

Jefferson Office of Human Research Policy Manual
Version: 6/21/2024

Signatures on File for the Approval of Revisions to the Policy and Procedures Manual

Table of Contents

100 General Administration (GA)	4
Policy GA 101: The Authority and Purpose of the Institutional Review Boards	4
Policy GA 102: Activities Requiring IRB Approval	8
Policy GA 103: Maintenance of Policies, Procedures, and Internal Forms.....	12
Policy GA 105: Use of a Single IRB in Multi-Site Research Studies	14
Policy GA 106: Conflicts of Interest.....	19
Policy GA 109: Roles and Responsibilities of Study Personnel and Department Chairs	21
Policy GA 110: Signatory Authority	26
Policy GA 112: Emergent Use of a Drug, Biologic, or Medical Device	28
Policy GA 113: IRB Reporting of Findings and Actions to Investigators.....	34
Policy GA 115: Management of Research Concerns	36
Policy GA 116: Use of Students and Employees as Key Personnel and Subjects in Clinical Trials.....	37
Policy GA 118: Protocol Inclusion/Exclusion Waivers	39
Policy GA 120: Reporting and Reviewing Unanticipated Problems Involving Risks to Subjects or Others.....	41
Policy GA 121: Documentation and Document Management	46
Policy GA 124: Good Clinical Practice for Investigators	50
Policy GA 125: Investigator Responsibility and Delegation of Responsibility	63
Policy GA 126: Sponsor Agreements	68
Policy GA 127: Subject Screening and Enrollment	70
Policy GA 128: Designation of the Institutional Official Responsible for the Human Research Protection Program	73
Policy GA 129: Protection of Privacy Interests of Research Subjects and Confidentiality of Subject Data.....	74
Policy GA 131: Research Device Acquisition, Use, and Tracking	83
Policy GA 132: Human Research Protection Program	86

Policy GA 133: Human Research Training.....	90
200 IRB Organization (OP)	92
Policy OP 201: IRB Membership.....	92
Policy OP 202: Recruiting, Appointing and Performance Evaluation of IRB Members, Chairs, and Vice Chairs.....	94
Policy OP 203: IRB Consultants.....	99
Policy OP 204: IRB Review of Protocols.....	100
Policy OP 205: IRB Member Responsibilities.....	102
Policy OP 206: IRB Meeting Administration	104
300 Quality Assurance (QA).....	109
Policy QA 301: Quality Assurance/Quality Improvement Program.....	110
Policy QA 303: Inspections by the FDA and Other Regulatory Agencies.....	113
Policy QA 304: Study Team Training	116
Policy QA 305: Verification by Outside Sources that No Material Changes Have Been Made to an IRB-Approved Protocol.....	120
400 Research Review (RR).....	122
Policy RR 401: Initial Review - Criteria for IRB Review and Approval.....	122
Policy RR 402: Continuing Review by Convened IRB.....	130
Policy RR 403: Review of Exempt Studies.....	135
Policy RR 404: Expedited Review of New and Continuing Research	137
Policy RR 407: Suspension or Termination of Human Subjects Research	139
Policy RR 408: Review of Amendments.....	141
Policy RR 409: Study Completion	145
Policy RR 410: Review of Advertisements	147
Policy RR 412: Recruiting Methods, Enrollment Incentives, and Subject Payment.....	149
Policy RR 413: Review of Research Involving Investigational Drugs and Devices	154
Policy RR 414: Institutional Conflicts of Interest.....	157
Policy RR 415: Undergraduate Research	159
500 Reviews Requiring Special Consideration (SC)	161
Policy SC 501: Determining Whether a Device Study Involves a Significant Risk or Nonsignificant Risk.....	161

Policy SC 502: Review of Cancer Trials Approved Under NCI Central IRB Independent Review Model.....	165
Policy SC 503: Review and Approval of a Humanitarian Device Exemption	168
Policy SC 504: Populations Requiring Special Consideration (Women, Prisoners, Children).....	171
Policy SC 507: The Enrollment of Women and Minorities as Subjects in Clinical Research.....	179
Policy SC 508: Pennsylvania Reporting Requirements.....	182
Policy SC 509: International Research.....	184
600 Guidance (G).....	187
Guidance G 601: Definition of Key Personnel in Human Subjects Research.....	188
Guidance G 607: Certificates of Confidentiality	190
Guidance G 608: Sociobehavioral Research	192
Guidance G 610: Quality of Life Issues	194
Guidance G 615: IRB Fees	196
Guidance G 616: Independent Monitoring of Investigator-Initiated Clinical Trials	198
Guidance G 618: HIPAA and Activities Preparatory to Research	201
Guidance G 619: Radioactive Materials.....	205
Guidance G 620: Department of Defense (DoD) Requirements for the Conduct of Human Subjects Research.....	212
Guidance G 621: Safeguarding and Protection of Children in Research Studies.....	220
700 Informed Consent (IC).....	224
Policy IC 701: Informed Consent and HIPAA Authorization: General Requirements ..	224
Policy IC 702: Documentation, Waiver and Alteration of Informed Consent.....	233
Policy IC 704: Child Assent and Parental Permission for Participation in Research ...	237
Policy IC 705: Informed Consent – Non-English Speaking Subjects and Translations	242
Policy IC 706: Waiver and Alteration of Informed Consent and HIPAA Authorization .	245
Policy IC 707: Surrogate Consent.....	249
Policy IC 708: Research in Emergency Settings (Prospective Review)	252
Policy IC 709: Treatment and Cost of Research Related Injury	256

100 General Administration (GA)
Policy GA 101: The Authority and Purpose of the Institutional Review Boards
Rev.: 5/22/2020

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. Responsibilities

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) or allied organizations which operate under a separate FWA but have agreed to adopt the Thomas Jefferson University policies.

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.

Jefferson 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.

