potential uses, limitations and the meaning of its results. (35 P.S. § 7605)

Blinded HIV-related testing for purposes of research performed in a manner by which the identity of the test subject is not known and may not be retrieved by the researcher is prohibited, unless reviewed and approved by the IRB established by the PA Department of Health. Consent requirements for HIV-related tests shall not apply to the following: (a) the performance of an HIV-related test on a cadaver by a health care provider which procures, processes, distributes or uses a human body or a human body part, tissue or semen for use in medical research, therapy or transplantation; or (b) the performance of an HIV-related test for the purpose of medical research if the testing is not prohibited by the Department and is performed in a manner by which the identity of the test subject is not known and may not be retrieved by the researcher. (35 P.S. § 7605)

5. Tools
Policy GA 129, Protection of Privacy Interests of Research Subjects by Investigators and IRB Members
Policy IC 701, Informed Consent and HIPAA Authorization: General Requirements
1. Purpose and Introduction
The purpose of this policy is to establish guidelines when Thomas Jefferson University (TJU) or Affiliates are conducting human subject research, for which one or all of the sites or participants, are outside the United States, regardless of funding.

2. Responsibility for Executing the Policy
Institutional Review Boards
Principal Investigators
Research Staff
Administrative Staff, OHR

3. Policy Statement
TJU international research requirements are consistent with the ethical principles set forth in its Human Research Protection Program (HRPP) and strive to meet equivalent levels of participant protection for research conducted within the United States. For federally funded research, the regulations of the sponsoring agency apply and the required protections must be provided. This policy is to ensure all human subjects research, regardless of whether the research is subject to U.S. federal regulations, will be guided by one of the following statements of ethical principles:


- Nuremburg Code.

- The World Medical Association’s Declaration of Helsinki (as adopted in 2001).

- Other appropriate international ethical standards recognized by U.S. Federal departments and agencies that have adopted the U.S. Federal Policy for the Protection of Human Subjects, known as the Common Rule.

The TJU Institutional Review Board (IRB) will review the research in accordance with the applicable Department of Health and Human Services (DHHS) and FDA regulations. If the IRB chooses to rely on the local Ethics Committee (EC), it must be established that the EC is guided by one of the above stated ethical documents. If the study is federally funded, the IRB will not rely on the local IRB.
OHRP provides guidelines that govern human subjects research in other countries, as well as standards from a number of international and regional organizations. The TJU HRPP directs researchers to these guidelines and requires compliance when conducting international research in applicable countries.


Conflicts arising between federal (or national) law and other applicable laws are referred to the TJU Office of University Counsel for guidance and resolution.

4. Responsibilities

4.1. Principal Investigators

Principal investigators must ensure that participants in research conducted outside of the U.S. have equivalent protections to participants in the U.S.

The PI must obtain TJU IRB approval in addition to approval from the local Ethics Committee should one exist in the host country in which the research will be conducted. If an Ethics Committee or other similar review committed does not exist, then a letter of support from a community leader or liaison must be obtained and submitted to the TJU IRB.

The PI also must obtain a letter of support from the facility at which research will be conducted, if it is not under the jurisdiction of the local Ethics Committee.

In addition, investigators are required to be knowledgeable about and comply with local laws while conducting their research and take into account the local customs and cultural context. Consultation with researchers familiar with the culture in which the research will take place is advised. Care must be taken to ensure that the cultural norms of the host country are respected and that the participants will not suffer adverse consequences from participation, such as being subjected to retaliation from local authorities or community members.

Principal investigators must assist their colleagues from the host country in obtaining a Federalwide Assurance (FWA) if the research is federally funded and requires that the international institution receive an approved FWA from the Office for Human Research Protections (OHRP).

4.2. IRB

The TJU IRB review of international human subjects research adheres to the same policies applied to US research, as appropriate. The PI must provide information about local research context to the IRB, so that the IRB can make an informed decision about whether the research is culturally appropriate. The amount of information necessary is commensurate to the level of risk presented by the research. This knowledge may be gained or supplemented by legal or cultural consultants to the IRB during its review of the research. In addition, the
IRB requires, when possible, documentation that the host country is aware of the research and has agreed for the research to be conducted in that country. When necessary, the IRB will communicate with the host country’s Ethics Committee or similar review committee or appropriate governmental agency, should any of these exist.

The IRB is responsible for:

- Confirming the qualifications of the researchers and research staff for conducting research in that country.

- Initial review, continuing review, and review of modifications to previously approved research.

- Post-approval monitoring.

- Handling of complaints, non-compliance, and unanticipated problems involving risk to participants or others.

Any problems encountered with the research should be reported to the study sponsor, relevant regulatory bodies and all reviewing Institutional Review Boards and Ethics Committees as appropriate. Research that is federally funded and is FDA regulated must comply with both DHHS and FDA regulations.

5. Consent
Obtaining consent in non-U.S. populations presents certain challenges. Especially in non-Western populations, conceptions of individuality and permission may be radically different. The investigator should be sensitive to differing norms pertaining to informed consent and design the consent process accordingly, while adhering to applicable regulations.

Consent forms, scripts or statements must be translated into the native language. These translations should be certified to be accurate and reflect appropriate cultural nuances. In some circumstances it may be inappropriate to document consent by using standard written consent. There also may be different laws regarding determination of who may serve as a Legally Authorized Representative (LAR) and the age of adulthood and consent that the IRB must take into consideration.

6. Payment
If subjects participating in international research will be compensated for their participation in the research, the IRB must ensure that the amount to be provided to subjects is appropriate and reflective of the standard of living in the country in which the research is being conducted as to not unduly influence subjects to participate.

7. Reference
OHRP International Compilation of Human Research Protections
1. Purpose
   This policy defines key personnel as listed on the Proposal Transmittal Form (OHR-1) for purposes of IRB oversight.

2. Responsibility for Understanding the Guidance
   Investigators
   Research Coordinators
   Departmental or Divisional Administrative Staff

3. Policy Statement
   Key Personnel in human subjects research are those individuals who are substantially involved in the research and who must be listed on the OHR-1, OHR-4, OHR-15 or OHR-18 as applicable. Key Personnel must have taken HIPAA training, have current IRB training, and must have completed the appropriate Conflicts of Interest (COI) Disclosure.

Examples of activities performed by key personnel include but are not limited to:

- Are involved in the conduct of study procedures
- Are able to view PHI
- Have access to study-related data that is not de-identified for statistical analysis or other study-related activities
- Interact with research participants
  - During recruitment
  - During the study (including administration of questionnaires)

Persons who are not Key Personnel are those who perform “contract” type duties or provide administrative support that does not require interaction with participants. Examples include but are not limited to:

- A nurse injecting a study medication according to orders but collecting no study-related data
- A pharmacist working in the Investigational Drug Service who dispenses study medication or maintains drug randomization schedules
- A statistician analyzing de-identified or aggregate data
• A technician drawing blood

• An administrator preparing IRB paperwork, study-related budgets, and case report form templates, etc.
1. Purpose
   This guidance addresses specific situations pertaining to reporting of adverse events (AEs) and Unanticipated Problems Involving Risks to Subjects or Others (UAPs).

2. Responsibility for Understanding the Guidance
   Investigators
   Research Coordinators
   IRB Members
   SAE Reviewers
   OHR Administrative Staff

3. Guidance for Reporting Adverse Events
   Due to lack of federal guidance on many of the specifics of what needs to be reported as an adverse event, the TJU Office of Human Research provides the following recommendations for particularly problematic reporting issues. This guidance represents our current thinking on this topic but may change as a result of new federal guidance.

3.1. Multiple causes for hospitalization – Many cooperative group studies (GOG, RTOG, etc.) require that in situations where a hospitalization has many contributing causes, the cause of highest severity (as per NCI’s grading system) should be reported as the primary cause. For these studies, this requirement should be followed. For non-NCI funded studies, OHR recommends that the cause of highest severity, as per the PI’s opinion, should be reported as the primary cause. Secondary causes may be described in the body of the report.

3.2. Multiple hospitalizations for the same cause – Because each hospitalization is a separate event, each should be reported as a separate adverse event.

3.3. Emergency Department visits should be reported as SAEs if:
   • The subject is admitted to the hospital
   • The subject is kept in the ED for more than 24 hours
   • The ED visit is probably or definitely related to the study drug
   • The ED visit is probably or definitely related to a study device and the problem is not listed in the device brochure, protocol or consent form
3.4. Protocol-specific AE reporting guidelines – If the adverse event reporting guidelines in a commercially sponsored or cooperative group protocol are more specific than those of the TJU IRB, the investigator should follow the protocol-specific guidelines. If protocol definitions are in conflict with those of the TJU IRB, the investigator should report according to the definition that is more protective of subject safety.

3.5. Reporting deaths – Subject deaths that occur 30 days after study treatment has ended do not require individual reporting unless it is believed that the death is study-related. Deaths of subjects on long-term follow-up who are not receiving experimental intervention should be reported in aggregate at the time of continuing review. (The OHR-9 includes a question pertaining to number of deaths.) These should also be addressed in the OHR-9, section C, question 2 narrative.

3.6. Laboratory or other test abnormalities should be logged as AEs and reported at the time of continuing review or reported as SAEs according to severity. In order to avoid unnecessary reporting, it is best to define laboratory abnormalities with respect to SAEs in the study protocol. For example, if a study is being done on patients undergoing major surgery but the major surgery is not part of the protocol, then events that are related to the surgery need not be reported as SAEs even if they meet criteria for grade 3 or above. Examples include:

- Laboratory abnormalities that are clearly expected during the recovery period from the surgery (especially relevant to those patients being monitored in the ICU after surgery),

- Expected ECG abnormalities after cardiac surgery,

- Return to the OR for surgical complications, or events related to recovery from anesthesia.

Similarly, an expected event of hypotension need not be reported if it is grade 3 [defined in CTCAE as sustained (up to or >24 hours without persisting physiologic consequences)] but should be reported as an SAE if grade 4 [shock (e.g., acidemia, impairment of vital organ function)].

4. How to Determine if an Adverse Event is Also an Unanticipated Problem that Must be Reported to the IRB

In most instances adverse events should be considered unanticipated problems involving risk to human subjects and reported to the IRB only if they are unexpected, serious, and have implications for the conduct of the study (e.g., requiring a significant or safety-related change to the protocol). An isolated unanticipated event that is serious and involves risk should be reported as such but may not require modification to the protocol or consent until a pattern is established.
Examples of adverse events that should be considered UAPs and reported to the IRB include:

- A serious unexpected (not in consent form) event that is uncommon and strongly associated with drug exposure such as angioedema, agranulocytosis, liver injury/failure, Stevens-Johnson syndrome, etc.

- A serious unexpected event that may occur once or a few times that is not commonly associated with drug exposure or found in the patient population under study, such as tendon rupture or progressive multifocal leukoencephalopathy.

- An event that occurs multiple times at a study site or is found on aggregate analysis of data from a multi-site study suggesting that these are not isolated occurrences but do pose risk to subjects.

- An adverse event described in the consent or other study documents that occurs at a rate or severity that is inconsistent with prior observations. Examples: Mild kidney function test abnormalities are expected to occur in about 5% of subjects but are being noted in 15% of subjects; Abnormal liver function tests are described as a risk in the consent, protocol, and Investigator Brochure, but hepatic necrosis is observed in a study subject in whom causality is at least possibly related, in the investigator’s opinion. In the latter example, the severity of the event is not reflected in the study documents.

- A serious risk described in the consent form occurs at a rate significantly greater than expected (e.g., noted as occurring at 1% but found in 10%).

- Any other event that requires modification of risks as listed in the Investigator Brochure.

Adverse events that are expected (listed in the Investigator Brochure, protocol and consent form) generally do not require reporting to the IRB as unanticipated problems but may require reporting as SAEs.

Examples of adverse events that do not represent unanticipated problems and do not need to be reported to the IRB as such include the following:

- Known complications of standard chemotherapy regimens in subjects participating in a study adding an experimental chemotherapy drug or placebo to standard of care with the known risks of chemotherapy listed in the consent form. An example would be a patient having severe neutropenia with development of sepsis and subsequent multi-organ failure and death. Since this clinical scenario in terms of the nature, severity, and frequency is expected, it need not be reported to the IRB as an UAP. However, the hospitalization would, under TJU rules, be reported as a SAE.
• A person in a multi-center study of a new non-steroidal anti-inflammatory drug (NSAID) for osteoarthritis develops abdominal pain and nausea and the work-up demonstrates gastric ulcers. The consent indicates that abdominal pain and nausea occur in about 10% of individuals taking NSAIDS, and gastric ulceration develops in about 20% of these patients. Medical review indicates that subjects across the study are experiencing nausea, abdominal pain and gastric ulceration at the expected frequency. This clinical scenario is not unexpected and therefore does not have to be reported as a UAP.

5. References
   OHR Policy GA 120 “Policy and Procedure for Reporting and Reviewing Unanticipated Problems Involving Risks to Subjects or Others”
1. Purpose
The language of medical science is precise, but contains terms that may be incomprehensible to the general public. The ability to convey these complex ideas to prospective study participants or to lay members of IRBs is an art that is difficult to master, yet it lies at the heart of informed consent. The following is a glossary of technical terms to suggest terminology more easily understood by lay people.