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 Office of Human Research, which oversees institutional IRB activity, 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 Jefferson
- 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.
- does not fit any of the categories above, but is judged to be congruent with the University mission

3.4.2 Each Jefferson 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 external funding, 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 become 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 Legal Office which will be responsible for investigating the allegation and taking corrective actions, as necessary.
- 4.2.3 In pre-review of a research study, the IRB personnel will check that the conflict of interest question in the application has been answered. If a significant financial interest is disclosed for any investigators on the study, the University's Conflict of Interest (COI) Committee will be notified. The COI Committee also learns about significant financial interests via the COI-Smart reporting system. IRB approval will not be issued for a given study until a significant financial interest of any investigator on the study has been reviewed by the COI Committee and a management plan issued by this Committee has been accepted by the investigator(s).

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, and the ethics of human subjects protection when reviewing proposed research.

The IRB policies do not affect any state or local laws or regulations (including tribal law passed by the official governing body of an American Indian or Alaska Native tribe) that may otherwise be applicable and that provide additional protections for human subjects.

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

Nothing in IRB policies is intended to limit the authority of a physician to provide emergency medical care, to the extent the physician is permitted to do so under applicable Federal, state, or local law.

100 General Administration (GA)
Policy GA 102: Activities Requiring IRB Approval
Rev.: 9/4/2020

1. Purpose

To describe the activities that require IRB review.

2. Responsibilities

OHR Personnel
Investigators and Key Personnel
IRB Members

3. Definitions

- **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 trial, clinical study, study, and clinical investigation are synonymous for purposes of FDA regulations. (21 CFR 50.3(c), 21 CFR 56.102(c), 45 CFR 46.102(b)).
- **Clinical trial** means a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes.
- **Human subject** means a living individual about whom an investigator (whether professional or student) conducting research:
 - (i) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or
 - (ii) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.
- **Interaction** includes communication or interpersonal contact between investigator and subject.

- **Intervention** includes physical procedures by which information or biospecimens are gathered (e.g., venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.
- **Private information** includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information that has been provided for specific purposes by an individual and the individual can reasonably expect will not be made public (e.g., a medical record).
- **Identifiable private information** is private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information.
- An **identifiable biospecimen** is a biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen.
- **Research** means a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge.

4. Policy Statement

4.1 Research Requiring IRB Review

Research activities involving human subjects research (see definitions above) may begin only after receiving IRB approval. A Jefferson IRB will approve the research or the Jefferson IRB may rely upon another IRB.

For activities that are considered exempt from IRB review, see OHR-18.

The OHR-34 is used to determine and document when an activity does not meet the definition of human subjects research and IRB review is not required. The OHR-36 is used by an investigator to delineate quality improvement activities from human research that must be submitted to the IRB.

If an activity previously determined to not require IRB review is subsequently thought to be human subjects research, the investigator must contact OHR immediately. If OHR determines that the activity meets the definition of human subjects research, the study must be submitted to the IRB for review. OHR will also determine if data collected prior to IRB approval may be used for research purposes and if any compliance issues must be investigated.

All activities meeting the definition of human subjects research may begin only after receiving IRB approval. Some specific examples of these include but are not limited to:

- 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.”
- Patient care or the assignment of normal participants to any intervention that is altered for research purposes in any way.
- A diagnostic procedure for research purposes that is added to a standard treatment.
- “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.
- One-time emergency uses of an investigational drug or device may proceed without prospective IRB review. Any subsequent use of the test article must have prior review by the full IRB. See OHR Policy GA 112.
- Research in Emergency Settings (Prospective Review) See OHR Policy IC 708.
- 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 the OHR-19 to determine whether research involving data, human cells or tissue requires IRB review.
- Investigator-Initiated Research
- Student Conducted Research: All activities conducted by students that meet the definition of human subjects research.

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. Three (3) or more case studies are considered human subjects research by Jefferson Center City IRB. Upon proposal of the 3rd case study, the research should be submitted to the IRB for review and approval. One or two case reviews do not require IRB review unless they meet the criterion of providing generalizable knowledge. If IRB review is not required, the case reviews should, however, be reviewed by the Privacy Officer in the Legal Office.

Research involving decedent tissue and a FDA regulated device does require IRB approval. For all other research on decedents, IRB approval is not required, however, for activities not requiring IRB approval, the Privacy Officer in the Legal Office should be consulted regarding protected health information (PHI) and privacy issues.

4.2 Tracking Active Studies

Every study meeting the definition of human research to be conducted in the Jefferson enterprise that receives either Jefferson IRB approval or exemption or external IRB approval or exemption is entered as a record in the IRB database. Those studies receiving a fixed approval period must receive a continuing review in order to remain active. Exempt studies and studies designated for no further continuing review (NFCR) do not have expiration dates. The IRB Portal automatically generates a monthly email notification that is sent to PIs of exempt and NFCR studies. The notification queries whether the study is active or closed and requests that the PI send an email response to OHR which will make appropriate notation in database.

In addition, all human research studies conducted at Jefferson fall under the purview of the Quality Improvement team in the Office of Human Research, and as such, whether approved for a fixed period, exempt, or NFCR, are subject to audit at any time.

5. References

45 CFR 46.101
45CFR 46.102
45 CFR 46.109

100 General Administration (GA)
Policy GA 103: Maintenance of Policies, Procedures, and Internal Forms
Rev.: 1/20/2020

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. Responsibilities

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 Quality Assurance/Quality Improvement team of OHR to create or revise policies, procedures and/or forms.

- 4.1.2 Policies, procedures and forms will be reviewed by the Director, OHR as needed.
- 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 Senior Compliance for Research Support Services and the Legal Office as necessary
- 4.1.4 Changes that are not substantive may be made without approval of the Director, OHR.

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. The announcements are intended to keep research personnel informed of new requirements related to their human subjects research. As appropriate the announcements are sent to the research community and are also available on the OHR website. Feedback from research personnel is solicited and is considered when making future policy and form revisions. When IRB members are notified of changes at an IRB meeting, this will be noted in the minutes for the meeting.

100 General Administration (GA)
Policy GA 105: Use of a Single IRB in Multi-Site Research Studies
Rev.: 5/22/2020

1. Purpose

To define the procedure for use of single IRB (sIRB) oversight in multi-site research studies.

2. Responsibilities

Director/Associate Director, OHR
OHR Administrative Staff
Investigators and Key Personnel

3. Definitions

- 3.1 sIRB: A single IRB, also termed “central” IRB. An IRB that provides IRB review and oversight for two or more participating sites in multi-site research. The IRB may be associated with an academic, private, non-profit, governmental, or commercial entity.
- 3.2 Multi-Site Research: Multi-site research projects are those that involve more than one institution. In the conduct of multi-site research projects, each institution is responsible for safeguarding the rights and welfare of human subjects.
- 3.3 Reliance Agreement: A written agreement between entities participating in multi-site research. The agreement contains terms that describe what each entity is responsible for in the review, oversight, and conduct of the research including responsibilities related to local requirements, state law, and federal regulations. Previously these agreements were referred to as IAAs or “IRB Authorization Agreements.”
- 3.4 Reviewing IRB: A term used in Reliance Agreements to identify the party to the agreement that acts as the sIRB in providing IRB review for all sites participating in the conduct of the same multi-site protocol. This is sometimes also termed the IRB of Record.
- 3.5 Relying Institution: A term used in Reliance Agreements to identify the party to the agreement that will rely on an IRB outside of its own entity. This is sometimes also termed the Relying Site or Participating Site.

- 3.6 Unaffiliated Investigator: A non-Jefferson investigator conducting research under the oversight of Thomas Jefferson University's IRB under the terms of an Individual Investigator Agreement.
- 3.7 Individual Investigator Agreement (IIA): A formal agreement between Jefferson and a single independent investigator not routinely "engaged" in research that allows such a single investigator to conduct collaborative human subject research under the TJU IRB.

4. Procedure

4.1 Introduction

As part of the Jefferson Human Research Protection Program (HRPP), the Jefferson IRB provides review and oversight of human subjects research conducted by Jefferson faculty, staff and students. The IRB provides this oversight unless an alternate IRB has been authorized to serve as the reviewing IRB through a formal written reliance agreement between Jefferson and the alternate IRB. The Jefferson Office of Human Research (OHR) executes and ensures adherence to reliance agreements.

IRB oversight for multi-site research studies may be provided via a sIRB model or with each site providing its own local IRB oversight. All research that is funded by NIH and falls under the NIH sIRB Policy (effective January 25, 2018) must use a sIRB for the research conducted in the United States as designated in the funding application. All research that falls under the DHHS regulations related to Cooperative Research (effective January 20, 2020) must use a sIRB for the research that is conducted in the United States. This includes other agencies that have signed onto the Common Rule.

The following research is not subject to this provision:

- (i) Multi-site research for which more than a single IRB review is required by law (including tribal law passed by the official governing body of an American Indian or Alaska Native tribe); or
- (ii) Multi-site research for which any Federal department or agency supporting or conducting the research determines and documents that the use of a single IRB is not appropriate for the particular context.

Regardless of which IRB will be serving as the sIRB for a given study, requisite documents for research performed within the Jefferson enterprise must be provided to OHR by submission through the IRB portal. Also, all Jefferson investigators and key personnel must adhere to Jefferson human subjects training and conflict of interest disclosure requirements.

When serving as the reviewing IRB, Jefferson IRB will follow its policy for reporting of unanticipated problems involving risks to participants, serious or continuing non-compliance, or suspension or termination of IRB approval. When ceding review to an external IRB, Jefferson IRB will follow the policies established by the external IRB.

4.2 Reliance on Jefferson IRB

4.2.1 Jefferson Investigator is the Principal Investigator on a Multi-Site Research Study

When a Jefferson investigator is responsible for the overall conduct of a multi-site study, the investigator must:

- Upload required documents in IRB portal as per Jefferson sIRB SOPs;
- Obtain all required ancillary institutional reviews and submit all requisite documents;
- Ensure that a Reliance Agreement between Jefferson and the external site(s) has been established and obtain study activation authorization for external site(s) from OHR prior to initiation of study activities at external site(s);
- Ensure that external site Principal Investigator and Key Personnel satisfy Jefferson's training and conflict of interest disclosure requirements;
- Be responsible for disseminating protocol information to site(s). Such protocol information includes initial study approval, annual review approvals, protocol modifications, unanticipated problems involving risks to participants or others, a finding of serious or continuing non-compliance, or the suspension or termination of IRB approval;
- Report to the Jefferson IRB any unanticipated problems occurring at external site(s) that are related to the research study.

4.2.2 Jefferson Investigator is the Principal Investigator on a Single or Multi-Site Research Study that Utilizes an Unaffiliated Investigator

When a Jefferson investigator's study team includes an Unaffiliated Investigator, the Jefferson investigator must:

- Ensure that the external investigator is not affiliated with an entity that regularly conducts research, is not acting as an agent of that entity, and is not acting as an agent of Jefferson through his/her participation in the

protocol (i.e., the investigator is not on Jefferson's payroll, not operating as an employee of Jefferson for this protocol specifically, not a student of Jefferson receiving academic or practicum credit, and not acting as an intern of Jefferson);

- Ensure that the unaffiliated investigator(s) satisfies Jefferson's training and conflict of interest disclosure requirements;
- Establish an Individual Investigator Agreement prior to the initiation of any research activities by the Unaffiliated Investigator.

4.3 External Site Utilization of Local IRB Review

Jefferson Investigator is the Principal Investigator on a Multi-Site Research Study

When an external site has an IRB and does not plan to rely on Jefferson IRB, the investigator must:

- Obtain Jefferson IRB approval for research activities to occur at Jefferson;
- Provide to OHR documentation of the external site's IRB initial and continuing approval of the investigator's research at that site.