2. Responsibilities for Understanding the Guidance
Investigators
Research Coordinators
IRB Members
OHR Administrative Staff

3. Informed Consent Glossary

Abdomen – belly, stomach
Ablation – removal
Abstain from – avoid
Acute – short-term, sudden onset
Adverse Event – side effect
Alopecia – hair loss
Amnesia – loss of memory; inability to remember
Analgesic – pain-relieving medication
Anaphylaxis – a severe allergic reaction that could result in injury or death
Anesthetize – make numb; put to sleep
Angioplasty – operation to open clogged blood vessels
Anorexia – loss of appetite
Antibodies – cells or substances in the body that fight infection
Anus – rectum
Artery – blood vessel
Arrhythmia – irregular or “skipped” heartbeat
Arthralgia – joint pain
Aspiration – inhalation; sucking in; removal of fluid from [location] through a tube or needle
Asthenia – loss of energy; weakness
Asymptomatic – without signs or symptoms of disease
Ataxia – unsteady movement

Bacteria – germs
Benign – not cancerous
Biopsy – removal and examination of a small part of [a tissue or organ]
Bone density – bone thickness; hardness of bone
Bradycardia – slow heart rate
Cardiac – involving the heart
Cardiac catheterization – procedure in which a small tube, called a catheter, is inserted through the blood vessels into the heart and a doctor uses a special fluid to look at the blood vessels in the heart
Cardioversion – procedure that uses electricity to stimulate the heart and to make it return to its normal rhythm
Catheter – flexible plastic tube that is inserted into the [location]
Central nervous system – the brain and spinal cord
Chronic – long-term
Coerced – pressured; forced
Cognitive status – levels of awareness and thinking
Colon – large intestine; bowel
Colonoscopy – procedure that uses a special camera at the end of a long tube
Confidentiality will not be compromised – the staff protects your privacy
Consent – agreement
Contrast material – fluid put into blood vessels or an area of the body to highlight the blood vessel or area for an x-ray picture
Convulsions – seizures
Coronary – involving the heart
Creatinine clearance – a test of kidney function
Computed tomography (CT) scan – computer enhanced x-ray; a special type of x-ray
Culture – a test for the presence of germs

Defecate – to have a bowel movement; to pass stools
Defibrillation – a procedure that uses electricity to stimulate the heart and to make it return to its normal rhythm
De novo – new
Deteriorate – to get worse; to lose function
Diastolic blood pressure – pressure when the heart rests between beats; the bottom number of a blood pressure reading
Diplopia – double vision
Distended – bloated; swollen; inflated
Double-blind – neither the subject nor the doctor will know what drug the subject is taking
Duodenum – beginning of the small intestine which is attached to the stomach
Dyspepsia – gas; upset stomach
Dyspnea – difficulty breathing; shortness of breath
Dysrhythmia – abnormal or irregular heart beat

ECG, EKG, or electrocardiogram – picture and measurement of a heartbeat
Echocardiogram – procedure using sound waves to take pictures of the heart chambers and measure of its pumping strength
EEG – measurement of electrical activity of the brain
Edema - swelling
Efficacy – effectiveness; usefulness
Electrode – wire
Electrophysiology study – heart rhythm study
Elucidate – to make clear; to determine; to find out
Embryo – animal in the earliest stages of development
Enema – medication given through the rectum that cleans out the bowel
**Enzyme abnormality** – blood test result that suggests abnormal organ function or injured cells

**Exclusion criteria** – reasons that one cannot be included

**Excreted** – made; given off; put out

**Fast** – do not eat or drink

**Fatigue** – tire; tiredness

**Fetus** – developing human

**Flatulence** – gas passed through the anus/rectum

**Flushing** – to become red in the face or other part of the body because of rush or blood to the skin; blushing of the skin

**Fracture** – break

**Gastric** – relating to the stomach

**Gastrointestinal** – relating to the stomach and intestines

**Glucose** – sugar

**Hematoma** – a bruise; bleeding into the body tissue around a blood vessel

**Hemodynamic measurement** – test to measure blood flow

**Hepatic** – relating to liver

**Hepatitis** – inflammation or swelling of the liver

**Holter monitor** – a machine, the size of a pocket radio that records the beats of a heart

**Hypertension** – high blood pressure

**Hypotension** – low blood pressure

**Hysterectomy** – removal of the womb

**Immobilization** – making something unable to move

**Immobilized** – unable to move

**Immunological** – relating to the body’s ability to fight infection

**Implantation** – operation to place a [device] inside the body

**Incision** – cut

**Indicated** – suggested; necessary

**Induce** – cause

**Inert** – not active

**Inert substance** – has no known effect on this disease

**Inflamed** – swollen, red and warm

**Inflammation** – swelling and redness

**Inflation** – filling with air

**Infused** – dripped in; put in

**Ingest** – swallow eat or drink

**Inject** – to put into by way of a needle (or other device)

**Insomnia** – unable to sleep

**Instilled** – put into; dripped into

**Intensity** – degree; amount

**Intramuscular injection** – putting something into muscle with a needle

**Intravenous** – in a blood vessel

**Intravenous infusion** – putting something into a blood vessel through a plastic tube and needle

**Isolated** – separated; closed off
Office of Human Research  
Office of Human Research Policy and Procedure  
Manual

*Lactating* – making breast milk; breastfeeding  
*Lesion* – site of an injury; site of a disease  
*Leukocyte* – blood cell that fights infection  
*Libido* – sexual desire; sex drive  
*Local anesthetic* – medicine to numb an area of the body  
*Lumbar puncture* – a needle inserted between the bones of the spine to put in a drug or to take a sample of the spinal fluid  
*Lumbosacral* – lower back  

*Maintenance dose* – one’s usual daily dose  
*Malignancy* – tumor; cancer  
*Manifested* – showed  
*Meningitis* – infection or irritation around the brain  
*Metabolism* – process by which food is used to supply energy for the body; the energy the body uses when it works; the way the body breaks down food or a drug  
*Metastasize* – spread  
*Magnetic Resonance Imaging (MRI)* – pictures of the inside of the body taken with large magnet and radio waves (radiation is not used)  
*Mucosa* – the lining inside [an organ]  
*Myocardial infarction* – heart attack  

*Nasal congestion* – stuffiness of the nose  
*Nasal* – relating to the nose  
*Nasogastric (NG) tube* – a flexible plastic tube that is inserted through the nose or mouth into the stomach  
*Nausea* – feeling sick to one’s stomach  
*Negative finding* – a normal result; the usual result for a healthy person  
*Neurological examination* – test of the brain, spinal cord and reflexes  
*New indication* – new use  

*Occult blood test* – a test for small amounts of blood in the stool  
*Open-label* – a scientific study in which the identity of the drug, device or procedure is known to both the subject and to the doctor; the subject will know which drug she or he is taking  
*Optimum or optimal* – best  
*Oral* – spoken; by mouth  
*Osteoarthritis* – bone and joint pain  
*Over-the-counter drugs* – drugs that one can buy without a doctor’s prescription  
*Overnight fast* – nothing eaten or drunk after [time] p.m.  

*Palpitation* – irregular or “skipped” heartbeat that one can feel  
*Paresthesia* – tingling in the [location]  
*Perception* – one’s view; one opinion  
*Perforation* – hole; tear  
*Pharmacological* – relating to the drug  
*Physiologically capable* – able to function  
*Plasma* – blood  
*Pneumonia* – lung infection  
*Pneumothorax* – collapsed lung  
*Polyps* – abnormal lumps that can sometimes be cancerous

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Positive history – in one’s past history; condition that one ever had
Positron Emission Tomography (PET) – special camera that uses energy rays to show how well the internal parts of the body are working
Predictive value – expected value
Prognosis – expected course of a disease
Prone – lying flat facing down; lying on one’s stomach
Prorated compensation – less if one does not complete the study
Protocol – study plan
Psychological test – test of one’s behavior
Pulmonary – relating to the lung
Puncture – to make a hole
Pyelogram – a series of x-ray pictures of the kidneys

Quantify - measure

Radioactive isotope – a chemical or substance that gives off radiant energy or rays similar to x-rays
Randomly – like picking numbers out of a hat; like flipping a coin (indicate the chance of being assigned to each group)
Recuperate – to get better; to heal
Reliable method of contraception – a way to prevent pregnancy such as using birth control pills; Norplant or Depo-Provera; using an intrauterine device (IUD); or using a condom or diaphragm with a sperm-killing jelly
Renal – relating to the kidney
Render one ineligible – make one unable to participate
Respiratory – relating to breathing

Saline – salt water
Secretion – one of the fluids made by the body
Sedation – making drowsy or sleepy
Somnolence – sleepiness; drowsiness
Sputum – thick saliva; spittle
Standard of care – the usual treatment for a disease
Stent – a small tube that keeps a blood vessel open
Subcutaneous – under the skin
Subsequent – later; following; or as a result
Superficial – near the surface
Supine – lying flat facing up; lying on the back
Sutures – stitches
Symptoms – signs or symptoms
Syncope – fainting or lightheadedness
Systemic – involving the whole body
Systolic blood pressure – the blood pressure during a heartbeat; top number of a blood pressure reading

Tachycardia – fast heartbeat
Telemetry – monitoring the [organ or location] from a distance
Therapeutic dose – the amount of medication needed to treat a condition
Third party payors – health insurance; Medicare or Medicaid
Tinnitus – ringing in the ears
Titration – adjusting the amount of drug one should take
Topical – applied to the surface of the skin
Triglyceride – fat in the blood
Tubal ligation – tying the Fallopian tubes to prevent pregnancy

Unable to comply with – unable to follow study directions or the study requirements
Ureter – the tube that carries urine from the kidneys to the bladder
Urethra – the tube that carries urine from the bladder outside the body
Urinalysis – urine examination

Vaginitis – infection in the vagina or birth canal
Vein – blood vessel
Venipuncture – to put a needle into a blood vessel
Verbal – in spoken or written words
Vertigo – a feeling of losing one’s balance; dizziness
Void – to make or to pass urine

Waive – give up
Withdraw – leave the study; quit

4. Reference
Informed Consent Glossary, Applied Clinical Trials. May 1997; 71-73
1. **Purpose**
   To provide an overall discussion of the use of Certificates of Confidentiality in research and a description of how to obtain an application for a certificate.

2. **Responsibility for Understanding the Guidance**
   - Investigators
   - Research Coordinators
   - IRB Members
   - OHR Administrative Staff Members

3. **Guidance**
   Investigators generally do not disclose identifying information about research subjects to individuals or entities not associated with the research. However, there may be occasions where, because of a court or administrative agency subpoena, the investigator may be required to disclose records of a subject's participation in a clinical research study that could include name, address, and medical history.

   Congress, realizing that individuals would not be willing to participate in research involving sensitive issues unless their privacy was protected, enacted a law allowing researchers to obtain Certificates of Confidentiality. Public Health Service Act (301 (d)), Title 42 US Code, permitted investigators to protect the privacy of subjects by refusing to disclose their names or other identifying characteristics, even if asked to do so by courts or governmental agencies. As long as a Certificate of Confidentiality is in place when a subject enrolls in a study, information identifying the subject will never be disclosed unless the subject or in certain specific circumstances, investigator volunteers it.

   A Certificate of Confidentiality can help to promote recruitment into a study involving sensitive issues. The IRB can suggest that an investigator apply for one when appropriate.

   The OHRP has determined that the research is of a sensitive nature if it involves collecting information:

   3.1. **How is a Certificate of Confidentiality Obtained?**
   A request for a certificate of confidentiality must be made for a particular study to the agency responsible for the funding, and is not transferable to any other study. Certificates of Confidentiality are not limited to federally-funded studies. FDA accepts applications for certificates of confidentiality for research that is of a sensitive nature and involves an investigational drug exemption.
3.2. Limitations on Certificates of Confidentiality
It is important to note that the certificate of confidentiality does not apply to voluntary disclosure of identifying information by either the subject or the investigator; even if the study is covered by a certificate, the subject may voluntarily disclose information about himself or herself. The investigator may also voluntarily disclose specific urgent issues such as child abuse involving a subject or a subject's threats about violence to self or others. Subjects should be advised about the exceptions to the protections the certificate offers.

3.3. Mechanics of Certificates of Confidentiality
A researcher may obtain a certificate of confidentiality only if it is determined that the research is of a sensitive nature and protection is necessary to reach the objectives of the research. Certificates of Confidentiality are valid from the date of issue to the date of study expiration, and if the research is not completed by the termination date of the certificate, the recipient must make a written application for an extension. A Certificate of Confidentiality is not transferable from one study to another. Any significant changes to the protocol, study personnel, or the test article to be administered requires notification of the issuing agency by the submission of an amended application.

Once a subject enrolls in a study in which a certificate of confidentiality is in place, the protection afforded by the certificate is permanent and information identifying that subject will never be disclosed unless it is volunteered by the subject or the investigator for certain urgent issue, or it expires.

3.4. Contacts for Information about obtaining a Certificate of Confidentiality
The OHRP website contains a list of contacts at different federal agencies for information about obtaining an application for a Certificate of Confidentiality.
1. Purpose
   To provide information regarding issues critical in the performance of behavioral research.

2. Responsibility for Understanding the Guidance
   IRB Members
   IRB Reviewers
   Investigators
   Research Coordinators

3. Guidance
   3.1. Federal Regulations
   Federal regulations apply to research involving human subjects that is conducted not only in medical therapeutics, but in areas such as human behavior, social science, anthropology, epidemiology, and education. Studies of these types often present only slight to minimal risk and in these cases may be exempt from IRB review or given an expedited review, as per Policies RR 403 and RR 404, respectively.

   3.2. Psychological/Social Risk
   Behavioral research generally does not involve any physical risk to the subject because there is no physical intervention. However, they do carry concerns for other types of potential harms, including psychological, economic, social and legal risks to the subjects that may be as harmful as any risk faced by a subject in a medical study.

   The risks of psychological harm range from temporary anxiety and distress to a relapse in a behavioral disorder or the precipitation of a disorder. Social harms include personal embarrassment, ostracism, stigmatization or possible loss of social status. Economic risks include decreased employability and possible job loss. Among the possible legal risks are arrest, prosecution and civil or criminal liability. Many of these potential harms would be the result of another risk: breach of confidentiality.

   In assessing the potential risks presented by a behavioral study, investigators and IRBs should ensure that the design of the study provides an adequate level of protection against these potential risks. In behavioral studies, the traditional risk/benefit balance is changed such that benefits rarely accrue to the subject, but rather to science or society.
3.3. Deception in Behavioral Research
Deception in a clinical research study involves intentionally misleading subjects or withholding full information about the study in order to achieve study aims. Misleading or omitted information might include withholding or misrepresenting the purpose of the research, the role of the investigator, or what procedures are experimental. Deception interferes with the ability of the subject to give informed consent and presents a limitation on the protection afforded by informed consent. However, it is important to note that humans act differently depending on the circumstances, and that in some cases the subjects’ full knowledge of the study would bias the results. In such instances of behavioral research, deception may be necessary. Under the federal regulations, deception is permitted with the limitations that it must be ethically and scientifically justified by the investigator and approved by an IRB.

Approval of research involving deception requires the investigator to obtain a waiver or alteration of the consent process from the IRB. If the IRB approves deception in the consent process or conduct of the study, the subjects must be fully debriefed at the end of the study. Furthermore, the subject must be given the opportunity to ask questions about the new information and the opportunity to withdraw both themselves and their data from the study.

3.4. Vulnerable Subjects
Additional protections are required for vulnerable persons participating in research. These added protections may include the use of witnesses, requiring consultants and/or advocates, review of consent at specified stages in the study, and limiting the scope of certain research projects.

3.5. Privacy and Confidentiality
Privacy and confidentiality are central considerations in all types of research. A violation of an individual’s privacy is not only a harm, but also may result in loss of personal protection. Breaches of privacy involving public exposure erode trust on all levels. Investigators must design studies to maximize confidentiality of data, and should avoid violations of privacy by removing identifiers or making data anonymous, unless there is a valid rationale for not doing so.
1. **Purpose**
   To provide an awareness of quality of life issues as they pertain to a research protocol involving human subjects, and a list of some specific quality of life issues that should be addressed in the design of a protocol, with the intent to minimize the effect on the research subject to the greatest possible degree.

2. **Responsibility for Understanding the Guidance**
   - Investigators
   - Research Coordinators
   - IRB Members

3. **Guidance**
   The demands of participation in a research study have the potential to disrupt the normal daily life of a participant. Well-known side effects such as prolonged pain and suffering may decrease the quality of life. However, even surveys and questionnaires can potentially cause psychological distress leading to a decline in aspects of life style.

   But beyond the design or requirements of the protocol, the quality of life issues imposed by the research, while not properly designated as risk, may affect a research participant’s day-to-day activities. These issues, therefore, constitute added hardship and thus should be considered in the design of a human subject’s protocol, and be clearly communicated to the subject as possible experiences during their participation in the study.