4.4 Reliance on an External IRB

Jefferson Investigator is Relying on an External IRB for Regulatory Oversight on a Multi-Site Research Study

When a Jefferson investigator will utilize a non-Jefferson IRB for review of human subjects research, the investigator must:

- Upload required documents in the IRB portal as per Jefferson sIRB SOPs;
- Obtain all required ancillary institutional reviews and submit all requisite documents;
- Ensure that a Reliance Agreement between Jefferson and the external IRB has been established prior to initiation of study activities at Jefferson;
- Obtain study activation authorization from OHR prior to initiation of study activities at Jefferson;
- Ensure all Jefferson reporting requirements are maintained throughout the life of the study.

5. References

45 CFR 46.114
NOT-OD-16-094

100 General Administration (GA)
Policy GA 106: Conflicts of Interest
Rev.: 5/22/2020

1. Purpose

To define the procedure for managing conflicts of interest (COI) for individuals involved with human subjects research.

2. Responsibilities

Legal Office
Conflict of Interest Committee (COIC)
Investigators and Key Personnel
IRB Members
Director/Associate Director, OHR
OHR Personnel

3. Procedure

Conflicts of interest that may interfere with an individual's ability to carry out their study related responsibilities objectively must be managed. The main source of reference for procedures related to conflicts of interest is University Policy 107.03 Conflicts of Interest Policy for Employees (including attachments). All Jefferson employees must follow the University policy. In addition, individuals involved with human subjects research must follow this policy.

Non-employees involved with human subjects research must also complete a COI disclosure by emailing their name, email address, institution, and role in the research to JeffCOISmart@jefferson.edu. They will be sent instructions on completing the disclosure.

The system used is COI-SMART. It contains all the disclosures, definitions, and monetary amounts related to COI.

Investigators must also provide the COI information requested on the OHR-1 (initial review) and OHR-9 (continuing review).

The Conflict of Interest Committee (COIC) reports COIs and management plans to OHR as appropriate. The IRB may approve the management plan as received, impose additional requirements, or disapprove the plan.

Individuals involved with human subjects research should also report non-financial COIs to OHR. Non-financial COIs include:

- Personal beliefs and/or relationships.
- Institutional relationships.
- Career advancement.
- Any situation that could interfere with an individual's ability to carry out their study related responsibilities objectively
- Note: Individuals who are responsible for research development, such as employees in the Jefferson Office of Technology Transfer and Business Development or other administrators with business development interests are prohibited from serving as members of the IRB.

OHR ensures that the Chairs/Vice Chairs and reviewers are aware of any COI and/or management plan.

The IRB Chair/Vice Chair will ask if any members have a COI with any of the studies to be discussed and ensures that any investigator/key personnel COIs/management plans are discussed during the meeting as appropriate. Individuals who will be performing IRB activities outside of a convened meeting must notify the Director/Associate Director, OHR of any COI. The IRB will determine if the COI must be disclosed in the consent form. The IRB will not issue the approval letter for the study before the management plan is approved per Policy 107.03.

Individuals with a significant COI may not be present at an IRB meeting during the discussion, deliberation, or vote for that particular study. Members are recorded as absent with the reason of COI, and are not counted towards quorum for that particular study. The individual may be asked to return temporarily to the meeting to answer questions. These actions will be documented in the meeting minutes.

This Policy will be distributed to all IRB members annually and will be available for review at all IRB meetings.

4. References

OP 203: Use of IRB Consultants

100 General Administration (GA)
**Policy GA 109: Roles and Responsibilities of Study Personnel and Department
Chairs**
Rev.: 1/20/2020

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. Responsibilities

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. Changes in Principal Investigator, Co-Investigator and key personnel must be reported to the IRB as indicated in this policy.

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 Jefferson 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.

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 to the IRB. Changes to the protocol, consent form and other supplementary materials are submitted to the IRB using the OHR-12. Investigators, Co-Investigators and key personnel are added to the study by submitting the OHR-12B to the IRB. If a PI, Co-I or key personnel leaves the study, this must be documented by the study team (e.g. entering a stop date in JeffTrial, or for studies not in JeffTrial, submitting an OHR-12C to the IRB). In addition, all study personnel additions and removals will be reported on the OHR-9 at the time of continuing review. Note that if the only change to a consent form is the addition/removal of an investigator, a revised consent form does not need to be submitted to the IRB at that time. 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):

Investigator means an individual who actually conducts a clinical investigation. In the event an investigation is conducted by a team of individuals, the principal investigator is the responsible leader of the team. The principal Investigator must be approved by the IRB.

The principal investigator has 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)
- Jefferson 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 Jefferson prior to submission of the final report

Individuals from other institutions who hold an adjunct appointment allowing limited activities at Jefferson 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):

A Co-Investigator includes other members of the study team who have been approved as Co-Investigators by the IRB.

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"

OHR-34 "Research Not Requiring IRB Review: A Checklist"

100 General Administration (GA)
Policy GA 110: Signatory Authority
Rev.: 9/21/16

1. Purpose

To describe the signatory authority given to personnel of the Office of Human Research, for all actions of the IRBs.

2. Responsibilities

Senior Compliance Officer 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)

100 General Administration (GA)
Policy GA 112: Emergent Use of a Drug, Biologic, or Medical Device
Rev.: 5/22/2020

1. Purpose

To define the procedure for emergent use of a test article (drug, biologic, or device).

2. Responsibilities

Director/Associate Director, OHR
Investigators and Key Personnel
Practicing Physicians

3. Definitions

Emergency Use - The use of a test article on a human subject in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval (21 CFR 56.102).

Life Threatening - Diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes (21 CFR 312.81). The disease need not be immediately life threatening.

Severely Debilitating - Diseases or conditions that cause major irreversible morbidity (21 CFR 312.81). Examples include blindness, loss of arm, leg, hand or foot, loss of hearing, and stroke.

4. Procedure

FDA regulations allow for emergency use of a test article without prior IRB approval, provided that such emergency use is reported to the IRB within 5 working days. Any subsequent use of the test article at the institution is subject to IRB review (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.

HHS regulations require that all non-exempt research involving human subjects receive IRB review and approval. However, HHS recognizes that physicians have the authority to provide emergency medical care to their patients. HSS 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.

The IRB will follow both FDA and HHS regulations accordingly.

When possible, contact the OHR Director/Associate Director as soon as possible when considering emergent use.

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 debilitating.
- 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 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.

Some manufacturers may require an “IRB approval letter” before releasing the test article. If it is not possible to convene the IRB, the Director/Associate Director, OHR will provide the sponsor with a letter stating that the IRB is aware of the proposed use and considers the use to meet the criteria for emergent use. 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.

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 immediately after shipment is made. Note that an unapproved device may not be shipped in anticipation of an emergency. Nights and weekends, contact the FDA Office of Emergency Operations.

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 below).
- Notifying the Institutional Review Board (IRB).

- 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 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 Director/Associate Director, OHR will determine whether the emergent use met FDA regulations and will ensure that the use is not research under HHS regulations.

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 Jefferson.

The Director/Associate 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 and the required OHR forms should be submitted to the IRB.

100 General Administration (GA)
Policy GA 113: IRB Reporting of Findings and Actions to Investigators
Rev.: 11/1/2018

1. Purpose

To describe how the findings and actions concerning all research submitted to the IRB are to be communicated to investigators.

2. Responsibilities

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 staff.

The IRB's findings and actions are reported in writing to the investigator (and the institution when appropriate) including its decision to approve or disapprove the proposed research activity and any modifications required to secure IRB approval of the research activity. If the IRB decides to disapprove a research activity, it shall include in its written notification a statement of the reasons for its decision and give the investigator an opportunity to respond to the investigator and the institution.

4. Procedures

4.1 Investigator Notifications

- 4.1.1 Initial Submission: The IRB secretary will notify the Principal Investigator of the IRB's review comments and study approval status in general within the week following the IRB meeting. This is generally by email. 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 IRB member(s) charged with expedited review.

If the Principal Investigator's responses and/or revisions reviewed by the Board Secretary are satisfactory, an approval letter and stamped materials (if applicable) will be issued.

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 may 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, specifying the approval and expiration dates, 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 ensures archiving of approval letters.

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, Vice Chair, or designated IRB Member. 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 Senior Compliance Officer for Research Conduct and Compliance and/or 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 Senior Compliance Officer and the Chair of the COI Committee will be notified by the Director or Associate Director of the Office of Human Research.

100 General Administration (GA)
Policy GA 115: Management of Research Concerns
Rev.: 5/22/2020

1. Purpose

To describe how OHR handles concerns or complaints about a clinical research study from a subject, their relative, advocate, and/or surrogate, a study team member, government agency, or other individual.

2. Responsibilities

Director/Associate Director, OHR
IRB Chairs/Vice Chairs

3. Procedure

Once a possible concern has been identified, OHR management, an IRB Chair/Vice Chair, or other qualified individual will act as reviewer.

Concerns that involve non-compliance will be handled according to TJU Policy 110.15, Institutional Review Board Review of Noncompliance Issues.

Concerns that involve unanticipated problems involving risks to subjects or others will be handled according to OHR Policy GA 120, Reporting and Reviewing Unanticipated Problems Involving Risks to Subjects or Others.

The reviewer will work with the individual with the concern, making every effort to resolve the issue in a confidential manner. As needed, the reviewer will request and collect additional information and will involve the Legal Office and other individuals who are not affiliated with the specific study, such as the Institutional Official. The reviewer or other appointed person (e.g., representative from the Legal Office) will contact the individual to provide findings and/or a resolution. This process will continue and expand as needed until the individual is satisfied or Jefferson has determined that it has fulfilled its obligation to the individual.

100 General Administration (GA)
Policy GA 116: Use of Students and Employees as Key Personnel and Subjects in
Clinical Trials
Rev.: 3/24/2015

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

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.

100 General Administration (GA)
Policy GA 118: Protocol Inclusion/Exclusion Waivers
Rev.: 1/2013

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. Responsibilities

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

100 General Administration (GA)
**Policy GA 120: Reporting and Reviewing Unanticipated Problems Involving Risks
to Subjects or Others**
Rev.: 11/1/2018

1. Purpose

The purpose of this policy is to ensure prompt reporting to the IRB of Adverse Events (AEs), 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 FDA of any unanticipated problems involving risks to human subjects or others.”

2. Responsibilities

OHR Personnel
Investigators and Key Personnel
SAE and UAP Reviewers

3. Definitions

3.1 An **Adverse Event (AE)** is any untoward medical occurrence that occurs during the reporting time period (see more below). The occurrence does not have to be related to the study and includes abnormal laboratory findings. An adverse event is considered **serious** if, in the view of either the investigator or sponsor, it results in any of the following outcomes:

- Death
- A life-threatening adverse event
- Inpatient hospitalization (including emergency room visits lasting more than 24 hours) or prolongation of existing hospitalization
- A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions
- A congenital anomaly/birth defect.

Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious 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.

3.2 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. Please see the National Cancer Institute website for more information.

- Grade 1 = Mild
- Grade 2 = Moderate
- Grade 3 = Severe
- Grade 4 = Life-threatening or disabling
- Grade 5 = Death

3.3 A **Related Event** is one that is judged to be *possibly or definitely* associated with the test article (e.g. drug, device), procedures, conduct, or some other aspect of the study.

3.4 An **Unanticipated Problem (UAP)** is an **unexpected event that involves risk to the subject(s) or others but does not by itself meet the definition of an adverse event.**

Examples of UAPs which may **involve risk to the subject or others** are listed below. The risks may be physical or psychological or involve the loss of a subject's confidentiality or rights as a research subject.