   Some examples of quality of life issues to consider include the following:
   - Lengthy screening and enrollment procedures
   - Inconvenient scheduling/frequency of study visits
   - Requirement for extra procedures (blood draws between study visits)
   - Lengthy questionnaires that are hard to complete given the subjects pre-existing condition
   - Excessive or redundant questionnaires or study procedures
   - Travel time/cost of travel
• Imposition on family members, care givers, or parents particularly in pediatric studies

• Unnecessary visits, tests or measures

• Restricted diets

• Washout periods/withholding of certain medications during study participation
1. Purpose
   To provide an overview of the investigational use of approved marketed drugs, biologics and medical devices

2. Responsibility for Understanding the Guidance
   Investigators
   Research Coordinators
   IRB Members
   OHR Administrative Staff

3. Guidance
   3.1. Bioresearch Audit and Monitoring Program
   The Food and Drug Administration’s Bioresearch Monitoring Program involves site visits to clinical investigators, sponsors, contract research organizations, Institutional Review Boards, and pre-clinical laboratories (e.g. Phase I studies). All FDA product areas, i.e., drugs, biologics, medical devices, radiological products, food, and veterinary drugs, are involved in the Bioresearch Monitoring Program. While program procedures may differ slightly depending upon product type, all inspectional activities have as their objective to ensure the quality and integrity of data and information submitted to FDA as well as protection of human research subjects. FDA carries out three distinct, separate clinical investigator programs; 1) surveillance inspections; 2) bioequivalence study inspections and 3) “for cause” inspections.

   FDA field offices conduct surveillance inspections on the basis of assignments developed by the agency. The assignments are based most frequently, but not entirely, on studies that are important to product evaluation, such as a new drug application and product license applications pending before the agency. Once the key studies are identified, FDA personnel will forward all pertinent study information, including copies of the protocols and clinical case reports, to the local FDA District Office that is responsible for conducting the inspection.

   The headquarters scientist who developed the assignment is listed as the contact person during the full evaluation of the protocol, and is available to provide guidance and direction to the FDA investigator and clinician on an ongoing basis throughout development of the federal evaluation.
When a research investigator is selected for comprehensive inspection, a FDA investigator from one of the agency’s district offices schedules the initial contact and preliminary review with the investigator. The investigation consists of two basic parts. First, the agency must determine all facts surrounding the scientific conduct and clinical merit of the study. Questions are wide in scope, such as:

- Scope of performance, that is, who did what?; and when;
- The degree of delegation of authority (Ref: italicized section next page);
- Where specific aspects of the study were performed;
- How and where data were recorded;
- How test article(s) accountability was maintained (reference drugs or devices) and;
- How the monitor communicated with the clinical investigator and customarily evaluated the study’s progress.

The FDA then makes a comparative investigation of all data submitted to the agency and/or the sponsor with all available records that might support the data submitted. These records may come from the physician’s office, hospital offices, off-site facilities (e.g. nursing home), or various laboratories connected with the protocol (e.g. multicenter investigations, cooperative group studies). Patient records that pre-date the study as well as records covering a reasonable period after active study completion and closure of patient enrollment (e.g. Phase II and III longitudinal studies, and Phase IV post-market surveillance) are equally subject to review by FDA authorities. After a full report of the inspection has been evaluated by federal review, a written summary to the clinical investigator usually follows.

This summary of the protocol assessment can take the following forms:

- An observational letter indicating no significant deviations from federal regulations were observed;
- An informational letter that identifies deviations from regulations and good investigational practice, but may not require a response;
- A finding of significant deviations from federal regulations that is sufficiently important to require prompt, voluntary and thorough correction by the investigator.
In this “Notice of Adverse Finding”, the agency specifies the deficiencies. In such cases, the FDA may inform the study sponsor that the investigator’s procedural deficiencies indicate ineffective monitoring by the sponsor, the institution, the investigator or all three parties may share responsibility within their scope of oversight.

In addition to this notification of “Adverse Finding”, the FDA may exercise the full force of its federal authority and take formal action in the form of:

- Regulatory Sanctions
- Administrative Sanctions
- Both Regulatory and Administrative Actions
- Expanded Surveillance Inspection that Develops into a “For Cause” Action

In every case, FDA (and OHRP) holds the clinical investigator fully, and ultimately, liable for any deficiencies cited within his/her scope of supervision. Therefore, final responsibility for clinical integrity and daily administrative monitoring rests with the investigator, and is not to be delegated to subordinates even though there may have been multiple staff subordinates associated with the protocol now undergoing assessment.
1. **Purpose**
   To elucidate the issue of privacy of research subjects and potential research subjects and how it can best be respected.

2. **Responsibility for the Guidance**
   Investigators

3. **Guidance**
   Privacy is supported by “Respect for Persons” and “Beneficence”, two of the principles of research ethics identified in the Belmont Report. Both 45 CFR §46.111 and 21 CFR §56.111 require the IRB to determine, as part of its review of research, that privacy is protected when appropriate.

   Privacy is an individual’s desire to be left alone, not approached, or not contacted. This is embodied in the research setting most notably during the recruitment process, before an individual has given his/her consent to participate in the various procedures, visits, tests, and contacts that comprises a research study. In many cases, the individual will not know the recruiter, and it is at this point that the recruiter must be sensitive to the privacy wishes of the individual. But ultimately, if the individual says no, this means no. Any further pressure from the recruiter could be construed as coercion, and any individual enrolled under coercion has not given his or her true informed consent.

   By consenting to participate in a research study, an individual has accepted the commitments of time and effort that will be involved in the participation. The individual has a certain level of comfort with adhering to the various procedures that s/he has committed to. However, this commitment on the part of the individual should not dampen the researcher’s sensitivity to individual privacy. The researcher needs to maintain a level of flexibility when dealing with the individual, as the individual may have specific privacy needs, such as being contacted only at certain times of day or at a particular phone number. Also, if the individual withdraws from the research study, the expressed privacy wishes of the individual should continue to be observed.
1. **Purpose**
   To provide guidance regarding IRB fees.

2. **Responsibility for Understanding the Guidance**
   Investigators
   Research Coordinators

3. **Guidance**
   3.1. **Application of IRB Fees**
      IRB fees apply to all commercially sponsored studies unless fees are waived by prior agreement with the Director, OHR. The Office of Research Administration (ORA) insures that contracts with commercial sponsors reflect the current IRB fee schedule.

      IRB fees apply to only commercially-sponsored research studies as follows:
      - Full Board review of new proposals, continuing review, and amendments.
      - Expedited review of new studies, amendments and continuing reviews.

   3.2. **Departmentally Funded Investigator Initiated Trials (IIT)**
      IITs that are partially funded through grants from non-federal sources or foundations (such as the American Cancer Society, the Arthritis Foundation, etc.) are not assessed IRB fees.

      For IITs that are partially funded by grants from commercial entities, the ORA includes the IRB fees in the contracts as a line item expense that should not affect the amount of money received by the investigator. Waiver of fees for these partially funded studies requires approval of the Director, OHR.

      If a funding entity is supplying drug only and no additional funding, then IRB fees are usually waived. However, if the funding entity is receiving data collected in the IIT then, absent any extenuating circumstances, IRB fees are assessed by contract.

   3.3. **Other Clinical Research**
      IRB fees are not assessed for federally-funded studies, clinical studies that are sponsored by foundations such as the American Cancer Society, American Lung Association, etc., or clinical studies supported solely by departmental funds.
1. Purpose
To provide guidance to investigators for establishing acceptable monitoring procedures for investigator-initiated clinical trials.

2. Responsibility for Understanding the Guidance
Investigators
Research Coordinators
IRB Members/Chairs

3. Overview
Investigator-initiated trials are those in which the investigator is considered to be the sponsor, whether or not s/he receives partial funding from an external source to conduct the study. In those instances where there is partial funding, the funding agency, commercial or non-commercial, will not provide monitoring. Therefore, in the absence of professional sponsor monitoring, independent monitoring of investigator initiated trials (IIT) that employ new drugs, biologicals, or medical devices becomes an issue of great importance in order to ensure adequate protection of the rights and safety of human subjects and the quality and integrity of the resulting data.

The method and degree of monitoring needed is related to the degree of risk involved. Establishing a monitoring plan for clinical trials is required to address safe and effective conduct of the trial and to recommend conclusion of the trial when significant benefits or risks have developed, significant efficacy has been demonstrated, or the study is unlikely to be concluded successfully. Risk associated with participation in research must be minimized to the extent possible.

Monitoring may be conducted in various ways and by various individuals or groups, depending on the size, scope and risk of the research effort. These ways exist in a continuum that includes monitoring by the PI, a TJU-based DSMB for a small phase I study, or the establishment of an independent DSMB for a large phase III clinical trial.

Minimal risk trials in general do not require monitoring beyond that provided by the PI and annual review by the IRB, since the OHR-9 form addresses the required safety and enrollment elements pertinent to the trial.

Greater than minimal risk studies do require monitoring procedures that should include establishing a Data Safety Monitoring Plan (DSMP), appointing an individual as an Independent Study Monitor (ISM), or appointing a Data Safety Monitoring Board (DSMB).
3.1. Independent Study Monitor
An ISM should be an appropriately trained and qualified individual who is not involved in the study in any other way. The study monitor may be a TJU employee or someone who is not employed by the University. If the study is partially or wholly funded by a non-Jefferson entity, the ISM should not be an employee of that entity. The ISM should sign a confidentiality statement and, if not a TJU employee, a Conflict of Interest Disclosure (Attachment D of TJU Policy 107.03). The ISM should be familiar with the protocol and risks of the study and should provide periodic written reports that are in accordance with the monitoring plan to the PI and the IRB on a quarterly, bi-annual or other regular basis. The monitoring plan should be explained in the OHR-2.

3.2. Data Safety Monitoring Plan (DSMP)
Elements of a DSMP should include the following:
- Reviews of adverse events and unanticipated problems posing risks to subjects or others;

- Depending on the complexity of the research, the plan may include assessments of data quality, participant recruitment, accrual and retention; and

- Plan to assure data accuracy and protocol compliance.

- Parameters that would define the need for suspension of enrollment or closure of the study.

3.3. Data Safety Monitoring Board
The following research situations require the oversight of a DSMB:
- The study is intended to provide definitive information about the effectiveness and/or safety of a medical intervention;

- Prior data suggests that the intervention under study has the potential to induce a potentially unacceptable toxicity;

- The study is evaluating mortality or another major endpoint, such that inferiority of one treatment arm has immediate implications for research subjects regarding both safety and effectiveness; or

- The primary question has been definitively answered, even if secondary questions or complete safety information have not yet been fully addressed.
3.4. Composition of DSMB
The composition of a DSMB varies but should include multidisciplinary representation, such as physicians from relevant medical specialties, biostatisticians, and possibly other experts such as bioethicists, epidemiologists and basic scientists. Members must be free of significant conflicts of interest (i.e., financial, intellectual, professional, or regulatory).

4. IRB Review of the DSMB
The IRB will review the DSMB as described in the OHR-2, Section A, #6 at the time of initial review of the protocol and at each Continuing Review.
1. **Purpose and Scope**
   This Policy describes the procedures study personnel will use for ordering, distributing, storing, and maintaining an inventory of investigational devices used in human research.

2. **Definitions**
   See OHR Policy SC 501: Policy and Procedure to Determine Whether a Device Study Involves a Significant Risk or Nonsignificant Risk Device.

   See OHR Policy G 617: Research Device Acquisition, Use and Tracking.

3. **Persons Responsible**
   Principal Investigator: The Principal Investigator is responsible and accountable for the conduct of any human research employing an investigational device. The PI may delegate responsibility for use or deployment of the device to a qualified co-investigator, but may not delegate accountability.

   Research Coordinator

   TJUH OR Personnel - (Nurse Managers of the TJUH ORs, Satellite units (Endoscopy Suite, CVIR, etc.) are responsible for:
   - Documentation of the receipt, storage, and distribution of the investigational device,
   - Return, disposal, or destruction of the investigational device (if applicable).

4. **Costs Associated with Device Research**
   The Investigator and his/her team should, in collaboration with OR personnel, identify the costs associated with obtaining, storing and tracking the use and disposition of investigational devices and submit the figure(s) to Office of Research Administration for negotiating such costs with the study sponsor.

5. **Approval Procedures**
   IRB: No device may be ordered for or used in a human research study without prior IRB approval. When completing the IRB application, be certain that all OHR 2 questions related to device use are fully addressed (OHR 2 Part C, questions 1-3 and 11-21).
Value Analysis Committee Approval: No device may be ordered for or used in a human research study without the approval of the Value Analysis Committee. As soon as possible after beginning protocol development, a request for each product should be entered into the Value Analysis system, which is accessed from a link on the Administration home page of the TJUH intranet. If the product is to be provided at no cost, a 0 should be entered in the cost field. Otherwise, enter the estimated cost per unit of use. If the product is not being provided without cost, the Associate Chief Medical Officer responsible for research will work with ORA, the sponsor, the PI and hospital finance to define the nature and amount of the hospital’s contribution before the Value Analysis Committee can consider the request.

Both Supply Chain Management and the Value Analysis Committee recognize the nature and importance of research to the institution and make every effort to facilitate this process. Approval granted for use in IRB-supervised research is conditional and expires with the completion of the study. Re-application is necessary if the product is subsequently desired for routine clinical use.

6. Ordering Research Devices
   Sponsor supplied devices: Submit a $00.00 Request to Purchase (RTP) to TJUH Supply Chain Management.

   Departmentally supplied devices (non-sponsored research): Submit the appropriately completed RTP to TJUH Supply Chain Management.

Research devices will be delivered to the TJUH OR or to the relevant satellite suite.

7. Procedures
   7.1. Upon receipt of the study device, the shipment should be inventoried, verifying that the receipt date, lot number, device type, batch number, code mark and quantity on the packing slips is the same as what was actually received;

   7.2. Promptly bring any discrepancies to the attention of the Sponsor/supplier of the device(s);

   7.3. Retain a copy of the shipping inventory, packing slips and document inventory in the study files (Research Coordinator);

   7.4. The device will be stored in a secure environment according to requirements listed in the protocol or the investigator’s brochure. If controlled temperature is a requirement, the device should be stored in a temperature-monitored and alarmed area.

   7.5. Log device into the Pyxis® system for controlled monitored dispensing to the point of care.
7.6. At the conclusion of the study all documentation regarding receipt, storage, dispensing, and return of used containers, and accountability will be verified for completeness and accuracy.

7.7. An explanation of why and how many device units have been returned to the sponsor, repaired, or otherwise disposed of should be noted. When a device is disposed of, the identification of the person responsible should also be noted.

7.8. A copy of all accountability documents will be maintained in the regulatory files (Research Coordinator).

If for any reason a device to be used in human subjects research cannot be received, logged in and distributed as above, then the IRB must approve an alternative plan. The alternative plan should be submitted in detail in the OHR-2, Part C.