- A Protocol Deviation and/or Violation is a departure from the IRB-approved protocol. OHR does not make a distinction between protocol deviations and violations. They are considered a type of UAP. A protocol deviation/violation that is serious or recurrent and involves risk to the subject or others must be reported as a UAP. Any associated SAE must be recorded and reported as specified in this policy.
- Reports from other sites including AEs, SAEs and IND safety reports that individually or collectively suggest an unanticipated problem.
- Multiple occurrences of an AE that are not individually reportable but together are considered an unanticipated problem.
- 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.
- Any other event that may prompt action by the IRB to ensure the protection of human subjects.

3.5 **Unexpected** indicates that an event is not listed, or is listed with a different specificity or greater severity or frequency, in the investigator's brochure, device brochure, product insert, protocol or consent form.

4. Review of SAEs and UAPs

Reported SAEs and UAPs will be reviewed by OHR staff and/or designee with the intention of eliminating any immediate risks to the subjects and others.

Actions that may be taken include:

- Modification of the protocol, consent form or consent process
- Providing additional information to or re-consenting subjects
- Modification of the continuing review schedule
- Monitoring of the research and/or consent process by the OHR QA/QI program
- Suspension or termination of the research

- Referral to other organizational entities for further investigation

Notification and further action taken as per TJU Policy 110.15 “Institutional Review Board Review of Noncompliance Issues”.

5. Reporting of Adverse Events, Serious Adverse Events, and Unanticipated Problems

- 5.1 AEs, SAEs, and UAPs are reportable from the time the patient consents to 30 days after the last study intervention, or as specified in the protocol.
- 5.2 A log of all AEs, SAEs, and UAPs must be maintained. Often, the log of protocol deviations/violations is maintained separately from the other UAPs.
- 5.3 SAEs are reported in the SAE reporting system (i.e. eSAEy). UAPs are reported in the UAP reporting system (i.e. eazUP).
- 5.4 If an event is ongoing or unresolved when it is initially submitted, an additional report should be submitted when the event is resolved.
- 5.5 If an event necessitates a change to the protocol and/or consent form, submit an amendment (OHR-12) to OHR.
- 5.6 The timeframes for reporting AEs, SAEs, and UAPs starts when anyone on the study team becomes aware of the event. The event is not considered reported to the IRB until the investigator signs off on the event in the reporting system.
- 5.7 AEs, SAEs, and UAPs must be recorded and reported per the agreement with other IRBs of record (e.g. commercial IRBs, other institutions IRBs).
- 5.8 Generally, reports of external events (e.g. IND safety reports) do not need to be submitted to the IRB. For external events that necessitate a change to the research (e.g. protocol, consent), an amendment must be submitted to the IRB
- 5.9 If Jefferson is acting as the coordinating site for a multi-center study:
 - 5.9.1 If the sponsor, DSMB, or other entity is monitoring safety across all sites, events that necessitate a change to the research (e.g. protocol, consent), an amendment must be submitted to the IRB.
 - 5.9.2 If no other entity is monitoring safety across all sites, events at all sites must be reported to the IRB as indicated in the table below.

The following events are reportable to the IRB in the timeframes indicated below:

Timeframes for AE, SAE and UAP Reporting

EVENT	Business Days
<p>An adverse event that meets ALL of these criteria:</p> <ul style="list-style-type: none"> • Serious [Grades 3,4,5 (death)] • Unexpected (in specificity / severity / frequency) • Possibly or Definitely Related 	<p>5</p>
<p>An unanticipated problem (UAP) that meets ALL of these criteria:</p> <ul style="list-style-type: none"> • Involves risk to the subject(s) or others • Is serious 	<p>5</p>
<p>All AEs, SAEs, and UAPs</p>	<p>Report with the next continuing review or final report (whichever comes first): All SAEs and UAPs that have occurred since the initial submission or last continuing review (whichever was more recent). This includes SAEs and UAPs that have already been submitted to the IRB. Note that grade 1 and 2 AEs do not have to be reported to OHR.</p>

6. 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 312.32 IND Safety Reporting
- 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

100 General Administration (GA)
Policy GA 121: Documentation and Document Management
Rev.: 6/21/2019

1. Purpose

To describe the requirements for management of all OHR and IRB documents including: document retention; administrative documents; and archiving.

2. Responsibilities

Director/Associate Director, OHR
OHR Administrative Staff

3. Policy Statement

Each hard copy of study files 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 46.108; 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

The IRB and Investigators must follow University Policy 102.39, Policy on Retention of University Records. Records must be retained longer if specified in the contract. For sponsored studies, when the retention period ends, the investigator should contact the sponsor before destroying any records. To ensure subject privacy, the investigator must consider the prompt destruction of PHI after the retention period ends. Records must be destroyed as specified in

the University policy. Shredding or depositing records in locked confidential bins are acceptable methods. After records have been destroyed, this will be documented (e.g. in the appropriate study file or database).

IRB files are stored in locked rooms. Files are stored on-site in locked rooms. Hard copies of files exceeding the three year retention limit will be purged annually. Final entry into the study history in the database will be made indicating that the file has been purged. The study folder and its materials will be discarded by shredding.

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:
 - Waiver or alteration of consent process
 - Research involving pregnant women, fetuses, and neonates
 - Research involving prisoners
 - 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:
 - The specific permissible category;
 - A description of the action taken by the reviewer
 - Any determination required by the regulations along with protocol-specific findings justifying those determinations.

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), IRB member training records, and voting status.
- 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.

5. References

45 CFR 46.103(a)
45 CFR 46.108
21 CFR 56.115
21 CFR 312.62
45 CFR 46.115

100 General Administration (GA)
Policy GA 124: Good Clinical Practice for Investigators
Rev.: 5/22/2020

1. Purpose

To provide guidance to investigators and key personnel on Good Clinical Practice (GCP) for human subjects research. This guidance is taken from the International Congress for Harmonization (ICH) E6 Guidelines for Good Clinical Practice.

2. Responsibilities

Investigators and Key Personnel

3. Policy

Investigators and key personnel should follow the following guidance when conducting human subjects research. Although they appear below, the most current version of the ICH guidelines should be referenced.

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

Attachment A - OHR Policy GA-124

Regulatory Binder Index

<p>1. Protocol</p>	<ul style="list-style-type: none"> • Study Protocol and Amendments • Protocol or Amendment Signature Pages • Non-Disclosure Agreement • Investigator Drug Brochure
<p>2. 1572 / Regulatory Forms / CV</p>	<ul style="list-style-type: none"> • Form FDA 1572 (If applicable) • Curriculum Vitae of investigator(s) • Medical Licenses (US only, if applicable) • Financial Disclosure Agreement (if applicable) • Copies of IRB & HIPAA training certificates
<p>3. Original IRB-Approved Consent Form(s)</p>	<ul style="list-style-type: none"> • Original Informed Consent(s) (with red IRB stamp)
<p>4. IRB Approval letters and Correspondence</p>	<ul style="list-style-type: none"> • IRB/IBC/RAC Approvals for Protocol • Copies of OHR-12 (Amendments, Advertisements), OHR-9 (continuation) • Other IRB Correspondence (copies of OHR-20 for deviations/violations, etc.)
<p>5. Laboratory</p>	<ul style="list-style-type: none"> • Lab Certifications as applicable (CAP & CLIA) • Laboratory Normal Ranges • CV of pathologist, if applicable
<p>6. Study Logs</p>	<ul style="list-style-type: none"> • Printouts of SAE reports • Investigator Personnel Team Signature Page • Site Visit Logs • Site Signature Logs • Master Subject Logs • Screening Logs • Training Logs (Site initiation Visit attendance log & training certificates)
<p>7. Correspondence</p>	<ul style="list-style-type: none"> • Study related correspondence between the site, sponsor, CRO, etc.
<p>8. Serious Adverse Events (SAE)</p>	<ul style="list-style-type: none"> • Printouts of SAE reports • IND Safety Letters
<p>9. Drug / Device Accountability (if applicable)</p>	<ul style="list-style-type: none"> • Receipt/packing invoices • Accountability Form • Supply Forms
<p>10. Miscellaneous</p>	<ul style="list-style-type: none"> • Miscellaneous (CRF transmittal logs, etc.)

100 General Administration (GA)
Policy GA 125: Investigator Responsibility and Delegation of Responsibility
Rev.: 5/22/2020

1. Purpose

To define the responsibilities of the principal investigator and the delegation of authority to members of the study team.

2. Responsibilities

Investigators and Key Personnel

3. Procedure

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 GA 124, 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 Legal Office and any other appropriate authorities, and mitigated where possible (Reference GA 106, 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 GA 124, Good Clinical Practice for Investigators).
- 3.1.10 Ensures the proper use, storage and accountability of investigational products (Reference GA 124, Good Clinical Practice for Investigators, Section 4.6, Investigational Products).
- 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, 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, 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, Good Clinical Practice for Investigators, Section 4.12 Premature Termination or Suspension of a Trial and RR 407, Suspension or Termination of Human Subjects Research).
- 3.1.14 Protects the rights and welfare of study participants and ensures initial and ongoing review by the IRB and any other relevant institutional participant safety committees. (References: Policy IC 701, Informed Consent and HIPAA Authorization: General Requirements; Policy IC 702,

Documentation, Waiver and Alteration of Informed Consent and HIPAA Authorizations; Policy GA 119, Submission and Review of Human Gene Transfer and Vaccine Trials).

- 3.1.15 Ensures that each participant signs the current version of the Jefferson 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, Documentation, Waiver and Alteration of Informed Consent and HIPAA Authorizations).
- 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 127, Subject 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, Reporting and Reviewing 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 301, Quality Assurance/Quality Improvement Program; QA 303, Inspections by the FDA and other Regulatory Agencies).
- 3.1.20 Cooperates with regulatory authorities (e.g., FDA, OHRP) in their assessment of the clinical research program's compliance with applicable regulations (Reference Policy QA 303: Inspections by the FDA and Other Regulatory Agencies)

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 Except where noted in these policies, the Investigator has the authority to delegate any study-related task and responsibility to any qualified 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)

100 General Administration (GA)
Policy GA 126: Sponsor Agreements
Rev.: 9/21/2016

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. Responsibilities

Director/Associate Director, OHR
OHR Administrative Staff
IRB Chairs/Vice Chairs
Director, Office of Research Administration
Senior Compliance Officer

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 Senior Compliance Officer, 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 Jefferson 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 Jefferson 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 Jefferson 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 Jefferson, then, as appropriate, from Jefferson to participants, when those results directly affected the participants' safety or medical care.
- 4.3 The Legal Office 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.

100 General Administration (GA)
Policy GA 127: Subject Screening and Enrollment
Rev.: 11/1/2018

1. Purpose

This policy describes the process to be followed for confirming the eligibility of subjects to enroll in human subjects research.

2. Responsibilities

OHR Personnel
Investigators and Key Personnel

3. Policy Statement

Every subject who is considered for enrollment in human subjects research must have his/her eligibility confirmed to participate

4. Procedures

4.1 General Instructions and Responsibilities

The 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.

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 To allow for the review of possible study candidates in the electronic medical record, an OHR-3 must be submitted to the IRB. The submission should also include the script/letter that will be used to contact patients. Obtaining statistics on a general number of patients from the electronic medical record with a specific condition/parameters, but without permanent record of specific patients is allowed. This can be performed as preparatory to research and does not require IRB approval
- 4.3.2 A Jefferson researcher may contact any patient in the Jefferson electronic medical records. The individual contacting the patient
- 4.3.3 If the patient shows interest, the consent process is then followed before any study specific procedures are done.
- 4.3.4 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. Summary statistics on the number of subjects pre-screened can be kept, but the actual list with patient names should be secured and destroyed when no longer needed.
- 4.3.5 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.
- 4.3.6 The Investigator/designee should record the status (e.g. screen failure, enrolled, etc.) of all potential subjects on the screening and enrollment log.
- 4.3.7 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.
- 4.3.8 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.