8. **Tracking**

Device manufactures are responsible for tracking devices used in clinical trials being done under an approved IDE (Investigational Device Exemption). Local tracking should be done using the OHR 21 form (OHR website) which may be modified to meet the needs of the research study. Completed forms should be kept in the subjects study file.

9. **References**

OHR Policy G 617 Research Device Acquisition, Use and Tracking

21 CFR 812


TJUH Policy 108.11 “Value Analysis Committee - Product Request Process”
1. **Purpose**  
To define and provide guidance regarding HIPAA permitted activities preparatory to research and some recruitment activities.

2. **Responsibility for Understanding the Guidance**  
Investigators  
Research Coordinators  
IRB Members/Chairs  
Privacy/Compliance Officer

3. **Definitions**  
3.1. "Activities Preparatory to Research" means activities involved in preparing for research such as: (1) preparing a research protocol; (2) developing a hypothesis; (3) writing a grant application; (4) requesting a query of a Covered Entity’s billing records to determine whether there is a sufficient number or type of records to conduct the research; and (5) identifying potential subjects or records of potential subjects who might be recruited to a research study.

3.2. “Covered Entity” under this guidance means Jefferson University Physicians (JUP) and Thomas Jefferson University Hospital (TJUH).

3.3. “Individually Identifiable Health Information” is information that is a subset of health information, including demographic data collected from an individual, and (1) is created or received by a Covered Entity; and (2) relates to the past, present, or future physical or mental health or condition of an individual; the provision of health care to an individual; or the past, present or future payment for the provision of health care to an individual; and (i) that identifies the individual, or (ii) with respect to which there is a reasonable basis to believe the information can be used to identify the individual.

3.4. “OHR-29” means the OHR form to be used by Researchers to request to engage in Activities Preparatory to Research.

3.5. “Protected Health Information” or “PHI” means Individually Identifiable Health Information transmitted or maintained in electronic or any other form.

3.6. “Researchers” means TJU investigators and research coordinators conducting research at JUP or TJUH under the auspices of Thomas Jefferson University (TJU).
3.7. “Records” means paper or electronic patient treatment records or billing records maintained by JUP and TJUH.

4. OVERVIEW
For Activities Preparatory to Research, JUP and TJUH, as Covered Entities, may use PHI or disclose PHI to a Researcher without securing a patient’s authorization, a waiver or alteration of Authorization, or a Data Use Agreement. A Researcher, making a request to a Covered Entity for a disclosure of Records or to provide Researcher access to Records for information preparatory to research, must represent that:

- The use or disclosure is requested solely to review PHI as necessary to prepare a research protocol or for similar purposes preparatory to research;
- The PHI will not be removed from the Covered Entity in the course of review; and
- The PHI for which use or access is requested is necessary for the research.

5. POLICY SPECIFICS
This policy addresses Activities Preparatory to Research as defined above and is specific to JUP and TJUH as the Covered Entities. If Researchers desire to use or access the records of other covered entities, Researchers will need to comply with the policies of those covered entities.

Application: Researchers must complete a form OHR-29 to request Records. The Covered Entity must receive a completed form OHR-29 from the Researcher. This form certifies that:

- The use of disclosure is requested solely to review PHI as necessary to prepare a research protocol or for similar purposes preparatory to research;
- The PHI will not be removed from the Covered Entity during the course of review;
- The PHI will not be subsequently disclosed once it is determined that there is sufficient basis for a clinical trial or research study;
- The PHI for which use or access is requested is necessary for the research; and
- The appropriate IRB forms will be submitted for IRB review and approval if it is determined that the information obtained will be used to conduct a research study.

PHI may not be removed from the Covered Entity. Researchers may record information using the PHI from the Covered Entity; such information must be de-identified.
A Researcher may not disclose PHI secured under a OHR-29 with a non-TJU Researcher unless and until the Researcher requests and obtains a Waiver of Authorization (OHR-3), a Limited Data Set Use Agreement (OHR-6B), or a Business Associates Agreement (BAA). Please consult Jefferson’s Office of Legal Counsel for a BAA.

The completed OHR-29 may be submitted by FAX or as a PDF attachment to an e-mail to the TJU/JUP privacy officer at FAX 215-923-3613 or doreen.kornrumpf@jefferson.edu or to the TJUH privacy officer at FAX 215-503-7867 or ann.powers@jefferson.edu.

In addition to the submission of the OHR-29 form to the Covered Entity, the Researcher must comply with the Covered Entity procedures to receive information or gain access to PHI. For example, if a Researcher desires to obtain a patient count for specific diagnosis code(s) to determine study feasibility, the Researcher may request JUP to provide the Researcher with a report of such findings. To request this report, the Researcher should submit an IDX Custom Request Form to the JUP administrator(s) listed on the form. In addition, if the Researcher desires to access the JUP EMR to review JUP patient electronic medical records to pre-screen records of patients who may qualify for an IRB-approved study, the Researcher will be required to complete a JUP EMR Custom Request form prior to accessing the JUP EMR. When Researchers submit either an IDX Custom Request Form or an EMR Custom Request Form to JUP, Researchers will be required to provide to JUP the plan the Researcher has in place to ensure the confidentiality of PHI.

6. RECRUITMENT AND CONTACTING POTENTIAL SUBJECTS
Following approval of the OHR-29 form by the Covered Entity’s privacy officer, the Researcher may conduct activities preparatory to research. Only if the Researcher decides to pursue a clinical study and secures IRB approval may the Researcher contact potential subjects to seek further Authorization for use of those individuals’ PHI and to obtain informed consent to participate in a research study. IRB requirements for contacting subjects must be followed and should include collaboration with the potential subject’s treating physician. For example, the treating physician contacts his/her patient regarding the research study in question or for patient permission for contact by the researcher. See GA 123, Protection of the Confidentiality of Identifiable Data by the Investigator and the IRB and GA 129, Protection of Privacy Interests of Research Subjects and Confidentiality of Subject Data.

7. ACCOUNTING FOR DISCLOSURES
Each Covered Entity must maintain a log of PHI disclosures whether such disclosures were for internal or external research-related purposes. Researchers must comply with the Covered Entity’s Accounting of Disclosures of Protected Health Information policies. (For JUP/TJU, see Policy No.: 122.08, HIPAA Privacy Policy and for TJUH, see Policy No.: 111.20, Accounting of Disclosures of Protected Health Information (PHI) Policy and Forms.)
8. **TOOLS**

45 CFR 164.512(i)(1)(ii)
OHR-29 “Review Preparatory to Research Request Form”
JUP EMR Custom Report Request Form
JUP IDX Custom Report Request Form
DHSP Policy GA 127 “Subject Recruitment and Enrollment”
1. **Purpose**
   To define and provide guidance regarding (1) the use of radioactive materials in human subjects research, and (2) the approval required to use such materials in research.

2. **Responsibility for Understanding the Guidance**
   - Investigators
   - Research Coordinators
   - IRB Members/Chairs
   - Director, Office of Radiation Safety

3. **Background**
   Various aspects of the use of radioactive materials in human research are regulated by the US Food and Drug Administration (FDA) and by the US Nuclear Regulatory Commission (NRC). Under NRC regulations, the NRC may enter into agreements with individual states, effectively transferring regulatory authority to the states, provided that state regulations are compatible with NRC regulations. Pennsylvania is a so-called Agreement State and directly incorporates NRC regulations by reference. The FDA regulates the manufacturers of radiation-producing machinery (e.g., sets performance standards for x-ray equipment) and medical devices that incorporate radioactive materials. The individual states regulate the use of radiation producing machinery. Regulatory authority in Pennsylvania for radioactive and machine-produced sources of radiation rests with the Pennsylvania Department of Environmental Protection (DEP), Bureau of Radiation Protection.

   “Radioactive drug” is defined in 21 CFR §310.3(n) and includes “radioactive biological product” as defined in 21 CFR § 600.3. Radioactive materials in NRC regulations are defined under the term “byproduct material” (see definition in 10 CFR § 20.1003).

4. **Categories of Use**
   The use of ionizing radiation sources in or on human research studies can fall into one of the following categories:
   - Radioactively labeled drugs used to obtain basic information regarding the metabolism (including kinetics, distribution, and localization) of the radioactive drug or regarding human physiology, pathophysiology, or biochemistry (see 21 CFR § 361.1).
   - To study the safety and effectiveness of a radioactive drug or radiation emitting device for diagnostic, therapeutic, or similar purposes (i.e., clinical trials).
• To use already FDA-approved radiopharmaceuticals for uptake, dilution, or excretion studies or for imaging and localization studies, or to use FDA approved x-ray imaging equipment as a means of assessing the effectiveness of a clinical regimen (e.g., use of a non-radioactive study drug) or physiologic process being studied.

• To use a non-radioactive study drug or a regimen not involving a radiation source in conjunction with a standard radiation therapy or diagnostic radiation procedure used to assess whether the study drug or regimen increases the efficacy of a standard therapeutic or diagnostic modality (i.e., the subject/patient would undergo the radiation procedure regardless of participation in the study).

4.1. Guidance re Category 1

Each proposed human subjects research protocol involving the research-related use of radioactive material and/or other sources of ionizing radiation (i.e., not clinically indicated procedures) requires the approval of (1) the Thomas Jefferson University Hospital/Thomas Jefferson University (TJUH/TJU) Radiation Safety Committee (RSC) or the Radiation Safety Officer (as appropriate – RSC procedures permit RSO only approval in limited circumstances), (2) the Jefferson Radioactive Drug Research Committee (RDRC), and (3) the Thomas Jefferson University (TJU) Institutional Review Board (IRB). The use of radioactive materials for research use is permitted only by or under the supervision of an authorized user approved by the TJUH/TJU Radiation Safety Committee (RSC).

When research involves investigational or unlicensed test articles, TJU must confirm that the test articles have appropriate regulatory approval or meet exemptions for such approval. (AAHRPP Element I.7.A as of 3/1/2010)

FDA regulations found in 10 CFR §21.361.1 apply to this category of research. Oversight at TJU/TJUH is handled by the Radioactive Drug Research Committee which is chartered by the FDA under 21 CFR § 361.1 to review both basic science and human subjects research in which radioactive devices or drugs are employed. The research study is approved the Radioactive Drug Research Committee based on the following requirements [§61.1(b)(1)(iv)]:

• Qualified study investigators

• Appropriate selection and consent of research subjects

• Appropriate quality assurance of radioactive drug administered

• Sound research protocol design
• Reporting of adverse events by the investigator to the RDRC

• Approval by the IRB

• Approval by the RSC

• The pharmacologic dose of the radioactive drug to be administered is known not to cause any clinically detectable pharmacologic effect in humans [§361.1(b)(2)].

• The radiation dose to be administered is justified by the quality of the study being undertaken and the importance of the information it seeks to obtain [§361.1(b)(1)(iii)] and is within the limits specified in § 361.1(b)(3) as shown below.

Radiation Dose Limit Guidelines (for this category)

<table>
<thead>
<tr>
<th>Age of Subject</th>
<th>Radiation Dose Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Under 18 years</td>
<td>300 mrem to the whole body (i.e., “effective dose”), active blood forming organs, lens of the eye, and gonads from a single administration, and 500 mrem annually.</td>
</tr>
<tr>
<td>18 years or older</td>
<td>3,000 mrem to the whole body (i.e., “effective dose”), active blood forming organs, lens of the eye, and gonads from a single administration, and 5,000 mrem annually.</td>
</tr>
<tr>
<td></td>
<td>5,000 mrem to other organs from a single administration, and 15,000 mrem annually.</td>
</tr>
</tbody>
</table>

[Note: Any radiation doses received by a participant from any imaging (e.g., x-ray) studies that would not have occurred but for participation in the study, must be included in the dose assessment.]

Use of radioactive materials in research subject to 21 CFR § 361.1 is also subject to NRC (or Agreement State) regulations. The TJUH/TJU RSC (or RSO in limited circumstances) approves the research based on the following considerations:

• Properly licensed facility to possess and handle radioactive materials

• Properly licensed facility for the administration of radioactive materials or application of radiation to humans

• Physician(s) appropriately authorized to supervise the administration of radioactive materials to humans
• Appropriate radiation safety procedures/precautions

• Appropriately trained personnel

• Appropriate provision for radioactive waste disposal and (where necessary) shipping radioactive samples.

• Appropriate radiation doses

• Approval by the IRB

• Approval by the RDRC

4.2. Guidance re Category 2
Most human subject research involving radiation is conducted under the terms of an Investigational New Drug (IND) or an Investigational Device Exemption (IDE) issued by the FDA, and must also be reviewed and approved by an IRB.

As defined in 21 CFR § 361.1 the RDRC has no oversight responsibility or authority over an investigation carried out under an IND exemption. This authority is retained by the FDA. If a radiopharmaceutical cannot be classified as “generally recognized as safe and effective,” (see FDA Guidance for use of Radiology Devices and Radioactive Materials in Research Protocols) the RSC may not review and approve the research, and an IND may be needed.

Regulation 21 CFR § 361.61 specifically does not apply to:
• Research intended for immediate therapeutic, diagnostic or similar purposes (e.g. preventive benefit to the study subject from the research).

• Research intended to determine the safety and effectiveness of a radioactive drug in humans.

Approval by the RDRC is therefore not required.

Use of radioactive materials and radiation producing machines or devices in research is however subject to NRC (and/or State) regulations. The TJUH/TJU RSC (or RSO in limited circumstances) approves the research based on the following considerations:
• Properly licensed facility to possess and handle radioactive materials or radiation producing device

• Properly licensed facility for the administration of radioactive materials or application of radiation to humans
• Physician(s) appropriately authorized to supervise the administration of radioactive materials or ionizing radiation to humans

• Appropriate radiation safety procedures/precautions

• Appropriately trained personnel

• Appropriate provision for radioactive waste disposal and (where necessary) shipping radioactive samples.

• Appropriate radiation doses (e.g., similar to that received from similar, already approved diagnostic or therapeutic uses, justified by the aims of the research)

• Approval by the IRB

4.3. Guidance re Category 3
This category applies to uses of standard techniques already in clinical use (e.g., imaging procedures involving FDA approved radiopharmaceuticals, standard x-ray or CT imaging techniques) in research on other new non-radioactive/radiation drugs or regimens, for the purpose of assessing the efficacy of the study drugs or regimen. All uses of ionizing radiation are subject to federal and/or state regulation. However, whether RSC (or RSO) approval is needed for is based on one criterion: “Would the research subject undergo any procedures involving radiation exposure that the subject would not receive if he/she did not participate in the study?” If yes, IRB and RSC (or RSO) approval is warranted.

The TJUH/TJU RSC (or RSO in limited circumstances) approves the research based on the following considerations:

• Properly licensed facility to possess and handle radioactive materials or radiation producing device

• Properly licensed facility for the administration of radioactive materials or application of radiation to humans

• Physician(s) appropriately authorized to supervise the administration of radioactive materials or ionizing radiation to humans

• Appropriate radiation safety procedures/precautions

• Appropriately trained personnel

• Appropriate provision for radioactive waste disposal and (where necessary) shipping radioactive samples.
• Appropriate radiation doses (e.g., similar to that received from similar, already approved diagnostic or therapeutic uses, justified by the aims of the research)

• Approval by the IRB

4.4. Guidance re Category 4
In this category the radiation doses received by the subject are part of the clinical standard of care and would be received regardless of participating in the study. Review and approval by the RSC (or RSO) is NOT required. IRB review and approval based on considerations other than radiation exposure is required as per federal regulations.

5. Policy Specifics
All human research studies involving use of radioactive materials or radiation emitting devices that exceed expected radiation exposure encountered in usual clinical care require review and approvals as described above prior to initiating the research.

Pregnant subjects may not participate in research studies using “radioactive research drugs” as described under Category 1 above. Likewise, pregnant subjects may not participate in research studies using radioactive drugs or radiation emitting devices as described under Categories 2 and 3 above, unless a purpose of the study is specifically aimed at the pregnant female population. Pregnant subjects are not required to be denied participation for Category 4. It is the responsibility of investigator to ensure female subjects of child-bearing age are not pregnant at the time of dose administration. Either urine or blood pregnancy test is recommended to be performed prior to the administration of study drug.

As with employees and the general public, radiation dose to research subjects is required to be “as low as reasonably achievable” (ALARA). Specifically, radiation doses administered should be the minimum necessary to achieve the desired research objectives. For imaging studies performed on human research subjects, as with patients, radiation doses should be optimized such that the lowest radiation dose necessary to produce adequate quality images is utilized.

Informed consent forms should address all required consent elements including appropriate precautions for pregnant subjects and risks of radiation.

6. Tools
Form OHR-32: Research in humans using radioactive drugs or devices

Submit completed OHR-32 form to:
1. Purpose
This Guidance describes requirements for IRB review and investigator responsibilities when conducting human subjects research sponsored or funded by the DoD.

2. Responsibility for Understanding the Guidance
OHR Staff
Investigators
Research Coordinators
IRB Members
IRB Chairs/Vice Chairs

3. Background
Research sponsored or funded by the DoD must be reviewed by the IRB under an additional set of regulations found at 32 CFR 219 and in DoD Instruction 3216.02 accessible at the following web address http://dtic.mil/whs/directives/corres/pdf/321602p.pdf. The Principal Investigator must meet these additional DoD requirements prior to initiation of the research.

Investigators contemplating research supported by the DoD should contact the Director or Associate Director, OHR, prior to submitting materials for IRB review.

4. Guidance
4.1. Training and Education
- All personnel who conduct, review, approve, oversee, support, or manage human subjects research are required to undergo initial and continuing research ethics education.

- There may be specific DoD educational requirements or certification required.

- DoD may evaluate the organization’s education policies to ensure the personnel are qualified to perform the research, based on the complexity and risk of the research.

- As the investigator must be aware of the specific requirements contained in DoD regulations and requirements and educated about these requirements when appropriate.

4.2. Scientific Review
The IRB must consider the scientific merit of the research.

The IRB may rely on outside experts to provide an evaluation of the scientific merit.

4.3. International Research

The researcher or the organization must obtain permission to conduct research in the specified country by certification or ethics review by the appropriate entity or official.

- Copies of such permissions, certifications or other documentation must be provided prior to IRB approval.

The researcher must follow all local laws, regulations, customs, and practices as pertinent to conducting research.

4.4. Reporting: The following finding in DoD-supported research must be reported to the DoD human research protection officer within 30 days:

- Determinations of Serious or Continuing Noncompliance
- Significant changes to the research protocol have been approved by the IRB
- The results of the IRB continuing review
- Change of reviewing IRB
- Notified by any Federal department, agency or national organization that any part of an HRPP is under investigation for cause
- Any Unanticipated Problems Involving Risk to Subjects or Others
- Suspension of IRB approval
- Termination of IRB approval

4.5. Survey Approval

Surveys performed on DoD personnel must be submitted, reviewed, and approved by the DoD after the research protocol is approved by the IRB.

4.6. Multisite Research

When conducting multi-site research, a formal agreement between organizations is required to specify the roles and responsibilities of each party.
4.7. Definition of Minimal Risk

- The definition of minimal risk based on the phrase “ordinarily encountered in daily life or during the performance of routine physical or physiological examinations or tests” must not be interpreted to include the inherent risks certain categories of human subjects face in their everyday life. For example, the risks imposed in research involving human subjects focused on a special population should not be evaluated against the inherent risks encountered in their work environment (e.g., emergency responder, pilot, soldier in a combat zone) or having a medical condition (e.g., frequent medical tests or constant pain).

- The organization applies this definition to all research regardless of funding.

4.8. Appointment of a Research Monitor:

Research monitor(s) may be appointed by the investigator but must be approved by the IRB.

The IRB considers the appointment of a research monitor:

- Required for research involving greater than minimal risk, although the IRB or organizational official can require this for a portion of the research or studies involving no more than minimal risk if appropriate.

- The research monitor is appointed by name and shall be independent of the team conducting the research.

- There may be more than one research monitor (e.g. if different skills or experience are needed.

- The monitor may be an ombudsman or a member of the data safety monitoring board. The IRB must approve a written summary of the monitors’ duties, authorities, and responsibilities.

- The IRB or HRPP official shall communicate with research monitors to confirm their duties, authorities, and responsibilities.

- The duties of the research monitor are determined on the basis of specific risks or concerns about the research, such as:
  - Perform oversight functions (e.g. observe recruitment, enrollment procedures, and the consent process, oversee study interventions and interactions, review monitoring plans and unanticipated problems involving risks to participants or others, oversee data matching, data collection and analysis).
  - Discuss the research protocol with researchers, interview human subjects, and consult with others outside of the study.
  - Report observations and findings to the IRB or a designated official.
• The research monitor has the authority to:
  o Stop a research project in progress
  o Remove individuals from a study
  o Take any steps to protect the safety and well-being of participants until the IRB can assess.

4.9. Recruitment of Service Members
• Officers are not permitted to influence the decision of their subordinates.

• Officers and senior non-commissioned officers may not be present at the time of recruitment.

• Officers and senior non-commissioned officers have a separate opportunity to participate.

• When recruitment involves a percentage of a unit, an independent ombudsman is present.

4.10. Compensation of Service Members
• Service member may not receive pay of compensation for research during duty hours.

• A service member may be compensated for research if the subject is involved in the research when not on duty.

• Federal employees while on duty and non-Federal persons may be compensated for blood draws for research up to $50 for each blood draw.

• Non-Federal persons may be compensated for research participating other than blood draws in a reasonable amount as approved by the IRB according to local prevailing rates and the nature of the research.

4.11. Consent
• The disclosure for research-related injury must follow the requirements of the DoD component.

• If the subject undergoes interactions or interventions for research purposes, the subject is considered an "experimental subject." For experimental subjects:
  o A waiver of the consent process is prohibited unless a waiver is obtained from the Assistant Secretary of DoD for Research and Engineering.
  o The Assistant Secretary for DoD for Research and Engineering may waive the requirements for consent when all of the following are met:
The research is necessary to advance the development of a medical product for the Military Services.

- The research may directly benefit the individual experimental subject.
- The research is conducted in compliance with all other applicable laws and regulations.
  - The IRB may waive the consent process for subjects who are not “experimental subjects.”

- If consent is to be obtained from the experimental subjects' legal representative, the research must intend to benefit the individual subject.
  - The determination that research is intended to be beneficial to the individual experimental subject must be made by an IRB.

- Waivers of consent are prohibited for classified research.


- Research involving pregnant women and fetuses as subjects is subject to HHS Subpart B except:
  - The phrase “biomedical knowledge” is replaced with “generalizable knowledge.”
  - The applicability of Subpart B is limited to research involving pregnant women as subjects in research that is more than minimal risk and included interventions or invasive procedures to the woman or the fetus or involving fetuses or neonates as subjects.

4.13. Research on Prisoners

- Research involving prisoners is subject to HHS Subpart C.

- Research involving prisoners cannot be reviewed by the expedited procedure.

- When the IRB reviews research involving prisoners, at least one prisoner representative must be present for quorum.

- In addition to allowable categories of research on prisoners in 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.
• When a subject becomes a prisoner, if the investigator asserts to the IRB that it is in the best interest of the prisoner-subject to continue to participate in the research while a prisoner, the IRB chair may determine that the prisoner-subject may continue to participate until the convened IRB can review this request to approve a change in the research protocol and until the institutional official and DoD Component office review the IRB’s approval to change the research protocol. Otherwise, the IRB chair must require that all research interactions and interventions with the prisoner-subject (including obtaining identifiable private information) cease until the convened IRB can review this request to approve a change in the research protocol. The convened IRB, upon receipt of notification that a previously enrolled human subject has become a prisoner, must promptly re-review the research protocol to ensure that the rights and wellbeing of the human subject, now a prisoner, are not in jeopardy. The IRB should consult with a subject matter expert having the expertise of a prisoner representative if the IRB reviewing the research protocol does not have a prisoner representative. If the prisoner-subject can continue to consent to participate and is capable of meeting the research protocol requirements, the terms of the prisoner-subject’s confinement does not inhibit the ethical conduct of the research, and there are no other significant issues preventing the research involving human subjects from continuing as approved, the convened IRB may approve a change in the study to allow this prisoner-subject to continue to participate in the research. This approval is limited to the individual prisoner-subject and does not allow recruitment of prisoners as subjects.

• Research involving a detainee as a human subject is prohibited.
  o This prohibition does not apply to research involving investigational drugs and devices when the same products would be offered to US military personnel in the same location for the same condition.

• Research involving prisoners of war is prohibited.
  o “Prisoner of war” includes any person captured, detained, held, or otherwise under the control of DoD personnel (military, civilian, or contractor employee). Such persons include: Enemy Combatant, Lawful Enemy Combatant, Unlawful Enemy Combatant, Enemy Prisoner of War, Retained Person, and Civilian Internee. Such persons do not include personnel of the DoD being held for law enforcement purposes. It does not include persons being held primarily for law enforcement purposes, except where the United States is the occupying power.
This prohibition does not apply to activities covered by investigational new drug or investigational device provisions the purpose of diagnosis or treatment of a medical condition in a patient. Such treatment (e.g., an investigational new drug) may be offered to detainees with the detainees’ informed consent when the medical products are subject to FDA regulations investigational new drugs or investigational medical devices, and only when the same product would be offered to members of the U.S. Military Services in the same location for the same medical condition and only when consistent with established medical practice involving investigational drugs and devices.

4.14. Research on Children
• Research involving children is subject to the HHS Subpart D.

• The exemption for research involving survey or interview procedures or observation of public behavior, does not apply to research with children, except for research involving observations of public behavior when the investigator(s) do not participate in the activities being observed.

4.15. Research on Fetal Tissue
• Fetal research must comply with US Code Title 42, Chapter 6A, Subchapter III, Part H, 289g.

4.16. Waiver of Informed Consent for Planned Emergency Research
• An exception from consent in emergency medicine research is prohibited unless a waiver is obtained from the Secretary of DoD.

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

4.18. Non-exempt Classified Research is not performed at TJU. In the unlikely event such research is contemplated by a Jefferson investigator, the investigator should carefully review DoD instruction 3216.02 (see link above) and contact the Director, OHR prior to initiating any aspect of a proposal.

5. References
DoD Instruction 3216.02
32 CFR 219
1. Purpose
   This policy describes the general requirements for obtaining and documenting informed consent.

2. Responsibility for Executing the Policy
   Director/Associate Director, OHR
   OHR Administrative Staff
   IRB Chairs/Vice Chairs
   Investigators
   Study Personnel

3. Policy Statement
   This policy pertains to all research submitted to the IRBs. Informed consent must be legally effective and prospectively obtained (45 CFR 46.116; 21 CFR 50.20). Except as delineated in Policy IC 706, Waiver of Informed Consent and HIPAA Authorization, no investigator may enroll a human being as a research subject unless s/he has obtained legally effective informed consent from the subject or the subject's legally authorized representative (LAR). Consent shall be sought only under circumstances that provide the prospective subject or the LAR sufficient opportunity to consider whether or not to participate in the study, and that minimize the possibility of coercion or undue influence.

   Subject authorization also must be obtained for prospective use or disclosure of protected health information (PHI) for research conducted within the University or the University Hospital. Except as described in Policy IC 706 no investigator may prospectively collect PHI unless s/he has obtained legally effective authorization of the subject or the subject's legally authorized representative.

   The IRB requires documentation of informed consent by use of a written consent form approved by the IRB and signed and dated by the subject or the subject's LAR. Authorization to collect PHI will also be obtained by the use of the IRB-approved consent form (OHR-8) that contains a federally-compliant HIPAA Confidentiality Section or, as appropriate, a separate HIPAA Authorization document.

4. Procedures
   The consent form document may be either of the following:
   - A written consent document that encompasses the elements of informed consent and the required elements of a HIPAA authorization. This form may be read to the subject or the subject's LAR. The investigator shall give the subject or the LAR adequate opportunity to read it before it is signed. The subject or LAR shall receive a copy of the signed and dated consent document.
• A “short form” written consent document stating that the elements of informed consent as required have been presented orally to the subject or the subject's LAR. When this method is used, there shall be an impartial witness to the oral presentation. The IRB must approve a written summary of what is to be said to the subject or representative. The subject or the LAR will sign the short form. The witness shall sign both the short form and a copy of the summary, and the person actually obtaining the informed consent shall sign the summary. A copy of the signed and dated summary and the signed and dated short form shall be given to the subject or the LAR.

4.1. Required Elements of Informed Consent
The following elements must be present in all IRB-approved informed consent documents:

• A statement that the study involves research, an explanation of the purposes of the research, the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental or investigational.

• A description of any reasonably foreseeable risks or discomforts to the subject.

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

• A disclosure of appropriate alternative procedures or courses of treatment, if any, that the subject can pursue outside of the study.

• A statement describing the extent to which, if any, the confidentiality of records identifying the subject will be maintained and that states the possibility that the Food and Drug Administration and representatives of the IRB may inspect the records.

• For research involving greater than minimal risk, or any study reviewed by the convened Board, an explanation as to whether any compensation is available and that medical treatments are available if injury occurs and where further information may be obtained.

• The informed consent document must not waive or appear to waive the rights of the participant or release, or appear to release, those conducting the study from liability for negligence.

• 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 and that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

Informed consent documents may not contain any exculpatory language through which the subject is made to waive or appear to waive legal rights or releases or appears to release the investigator, the sponsor, or the university from liability for negligence.

4.2. Additional Elements of Informed Consent
When appropriate, one or more of the following elements also may be required in the informed consent document:

- 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) which are currently unforeseeable.

- Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.

- Any additional costs to the subject that may result from participation in the research.

- The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject.

- A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject.

- The approximate number of subjects involved in the study at Jefferson and nationally if a multi-site study.

4.3. Elements of HIPAA Authorization
The following elements are required in a federally-compliant HIPAA Authorization. These elements should be part of the Confidentiality Statement in the OHR Informed Consent Document template:

- A description of the health information to be collected as part of the research.

- A description of the person or classes of persons authorized to use or disclose the protected health information.
• A description of the person or classes of persons who may receive the information, and the purpose(s) for each disclosure.

• An expiration date or the extent of the authorization for use or disclosure if any

• A statement of the subject’s right to revoke authorization and person to contact to revoke

• Reference to the covered entities Notice of Privacy Practices

• Notice that disclosure of protected health information to non-HIPAA compliant entities may result in subsequent loss of protection of PHI.

• Limitations, if any, on a subject’s access to their records during the study.

4.4. Documentation of Informed Consent
At some point in the consent process, an interview or session is held with the prospective subject and/or LAR so that all of the subject’s/LAR’s questions and concerns are answered before s/he makes the final decision on participation. This interview can be conducted by the PI, a Co-I, or any key personnel designated by the PI. When the subject or LAR signs the consent form, this is referred to as “obtaining informed consent.”

The ultimate responsibility for ensuring that informed consent is obtained, and that the consent interview is conducted in such a way that all of the subject’s/LAR’s questions and concerns are answered rests with the PI. However, because consenting situations are so varied, the IRB will only make specific determinations as to who can and cannot obtain informed consent on a case-by-case basis.

Whomever is designated to conduct the consent interview must describe the research study to the potential subject/LAR, discuss appropriate alternatives, and answer any questions regarding the research, and obtain the subject’s/LAR’s consent to participate prior to initiating any research procedure.

If the consent interview is conducted by key personnel other than the PI (or Co-I if the PI is unavailable), the PI or Co-I must be reachable by phone if the subject should have questions that cannot be answered by the person conducting the interview. If the research poses greater than minimal risk, the PI or a Co-I should make every effort to be present at some time during the consent interview.
When the subject signs and dates the consent form, the person conducting the consent interview will also sign and date. If the PI or Co-I is present at this time, s/he also will sign and date. If the PI/CO-I is not present, s/he should sign and date the consent as soon as is possible so that a copy with all signatures can be given to the subject.

The original consent form, signed and dated by the subject, or the subject’s authorized representative, and the PI or Co-I, and a witness if necessary, must be kept in the subject’s study file and a photocopy provided to the subject. The requirement for presence of a PI or Co-I during the consent process as noted above may be waived on a case-by-case basis, or as per OHR Policy IC706. Examples of situations where direct subject contact with the PI or Co-I may not be required are prospective community health research and questionnaires, focus group research, and minimal risk studies such as physical therapy studies done at a subject’s home or public gathering place.

4.5. Other Requirements

- **Second Person:** The consent document should use the second person (You/your) style so the consent form conveys a dialogue with information being provided and that there is a choice to be made by the subject rather than presumption of the subject’s consent with the use of the first person style (I/mine).

- **Simple Language:** The information provided in the informed consent documents must be in language understandable to the subject. The informed consent document should not use complex language that would not be understandable to all subjects. Technical and scientific terms should be adequately explained using common or lay terminology (See Guidance Document G 603).

- **FDA-Regulated Test Articles:** For research involving test articles regulated by the U.S. Food and Drug Administration (FDA), informed consent documents must include a statement that the purpose of the study includes evaluation of the safety and/or efficacy of the test article. The consent form must also include a statement that the FDA has access to the subject's medical records.

4.6. IRB Review of Consent Process

The IRB will take the following into consideration when reviewing the protocol and consent document:

- Who will conduct the consent process?

- Matters of timing of obtaining informed consent and the waiting period between informing the subject and obtaining consent.
• That the process provides ample time for the person conducting the consent interview and the prospective subject to exchange information and ask questions.

5. Tools
- OHR OHR-8 OHR Informed Consent Document Template
- OHR Policies IC 701, Informed Consent and HIPAA, and IC 702, IC documentation
- OHR Guidance G 603, Lay terminology
1. Purpose
This policy describes the requirements for documenting informed consent and the circumstances when the IRB may waive or alter the requirement to document informed consent.

2. Responsibility for Executing the Policy
Director/Associate Director, OHR
OHR Administrative Staff
IRB Chairs/Vice Chairs
Investigators
Study Personnel

3. Policy Statement
This policy pertains to all research submitted to the IRBs. Unless specifically waived by the IRB, informed consent for all subjects, or their legally authorized representatives, must be documented. DHHS provides for waiver or alteration of consent, and waiver of written documentation under certain conditions. FDA-regulated studies have no such provision because the types of research that qualify for waiver are not regulated by FDA or are covered by the emergency treatment regulations at 21 CFR 50.23.

4. Procedures
4.1. Documentation of Informed Consent (45 CFR 46.116; 45 CFR 46.117; 21 CFR 50.27)
Each subject or his/her legally authorized representative (LAR) must sign and date a copy of the current IRB-approved consent form prior to enrollment or any participation in any phase of a research study, unless the requirement is waived by the IRB. The subject must be given a copy of the signed document that has also been signed by the Principal Investigator or co-investigator and the person conducting the consent interview. At the discretion of the IRB, these signature requirements may be waived. For example, the signature of the principal or co-investigator may be waived for selected minimal risk studies.

The IRB may approve procedures for documentation of informed consent that involve: (1) a written consent form signed by the subject; (2) a short form written consent form with oral presentation; or (3) in limited circumstances a waiver or alteration of a written consent form. Each of these three options is described in detail below. It is the responsibility of the IRB to determine which of the procedures described below is appropriate for documenting informed consent.
4.1.1. Written Consent Form Signed by Subject or LAR:
In most circumstances, the IRB requires that informed consent is documented by the use of a written consent form approved by the IRB and signed by the subject or the LAR as well as by the Principal Investigator or co-investigator. The investigator should allow the subject or the LAR adequate opportunity to read the consent document before it is signed.

Some studies involving subjects with anticipated or fluctuating impaired decision-making capabilities may take place over extended periods. For these studies, the IRB should consider whether periodic re-consenting of individuals or their LARs should be required to ensure that a subject's continued involvement is informed and voluntary. Additionally, the IRB should consider whether and when to require a reassessment of subject's decision-making capacity.

The written informed consent document should contain, in a language understandable to the subjects of the study, all the elements necessary for legally effective informed consent (see OHR Policy IC 701). Subjects who do not understand English should be presented with an informed consent document written in a language understandable to them.

4.1.2. Research Data Retention
In accordance with FDA guidance

- When a subject withdraws from a study, the data collected on the subject to the point of withdrawal remains part of the study database and may not be removed. The consent document cannot give the subject the option of having data removed.

- The investigator may ask a subject who is withdrawing whether the subject wishes to provide continued follow-up and further data collection subsequent to their withdrawal from the interventional portion of the study. Under this circumstance, the discussion with the subject must distinguish between study-related interventions and continued follow-up of associated clinical outcome information, such as medical course or laboratory results obtained through noninvasive chart review, and address the maintenance of privacy and confidentiality of the subject's information.
  - The Researcher must obtain the subject's informed consent for this limited participation in the study (assuming such a situation was not described in the original informed consent form). The IRB must approve the consent document.
If a subject withdraws from the interventional portion of a study and does not consent to continued follow-up of associated clinical outcome information, the researcher must not access for purposes related to the study the subject's medical record or other confidential records requiring the subject's consent. However, a researcher may review study data related to the subject collected prior to the subject's withdrawal from the study, and may consult public records, such as those establishing survival status.

4.1.3. Short Form Consent(45 CFR 46.117(b); 21 CFR 50.27)

As an alternative to standard written informed consent documents, oral presentation of informed consent information may be used with a short form consent document. In such cases, the subject must be provided with: a) a short form informed consent document stating that the elements of consent have been presented orally to the subject or the subject's LAR; and b) a written summary of the information that is presented orally.

A witness to the oral presentation is required. When this method is used the IRB must review the written summary. The subject or the LAR must sign the short form written consent document.

The person obtaining consent must sign a copy of the written summary of the information that is presented orally. The person obtaining consent may not be the witness to the consent.

For potential subjects who do not speak English (Policy IC 705), where informed consent is documented using this short form procedure, the written informed consent document should contain, in language understandable to the subject, all the elements necessary for legally effective informed consent. When this procedure is used with subjects who do not speak English:

- The oral presentation and the short form written informed consent document should be in a language understandable to the subject;

- The IRB-approved English language informed consent document may serve as the summary; and

- For those subjects who are consented using a foreign language consent document, the witness should be fluent in both English and the language of the subject. For those studies, the IRB will receive all foreign language versions of the short form as a condition of approval. The information in the protocol must match the information in the informed consent document.
Expedited review of these versions is acceptable if the protocol, the full English language informed consent document, and the English version of the short form document have already been approved by the convened IRB.

4.1.4. Use of Facsimile of Mail to Document Informed Consent
The IRB may approve a process that allows the informed consent document to be delivered by mail or facsimile to the subject or LAR, and to conduct the consent interview by telephone when the subject or the LAR can simultaneously read the consent document as it is discussed. Consent may also be obtained by mail. When using this procedure, the subject or LAR will first sign and date the consent form and mail it to the investigator.

The investigator will then sign and date the consent form and mail a copy of this form to the subject or LAR.

5. Reconsenting
Re-consent of research subjects is required when there is new information about a trial that could affect the subject’s willingness to continue in the trial. Examples include increased or new risks and changes in the protocol that materially affect the subject, such as additional study visits, increased length of visits, new questionnaires or changes in treatment modalities.

Subjects should be presented with the amended IRB-approved consent form with added and/or deleted content denoted appropriately (e.g., hi-lighted or underlined). The changes also should be explained verbally to the subject. The subject should initial and date the pages containing the changes and also sign and date the signature page of the consent form. The subject should receive a complete copy of the signed and dated amended consent form.

6. References
Policy IC 705, Informed Consent for Illiterate and Non-English Speaking Subjects.
OHRP Compliance Activities: Common Findings and Guidance #45.
1. Purpose
   To provide information regarding the requirements for parental permission for a child’s participation in a research study. This policy is to be used in conjunction with Policy IC 704, Child Assent to be a Subject in Research.

2. Responsibility for Executing the Policy
   IRB Members
   IRB Reviewers
   Investigators
   Research Coordinators

3. Definitions
   3.1. Children: Both HHS and FDA define children as “persons who have not attained the legal age for consent to treatments or procedures involved in the research (or clinical investigations in the case of FDA), under the applicable law of the jurisdiction in which the research will be conducted.” [(45 CFR 46.402(a) and 21 CFR 50.3(o)]

   3.2. Assent: Both HHS and FDA define assent as “a child's affirmative agreement to participate in research (or clinical investigation in the case of FDA). Mere failure to object should not, absent affirmative agreement, be construed as assent.” [45 CFR 46.402(b) and 2a CFR 50.3(n)]

   3.3. Permission: Both HHS and FDA define Permission as “the agreement of parent(s) or guardian to the participation of their child or ward in research (or clinical investigation in the case of FDA)” [45 CFR 46.402(c) and 21 CFR 50.3(r)]

   3.4. Parent: Both HHS and FDA define Parent as “a child's biological or adoptive parent.” [45 CFR 46.402(d) and 21 CFR 50.3(p)]

   3.5. Guardian: HHS defines guardian as “an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care.” [45 CFR 46.402(e)]

   FDA defines Guardian as “an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care when general medical care includes participation in research.” [21 CFR 50.3(s)]
3.6. **Family Member**: FDA defines family member as “any one of the following legally competent persons: Spouse; parents; children (including adopted children); brothers, sisters, and spouses of brothers and sisters; and any individual related by blood or affinity whose close association with the subject is the equivalent of a family relationship.

3.7. **Ward**: FDA defines ward as “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.” [21 CFR 50.3(q)]

4. **Policy Statement**

4.1. Parental Permission for Enrollment of a Child in a Study

Children generally have not reached their full intellectual and emotional capacities and thus are legally unable to give valid consent. Consequently, when children or minors are involved in research, federal regulations require the assent of the child or minor and the permission of the parent(s). No individual can consent for someone else; she/he can only give permission. In the case of a parent wishing to enroll a child/adolescent in a research study, the parent must sign a parental permission that is similar to the adult consent form (OHR-8) except that the parent gives permission for his/her child/adolescent to participate in the research. Parental permission is treated the same as informed consent apart from some additional provisions found in 45 CFR 46.408. Parental permission along with child assent meets federal requirements for enrollment of a child in a research study.

While the default for parental permission is that both parents sign permission, federal regulations provide that an IRB may find that the permission of one parent is sufficient for research to be conducted if the research represents no more than minimal risk, or if the research involves greater than minimal risk, but presents the prospect of direct benefit to individual subjects. Where research is covered by 45 CFR 46.406 and 46.407 of the HHS regulations and 21 CFR 50.53 and 50.54 of the FDA regulations, 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.

4.2. Waiver of Parental Permission
Under the regulations at 45 CFR 46.408 (c), in addition to the provisions for waiver contained in 45 CFR 46.116 of subpart A, if the IRB determines that a research protocol is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children), it may waive the consent requirements in 45 CFR 46.116 (c) and (d), provided an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted, and provided further that the waiver is not inconsistent with federal, state, or local law. The choice of an appropriate mechanism 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.

4.3. Child Assent for Participation in a Research Study
As defined in Policy IC 704, Child Assent for Participation in Research, “assent” means a child's affirmative agreement to participate in research. Failure to object without affirmative agreement cannot be construed as assent. The child must actively show his or her willingness to participate in the research rather than just complying with directions to participate and not resisting in any way. The IRB shall make certain that adequate provisions are made for soliciting the assent of the child when in the judgment of the IRB the child is capable of giving it. When the child is judged intellectually capable of understanding the parental permission form, the child should read the parental permission form and sign it rather than signing the Child Assent form appended to the OHR 8D. The child's signature on the parental permission will then indicate his/her assent.

5. Tools
Parental Permission Form (OHR-8D), including Child Assent Form
Policy IC 704, Child Assent to be a Subject in a Research
OHR Policy SC 508, Differences in State and Federal Law
All tools are downloadable from the IRB web site.
1. Purpose
This policy describes the Federal and state laws and the requirements for assent of children for participation in research. The purpose of the policy is to ensure that the Principal Investigators and Institutional Review Boards (“IRB”) members comply with all federal regulations and state and local law regarding participation of children in research.

2. Responsibility for Executing the Policy
Principal Investigators
IRB Chairs/Vice Chairs
IRB Members

3. Policy Statement
Federal regulations at 45 CFR, Part 46 Subpart D (Additional Protections for Children Involved as Subjects of Research) and FDA regulations at 21 CFR, Part 50, Subpart D for the Protection of Human Subjects set standards for the informed consent process and assign the IRB with the responsibility for ensuring that any research involving children adheres to federal and state regulations.

The principle of respect for persons requires that the decision of an autonomous person be respected. However, as children are not fully autonomous individuals and have not developed full cognitive ability, the permission of the parent or parents (or legally authorized representative) is required (See, Policy IC 703, Parental Permission for a Child to Participate in a Research Protocol.)

4. Definitions
4.1. Assent: Consistent with the U.S. Department of Health and Human Services (“DHHS”) and the Food and Drug Administration (“FDA”), “assent” means a child’s affirmative agreement to participate in research (or clinical investigation in the case of FDA). Mere failure to object should not, absent affirmative agreement, be construed as assent. (See, 45 C.FR. Section 46.402(b) and 2a CFR 50.3(n))

4.2. Children: DHSS regulations define “children” as persons who have not attained the legal age for consent to medical or dental treatments or procedures involved in research under the applicable law of the jurisdiction in which the research will be conducted. (See, 45 CFR Section 46.402(a))

The FDA defines children as persons who have “not attained the legal age of consent to treatments or procedures involved in clinical investigations, under the applicable law of the jurisdiction in which the clinical investigation will be conducted.” (See, 21 CFR Section 50.3 (o)).
Under the laws of the Commonwealth of Pennsylvania, persons under the age of eighteen (18) generally meet the definition of children, and will be considered children for purposes of this policy, with the exceptions set forth below. As a result, permission of the child’s parent(s) or guardian(s) must generally be obtained prior to the participation of that child in research.

The following exceptions to the general rule noted above apply, where a person under the age of eighteen (18) does not meet the federal definition of “child” and may provide legally effective consent to participate in research if either:

- The research involves (i) the provision of medical, dental and health services, care or treatment, (including care or treatment deemed to be experimental) AND (ii) the person has married, has been pregnant, or has been graduated from high school may give effective consent and the consent of no other person shall be necessary.

- The person is an emancipated minor. A minor may be determined by a court of competent jurisdiction to be emancipated, i.e. is self-supporting, and does not live with parents. To demonstrate emancipation, such minor will be required to present appropriate documentation. If an emancipated minor provides consent for him/herself, the court order should be copied and included in the research records with the consent document.

4.3. **Parent:** Consistent with the DHHS and FDA regulations and the Commonwealth of Pennsylvania, a “parent” for purposes of this policy means either a child’s biological (natural or birth parent) or a person(s) adjudicated as an adoptive parent(s). (See, 45 CFR Section 46.402(d) and 21 CFR Section 50.3(p))

4.4. **Legally Authorized Representative (“LAR”):** DHHS regulation defines a LAR as “an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject’s participation in the procedure(s) involved in the research.” (See, 45 CFR Section 46.102(c). FDA regulation defines a LAR in the same way. (See, 21 CFR Section 50.3(l))

For purposes of this policy and consistent with the laws of the Commonwealth of Pennsylvania and Federal regulations, a “LAR” capable of providing consent on behalf of a child to participate in research studies is either a parent as defined in Section 4.3 above or a guardian as defined in Section 4.5 below.

4.5. **Guardian:** FDA defines guardian as an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care when general medical care includes participation in research. (21 CFR Section 50.3(s)).
DHHS defines guardian as “an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care.” [45 CFR Section 46.402(e)]

Consistent with the laws of the Commonwealth of Pennsylvania, a legal custodian may provide the effective consent on behalf of a child to general medical care. For purposes of this policy, a “guardian” means an individual appointed by a court of competent jurisdiction to serve in the capacity as a legal custodian who may consent on behalf of a child to general medical care when such includes participation in research. (See, 20 P.S. Section 5521). Except for research involving no greater than minimal risk, if a guardian provides consent on behalf of a child, the court order or legal authorization to consent to general medical care must be copied and included in the research records with the documentation of permission.

4.6. Ward: FDA defines ward as 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. (See 21 CFR Section 50.3 (q)) Under the laws of the Commonwealth of Pennsylvania, an agency must obtain consent from a ward’s parent or legal guardian for experimental procedures or treatment. (See, 55 Pa. Code Section 3680.52)

For purposes of this policy, a parent or a guardian must provide consent on behalf of a ward to enable the ward to participate in research studies. In the event the parent or guardian cannot be located, a court order authorizing participation in the research will be required.

5. Persons not Meeting the Definition of Children May Consent to Research on Their Own Behalf

All individuals defined as “children” will be afforded the protections under federal laws cited above and additional protections for enrollment of children in research as delineated in IRB policies. Subpart D protections are not applicable for persons who do not meet the definition of children. (See exceptions listed in Section 4.2 above.) The IRB may consider these subjects potentially vulnerable and may choose to apply additional protections. When a research protocol involves persons who do not meet the definition of children, the IRB will carefully balance the potential risks and benefits of the proposed research and will consult with the Office of University Counsel as deemed necessary.

For children, as defined in Section 4.2 above, parental permission as set forth in Section 6 below and assent as noted in Section 7 below shall be required.
6. Parental Permission Requirements

For children who are not legally capable of consenting to medical treatment as defined in Section 4.2 above, Federal regulations require parental permission for a child’s participation in any medical research study except where parental permission is waived. The regulations divide medical research involving children into four categories. In the first two categories (45 CFR Sections 46.404, and 46.405), permission of only one parent or legal guardian is required. In the third and fourth categories, (45 CFR Sections 46.406 and 46.407), permission of both parents, if legally possible, is required.

Both parents should provide permission, however, permission of only one parent may suffice for:

- Research not involving greater than minimal risk (45 CFR Section 46.404); or
- Research involving greater than minimal risk, but presenting the prospect of direct benefit to the individual subject (45 CFR Section 46.405).

Unless one parent is deceased, unknown, incompetent, or not reasonably available, or only one parent has legal responsibility for the child, permission from both parents is required for:

- Research that has a greater than minimal risk and no prospect of direct benefit to the child (45 CFR Section 46.406); or
- Research approved by the Secretary of DHHS that does not fit the above criteria, but presents an opportunity to understand, prevent or alleviate a serious problem affecting children’s health (45 CFR Section 46.407).

See also Policy IC 703: Parental Permission for a Child to Participate in a Research Protocol.

7. Assent Procedures

7.1. Soliciting Assent:
In instances where a child may not be capable of giving informed consent, the IRB must find that adequate provisions are made for soliciting the assent of the child subject when, in the judgment of the IRB, the subject is or has become capable of providing assent, unless assent has been waived by the IRB. (45 CFR Section 46.408)

7.2. Determining Capability of Assent.
IRBs’ have wide discretion in determining whether a child is capable of assent. In determining whether children are capable of assenting, the investigator and the IRB shall take into account the age, maturity, and psychological state of the child involved. This judgment may be made for all children to be involved in research under a particular protocol, or for each child, as the IRB deems appropriate. The IRB will determine for each protocol, depending on such factors as the nature of the research and the age, status, and condition of the proposed subjects, whether all or some of the children are capable of assenting to participation. Where appropriate, the IRB may choose to review on a case-by-case basis whether assent should be sought from certain individual subjects.

7.3. IRB Assessment of Risks and Benefits.
Federal regulations divide medical research involving children into four (4) categories. (See also Section 6 above.) The IRB shall classify research involving children into one (1) of the four (4) categories and consider the risks and benefits of the research study. In the first category, 45 CFR Section 46.404, research is considered research not involving greater than minimal risk. The second category, 45 CFR Section 46.405, research involves greater than minimal risk, but presents the prospect of direct benefit to an individual subject. Research in this category is approvable provided: (a) the risk is justified by the anticipated benefit to the subject and (b) the relationship of risk to benefit is at least as favorable as any available alternative approach. The third category, 45 CFR Section 46.406, concerns research involving greater than minimal risk with no prospect of benefit to individual subjects, but likely to yield generalized knowledge about the subject’s disorder or condition. Research in this category is approvable provided: (a) the risk represents a minor increase over minimal risk; (b) the intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social or educational settings; and (c) the intervention or procedure is likely to yield generalized knowledge about the subject’s disorder or condition that is of vital importance for the understanding or amelioration of the subject’s disorder or condition. The fourth category set forth at 45 CFR Section 46.407, is research that is not otherwise approvable, but which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children.

7.4. Assent Not Necessary.
If the IRB determines that the capability of some or all of the children is so limited that they cannot reasonably be consulted or that 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 subject and is available only in the context of the research, the assent of the subject is not a necessary condition for proceeding with the research. When the research offers the child the possibility of a direct benefit that is important to the health or well-being of the child and is
available only in the context of the research, the IRB may determine that the assent of the child is not necessary.

7.5. Child's Dissent.
In circumstances where a child might dissent, a child's dissent, which should normally be respected, may be overruled by the child's parent(s) at the IRBs' discretion if the research may provide direct benefit for the child.

7.6. Waiving Assent.
The IRB may waive parental permission and/or child assent under certain circumstances, for example:

- If the child is not capable of assent and
- If the research offers a prospect of direct benefit not available outside of the research (See Section 7.4 above and 45 CFR Section 46.408(a) waiver of assent of child); or
- If the same conditions are present under which parental permission may be waived. (See, 45 CFR Section 46.408 (a through c) and 45 CFR Section 46.116(d))

Even where the IRB determines that the children are capable of assenting, the IRB may still waive the assent requirement under specific circumstances in which consent may be waived. (See, 21 CFR Section 50.55 (b); 45 CFR Section 46.408(c)).

7.7. Parental Permission Inappropriate.
In certain research, for example research involving abuse or neglect, serious doubts as to whether parents' interest adequately reflect the child's interests may present. In these cases, the IRB may devise alternative procedures for protecting the rights and interests of the children asked to participate, including seeking a court appointment of a special guardian.


7.8.1. IRB Determination. When the IRB determines that assent is required, it shall also determine whether and how assent must be documented. (See, 45 CFR Section 46.408 (e)). IRBs are also given discretion as to whether and how child assent is documented. When children as defined in Section 4.2 above are involved in research, (1) the assent of the child, and (2) the permission of the parent(s) in place of the consent of the subjects are required.

7.8.2. Child's Decision. When assent is required, the decision of the child to assent or dissent should be respected and documented.
7.8.3. Use of Assent Form. The IRB requires the use of a Child Assent form (see OHR-8D Child Assent) to serve as an addendum to the Parental Permission form for children ages 7 through 17 who wish to participate in a research study.

7.8.4. Use of Parental Permission Form for Child. It is acknowledged that some children who are adolescents (15-17 years of age) should be able to adequately comprehend the information in the Parental Permission Form for the study, and so with the concurrence of the parent(s) may also sign and date that document. The child’s signature and date on the parental permission would then indicate his/her assent.

8. Procedure to Research Involving Children Being Conducted in States Other Than Pennsylvania

If the research includes enrollment of participants in other states or countries, the principal investigator is responsible for providing the IRB with sufficient information to (a) verify the age at which participants in such jurisdictions have the ability to consent to participation in research, including any medical treatments or procedures, if applicable and/or (b) verify the requirements for determining who may serve as a LAR, including a guardian for a child to participate in research. The principal investigator must also provide information on any state specific regulations on privacy requirements and genetic research. The principal investigator may consult with the Office of University Counsel for advice or direction.

Recognizing that state laws differ with respect to the definition of children, age of majority and what constitutes “emancipation”, or what constitutes a LAR including guardian, for research involving children conducted in states other than the Commonwealth of Pennsylvania, the principal investigator and the IRB shall contact the Director or Associate Director, OHR, who will refer the question(s) regarding children to the Office of University Counsel. The IRB may, if it appears advisable, require the submission of an opinion rendered by an attorney from any applicable jurisdiction on age at which an individual can consent to participation in research and/or who may serve as a LAR including a guardian with regard to a child’s participation in research.

9. References

45 CFR PART 46.408 (Subpart D)
21 CFR Part 50.55 (Subpart D)
Parental Permission Form (OHR-8 “Universal”), and Child Assent Form, OHR-8C
Policy IC 703: Parental Permission for a Child to Participate in a Research Protocol.
OHR Policy SC 506: Enrollment of Children, Neonates and Minors in Research OHR
Policy SC 508: Differences in State and Federal Law
1. Purpose
To delineate the policy and procedures for conducting the informed consent process when a potential subject cannot read English, is non-English speaking or is physically unable to sign a consent form.

2. Responsibility for Executing the Policy
Investigators
Research Coordinators
IRB Members
OHR Administrative Staff

3. Policy Statement
Department of Health and Human Subjects regulations require that informed consent information be presented in "language understandable to the subject" and, that, in most instances, informed consent be documented in writing unless appropriate waiver criteria are met (45 CFR §46.116 and §46.117). If a potential subject is non-English speaking, the consent form must be translated into the subjects' language. In the translation, particular attention must be paid to meanings and cultural nuances surrounding words and phrases as they may have different meanings or connotations in the potential subjects’ own language. If the translation is not accurate, the subject could be misinformed and this would undermine the ability of the subject to give truly informed consent.

4. Procedures
4.1. Persons Illiterate in English
An individual who understands, but does not read English may have the consent form read to him/her and s/he may “make his/her mark”. The signature of an impartial witness to the consent process and that of the person conducting the consent interview and the investigator are required (21 CFR §50.27(b)(2). The witness cannot be study personnel.

4.2. Individual Does Not Understand or Speak English
Having a translator present during the consent interview to do an ad hoc translation of the consent form is not permitted under federal regulations. If an individual meets the inclusion/exclusion criteria for the study, but does not speak English, s/he cannot be denied participation on the study, but must be offered the opportunity to read and understand a consent form translated into his/her native language. Federal regulations do not elaborate on who is qualified to translate the consent form into the required language. In situations where time does not permit a full translation to be prepared, the provisions for the short form consent process, as per 45. CFR 46.117(b)(2), are permitted.
However, the research summary and short form consent (OHR-8S) required by this regulation must be translated into the native language of the subject and a translator must be present at the consent interview. The translator may serve as the witness for the short form consent process. The short form documents must be approved by the IRB prior to being used. A translation of the full consent form should be provided to the subject as soon as possible.

The above procedure is allowable in circumstances where a non-native speaker who is not part of a targeted non-English speaking subject population presents as a potential research subject. When an investigator is specifically targeting particular non-English speaking populations for enrollment in a study, appropriately translated consent forms must be approved by the IRB prior to enrolling members of these populations.

4.3. Individuals Physically Unable to Sign a Consent Form

If a subject is cognitively capable of consent, but is physically unable to sign the consent form (e.g. paralyzed), the subject’s power of attorney or an impartial witness must be present for the entire consent interview. The witness cannot be study personnel. After the subject has indicated the intention to consent, the subject’s name and the current date may be written in the appropriate places on the consent form signature page. In addition, the signature page should include a statement with the following information: The subject is physically unable to sign the consent form. All pages of the consent form were reviewed with the subject, who voluntarily consented to participate in this study.

If able, the subject will make his/her mark on the signature line. The witness will complete the witness section of the signature page.

4.4. Translation of the Consent Form

For translation of the consent form, the investigator may use either: 1) A professional translator; or 2) an individual with special expertise in the particular language required.

Companies providing translation services will provide certification that the translation is an accurate representation of the original English consent form. For individual translators, the investigator must provide the IRB with the name and qualifications of the translator as well as a statement from the translator that the translation is accurate and contains the appropriate cultural nuances. For any study that plans to enroll a non-English-speaking subject, the IRB reserves the right to evaluate the translator’s credentials and, if deemed necessary, require translation of the consent form by another party.
4.5. Presence of a Translator
A translator should be present during the consent interview for a non-English speaker. The translator must be someone who can accurately translate between spoken English and the subject’s native language and who understands the cultural nuances of the language. The translator may be a member of the subject’s family or someone else who can adequately fulfill the duty. A translator should also be available during the full course of the non-English speaker’s participation in the study, so that the subject can always communicate reliably with the research team, which is a right of any research subject. The PI should assume responsibility for assuring that appropriate arrangements with the translator or translation service can be made before the non-English speaker is enrolled.

4.6. Short Form Consent
All foreign language versions of short form consent documents must be approved by the IRB under the provisions of §46.117(b)(2). Review of the foreign language versions of the documents may be carried out by expedited review, but only if the protocol, full English language informed consent document and the English language version of the short form document have been given prior approval by a convened IRB.
1. **Purpose**

To describe the procedures by which an IRB may waive documentation of informed consent or authorization to use and/or disclose protected health information.

2. **Responsibility for Executing the Policy**

Associate Director, OHR
IRBs

3. **Policy Statement**

The IRB has the authority to waive the requirement for the investigator to document the informed consent process with an IRB-approved signed consent form. The IRB also has the authority to waive authorization for the use and/or disclosure of protected health information.

4. **Procedure**

4.1. **Waiver of Informed Consent**

45 CFR 46.116 (c) states that an IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent, or waive the requirement to obtain informed consent provided the IRB finds and documents that:

- 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; and

- The research could not practicably be carried out without the waiver or alteration.

Or that [45 CFR 46.116(d)]

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

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

- The research could not practicably be carried out without the waiver or alteration; and

- Whenever appropriate, the subjects will be provided with additional pertinent information after participation.
When the IRB waives the requirement for informed consent, the IRB must document the specific criteria required by federal regulations in the minutes of the appropriate convened IRB meeting. This is not required for exempt studies.

If the research protocol meets the requirements for expedited review, the same documentation requirement holds when the waiver is granted through the expedited procedure.

FDA regulations have no provision for the waiver of informed consent, the alteration of the elements of informed consent, or the waiver of written consent. Therefore, if a study is FDA-regulated, these waivers are not permitted.

4.2. Waiver of Authorization to Use and/or Disclose Protected Health Information:
Investigators at Thomas Jefferson University may use and/or disclose protected health information of the covered entity for research purposes without prospective authorization, provided that they request such a waiver from the IRB by completion of an OHR-3, Request for Waiver of Authorization to Collect Protected Health Information. The following criteria must be adequately addressed:

The use or disclosure of the protected health information involves no more than minimal risk to the privacy of individuals based on:
- The provision of an adequate plan to protect the identifiers from improper use and disclosure;
- The provision of an adequate plan to destroy the identifiers at the earliest possible 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;
- The provision of adequate written assurances that the protected health information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research project, or for other research for which the use or disclosure of protected health information would be permitted by law;
- The research could not be practicably conducted without the waiver or alteration;
- The research could not be practicably conducted without access to and use of the protected health information.

4.3. Documentation of Waiver of HIPAA Authorization:
The IRB shall provide the following documentation for all waivers of HIPAA Authorization approved under Section 4.2 above:
• Identification of the IRB and the date on which the alteration or waiver was approved;

• A statement that the IRB determined that the alteration or waiver of HIPAA Authorization, in whole or in part, satisfied the criteria of Section 4.2 of this policy;

• A brief description of the protected health information for which use or access was determined to be necessary by the IRB;

• A statement that the alteration or waiver of HIPAA Authorization was reviewed and approved under expedited or full IRB review procedures; and

• The signature of the Director/Associate Director of the OHR or other designated authority of the IRB as described in Policy GA 110.

5. Tools
OHR Form OHR-3, Request for Waiver of Authorization to Collect Protected Health Information.
1. Purpose
To describe procedures to be followed in order to allow certain populations of patients (other than children who are covered under Policy IC 704: Child Assent for Participation in Research and Policy IC 703, Parental Permission for a Child to Participate in a Research Protocol), otherwise incapable of making autonomous choices, to participate as subjects in research where the potential for direct benefits exceeds the risk of harm.

2. Responsibility for Executing the Policy
Director/Associate Director, OHR
IRB Chair/Vice Chairs
IRB Members
Principal Investigators

3. Definition of Legally Authorized Representative (“LAR”)
Both the FDA and DHHS define a Legally Authorized Representative as “….an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research.” [45 CFR Section 46.102(c); 21 CFR Section 50.3(l)].

For purposes of this policy, the following individuals may be considered a LAR of the subject and capable of providing surrogate consent:

- A court appointed guardian authorized to consent to the subject’s participation in the protocol in a current court order issued within the subject’s jurisdiction;

- A health care proxy appointed by the subject in a power of attorney; or

- Where there has been no guardian appointed by a court or a health care power of attorney designated by the patient/subject, certain individuals may provide consent. Such individuals must be at least 18 years of age. There is a priority of order of individuals who may provide consent, which is noted below in Section 5. (See, 8 PA Code Section 103.22).

4. Policy Statement
1) Background

Federal regulations require that the researcher obtain the legally effective informed consent of the subject or the subject’s legally authorized representative prior to medical research. Federal law defers to state law to determine which individuals are legally authorized to provide surrogate consent for the research subject. Pennsylvania law requires the informed consent of the patient or the patient’s authorized representative before the administration of an experimental medication, the use of an experimental device, or the use of an approved medication or device in an experimental manner.

By statute, Pennsylvania authorizes surrogate consent for an experimental biomedical or behavioral medical procedure or participation in any biomedical or behavioral experiment by the subject’s court-appointed guardian pursuant to a court order issued after fact finding. Pennsylvania statutory law further authorizes a person named in the patient’s power of attorney to consent to medical, therapeutic and surgical procedures for the subject.

While Pennsylvania statutory law does not explicitly authorize surrogate consent in the absence of a power of attorney or court-appointed guardian, case law strongly supports substituted consent by close family members when patients lack capacity to make medical decisions. See, In re Fiori, 543 Pa. 592, 673 A.2d 905 (1996). When the patient is unable to give informed consent, the patient’s close family member is in the best position to determine the wishes of the patient regarding participation in therapeutic research.

2) Policy

The Office of Human Research (OHR) recognizes the research subject’s right to autonomy. The OHR also recognizes, however, that individuals with diminished capacity for decision-making require the consent of a surrogate decision maker (surrogate consent) in order to participate in research where the potential for direct benefit exceeds the risk of harm. This policy pertains to individuals with diminished capacity for making decisions including:

- Individuals under sedation
- Individuals who are semi-conscious or unconscious
- Individuals who are experiencing overwhelming stress or pain (e.g., women during childbirth, individuals presenting to the ER with acutely painful conditions, such as Sickle Cell crisis, etc.)
- Cognitively impaired individuals
- Decisionally impaired individuals
- Individuals who are inebriated or under the influence of drugs
Only studies given IRB approval specifically to enroll decisionally-impaired individuals with use of the surrogate consent form may do so. An investigator may not decide on an ad hoc basis to enroll a decisionally-impaired individual without prior IRB approval.

When evaluating studies that may involve individuals with decisional impairments, the IRB must evaluate whether: 1) the proposed plan for the assessment of capacity of the individual to consent is adequate, and; 2) assent of participant is required, and if so, whether the plan for assent is adequate.

With regard to surrogate authorization in abuse, neglect and endangerment situations, notwithstanding state law or any requirement of this policy or the HIPAA privacy regulations to the contrary, the IRB may elect not to treat a person as the LAR of an individual for surrogate if they have a reasonable belief that:

- The individual research subject has been or may be subjected to domestic violence, abuse, or neglect by such person; or

- Considering such person the LAR could endanger the individual; and, the Investigator, in the exercise of professional judgment, decides that it is not in the best interest of the individual to consider the person the individual’s LAR.

If such a decision is made not to treat a person as the patient’s LAR for these reasons, documentation of the factual basis for such decision should be noted in the medical and research record with the report or any other documentation of suspected domestic violence, abuse, or neglect.

5. Procedure
First, the investigator will determine whether a person who meets the study’s eligibility criteria is unable to provide informed consent due to one or more of the above-stated criteria. The investigator may consult with a psychiatrist in determining the patient’s capacity to make medical decisions. Secondly, the investigator will determine whether the risk of harm posed by the research to this patient is reasonable in relation to the potential for direct benefit to the subject. If both of these criteria are met, the investigator should seek surrogate consent for that person.

The investigator will complete the form, Thomas Jefferson University Surrogate Consent for a Research Protocol (OHR-8B) by documenting as thoroughly as possible the reason for the subject’s inability to provide informed consent. The following individuals may be considered legally responsible surrogates capable of providing substituted consent:

- a court-appointed guardian

- a health care proxy appointed by the subject to execute “power of attorney”
In the absence of a court order or a duly appointed health care proxy, the investigator will obtain the surrogate informed consent from one of the following individuals (health care representatives in priority order:

1) Spouse
2) Natural or adoptive parent
3) Adult child (individual over the age of 18 years)
4) Adult brother or sister
5) Any other available adult relative related through blood or marriage

This list is ordered according to legal preference and is congruent with TJUH policy for permission to administer medical care. The investigator should always seek out the available relative who is highest on the list.

The consent process will comply with the policies and procedures set forth by the IRB and by state and federal law. The surrogate should base his or her decision on the subject’s expressed wishes or, if unknown, what the surrogate believes the subject would have desired in light of his or her prognosis, values, and beliefs. When a surrogate provides consent, it is advised that s/he should remain the responsible party for all research decisions throughout the duration of the subject’s participation in the research.

In the event of a disagreement among potential patient surrogates, an attempt to reach consensus shall be made. If consensus cannot be reached, the subject cannot be enrolled in the study, unless further mediation is sought out for the parties in disagreement.

Subsequent to obtaining the surrogate consent, the investigator should obtain the assent of the subject once it is determined that the subject is capable of understanding that permission for his or her inclusion in a research study has been granted.

If the subject’s condition improves and he or she regains the capacity to provide informed consent after s/he has been enrolled in the study and undergone some or all study procedures, the investigator shall inform the subject of his or her participation in a research study and seek informed consent from the subject for continued participation in the research. If the subject agrees to continue participation, informed consent should be obtained. If the subject declines to participate, the subject will be withdrawn from the study, and the data obtained thus far will not be used in the research study, unless the subject agrees to allow the data already collected to be used. This agreement should be confirmed in writing with the subject’s signature.
If, on the other hand, the subject is capable initially of providing informed consent, but it is likely that the subject will lose this capacity during the study, the subject should be encouraged at the beginning of the study to appoint a surrogate who will have the authority to consent to continuing participation, amendments to the study, and withdrawal from the study if the subject loses capacity.

6. Applicability of the Laws of Other States
If the research includes enrollment of participants in other states or countries, the principal investigator is responsible for providing the IRB with sufficient information to verify the circumstances under which surrogate consent is allowable within in such jurisdictions. The IRB may, if it appears advisable, require the submission of an opinion rendered by an attorney or consultant from any applicable jurisdiction.

If the research is being conducted in jurisdictions outside of Pennsylvania, the Principal Investigator should contact the Director or Associate Director, OHR who will enlist the Office of University Counsel in determining the laws regarding priority of legally authorized representatives in the relevant states.

7. Tools
OHR Internal Form (0HR-8B) Thomas Jefferson University Substituted Consent for a Human Subject Research Protocol.
1. **Purpose**
   To describe the exception from informed consent requirements for emergency research and the requirement for prospective review. PLEASE NOTE: This policy does NOT apply Emergent Use of a Drug, Biologic, or Medical Device. That is addressed in OHR Policy GA 112.

2. **Responsibility for Executing the Policy**
   Director/Associate Director, OHR
   IRB Chair/Vice Chair
   IRB Members

3. **Policy Statement**
   21 CFR Part 50.24, permits an IRB, with the concurrence of a licensed physician who is either a member of the IRB or a consultant who is not participating in the research being reviewed, to approve emergency research, and in certain instances to waive the requirement for informed consent.

   In order to waive informed consent under these conditions, the IRB must find and document that:
   
   3.1.1. The human subjects are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific data, which may include data obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.

   3.1.2. 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 representatives is feasible; and
   
   - There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation.

   3.1.3. 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 pre-clinical studies have been conducted, and the information derived from those studies and related evidence support 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 potential 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.

3.1.4. The clinical investigation could not practicably be carried out without the waiver,

3.1.5. The proposed research plan defines the length of the potential therapeutic window based on scientific evidence;

3.1.6. The investigator has committed to attempting to contact a legally authorized representative for each subject within that window of time; and if feasible, to ask the legally authorized representative contacted for consent within that window rather than proceeding without consent.

The investigator will summarize efforts made to contact legally authorized representative(s) and make this information available to the IRB at the time of continuing review.

3.1.7. The IRB has reviewed and approved informed consent procedures and an informed consent document consistent with 21 CFR 50.25. These procedures and the informed consent document are to be used with subjects or their legally authorized representatives in situations where use of such procedures and documents is feasible.

The IRB has reviewed and approved procedures and information to be used when providing an opportunity for a family member to object to a subject’s participation in the clinical investigation consistent with paragraph (7) (v) of this section.

3.1.8. Additional protections of the rights and welfare of the subjects will be provided, including at least:

• Consultation carried out by the IRB with representatives of the communities in which the clinical investigation will be conducted and from which the subjects will be drawn;
• Public disclosure to the communities in which the clinical investigation will be conducted, and from which the subjects will be drawn, prior to initiation of the clinical investigation, of plans for the investigation and its risks and expected benefits;

• Public disclosure of sufficient information following completion of the clinical investigation to apprise the community and researchers of the study, including the demographic characteristics of the research population and its results;

• Establishment of an independent data monitoring committee to exercise oversight of the clinical investigation; and

• If obtaining informed consent is not feasible and a legally authorized representative is not reasonably available, the investigator has committed, if feasible, to attempting to contact, within the therapeutic window, the subject’s family member who is not a legally authorized representative, and asking whether s/he objects to the subject’s participation in the clinical investigation. The investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review.

The study plan must assure that, at the earliest feasible opportunity, each subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, will be informed of the subject’s inclusion in the clinical investigation, the details of the investigation and other information contained in the informed consent document.

The study plan must assure that there is a procedure to inform the subject, or if the subject remains incapacitated, a legally authorized representative of the subject or if such a representative is not reasonably available, a family member, that he or 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 legally authorized representative or family member is told about the clinical investigation and the subject’s condition improves, the subject is also to be informed as soon as feasible. If a subject is entered into a clinical investigation with waived consent and the subject dies before a legally authorized representative or family member can be contacted. Information about the clinical investigation is to be provided to the subject's legally authorized representative or family member, if feasible.
If the IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria provided in the above section or because of other relevant ethical concerns, the IRB will document its findings and provide these findings promptly in writing to the clinical investigator and to the sponsor of the clinical investigation.

4. Reference
   Federal Register 61(192): 51531-51533.