4.4 Subject Numbering

- 4.4.1 The investigator will ensure maintenance of 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 could include a site number if applicable, and sequential subject number. This procedure including any other protocol-specific subject

cohort assignment should be defined in the protocol or study-specific operations manual.

4.4.2 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.

4.4.3 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)

100 General Administration (GA)
**Policy GA 128: Designation of the Institutional Official Responsible for the Human
Research Protection Program**
Rev.: 5/22/2020

1. Purpose

To designate the Senior Compliance Officer as the Institutional Official (IO) with overall responsibility for the Human Research Protection Program (HRPP).

The Senior Compliance Officer may also be referred to as the Senior Associate Provost for Research Conduct and Compliance.

2. Responsibilities

Institutional Official (IO)
Director, OHR
The Provost of Thomas Jefferson University

3. Policy Statement

This Policy designates the Senior Compliance Officer as the Institutional Official (IO). The IO is the individual charged with responsibility for research, research integrity and science policy. The IO is responsible for general oversight of the University's HRPP and reports directly to the Provost of the University.

The Director, OHR reports directly to the IO, ensuring that there is direct accountability by the OHR to the IO.

100 General Administration (GA)
Policy GA 129: Protection of Privacy Interests of Research Subjects and
Confidentiality of Subject Data
Rev.: 1/20/2020

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. Responsibilities

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:

Jefferson 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 consent form document that contains the HIPAA- compliant Privacy Notice approved by the Legal Office.

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 and disclose PHI for research purposes pursuant to a documented waiver of authorization issued by the IRB. This document, known as a HIPAA waiver letter, includes the following information:
- Identification of the IRB approving the waiver and the date of approval.
 - A statement that the IRB has determined that the waiver satisfies the criteria in the Privacy Rule as stated above.
 - A brief description of the PHI covered by the waiver.
 - A statement that the waiver has been approved by a convened IRB or by expedited review.

An IRB approval letter for the study will always be issued simultaneously with a HIPAA waiver letter.

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 Legal Office 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 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.

100 General Administration (GA)
Policy GA 131: Research Device Acquisition, Use, and Tracking
Rev.: 6/21/2019

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 Jefferson premises.

2. Application

This policy applies to all medical research devices used or implanted on Jefferson 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”).

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 Jefferson 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 record of the device. 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 Jefferson IRB prior to study initiation. IRB approval will not be granted if the device section on 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 Jefferson 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.).

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.

8. References

21 CFR 812

FDA Information Sheet Guidance for IRBs, Clinical Investigators, and Sponsors, Significant Risk and Nonsignificant Risk Medical Device Studies, January 2006. Available at www.fda.gov/cdrh.

TJUH Policy 108.11, “Value Analysis Committee - Product Request Process”

100 General Administration (GA)
Policy GA 132: Human Research Protection Program
Rev.: 11/11/2021

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 Jefferson.

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 Jefferson, 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 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 improvement group conducts routine and for cause audits of clinical research studies. Consent observations are also conducted as needed. In addition, the group audits OHR files and processes on a regular basis.

The OHR is in the Jefferson corporate structure. The Senior Compliance Officer has general oversight responsibilities for the OHR. The Director of OHR reports to the Senior Compliance Officer at weekly meetings or on an *ad hoc* basis. The Senior Compliance Officer 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 of 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 Legal Office maintains all Jefferson policies including those on Conflicts of Interest (COI) for employees, COI for the Board of Trustees, HIPAA, and Noncompliance with human subjects regulations. A member from the Legal Office 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. The Legal Office 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 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 Jefferson 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 Senior Compliance Officer is the Senior Officer with oversight responsibility for research, research integrity and science policy. The Senior Compliance Officer 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 Sidney Kimmel Cancer Center quality improvement group conducts routine and for cause audits of oncology clinical research studies and will report serious and continuing compliance issues to OHR.
- 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 Jefferson.

4. Responsibility of the Offices and Personnel involved in the HRPP

The Director of OHR, the Senior Compliance Officer 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
- 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

100 General Administration (GA)
Policy GA 133: Human Research Training
Rev.: 5/22/2020

1. Purpose

The purpose of this policy is to explain training requirements for individuals involved in human subjects research.

2. Responsibilities

OHR Personnel
Investigators and Key Personnel
IRB Members

3. Procedure

All investigators, key personnel, and IRB Members must receive training prior to their involvement in human subjects research. This training is available through the Collaborative Institutional Training Initiative (CITI). OHR will maintain the training records. OHR will also ensure that study personnel have completed the appropriate training before issuing the approval letter for a new study or continuing review and before the addition of study personnel is approved for an existing study.

These training requirements apply whether Jefferson personnel are engaged in research reviewed by a Jefferson IRB or an external IRB.

OHR has the option of accepting certification of training that is comparable to that which is described in this policy.

Investigators and key personnel must complete the CITI training appropriate to their area of research. Those doing biomedical research must take the biomedical and GCP courses. Those doing socio-behavioral research must take either the socio-behavioral course or both the biomedical and GCP courses.

To maintain certification, active researchers must complete the refresher modules every 3 years following their initial certification.

Jefferson personnel who took CITI training elsewhere should log on to their accounts and make Jefferson an affiliate institution. This will provide OHR with access to your most current training and allow you to receive automated e-mail notifications of training status.

As of 5/16/19, all current IRB Members are grandfathered into training by virtue of their experience as IRB members. After 5/16/19, all new IRB Members and alternates must complete the CITI training for IRB Members. After the initial training, no refresher CITI training is required. Further relevant training is provided on a regular basis through the IRB continuing education program.

200 IRB Organization (OP)
Policy OP 201: IRB Membership
Rev.: 6/21/2019

1. Purpose

To ensure that the membership of the IRBs conforms to the requirements of 45 CFR Part 46.107 and 21 CFR 56.107(c).

2. Responsibilities

Director/Associate Director, OHR
IRB Secretary

3. Policy Statement

The membership of the IRB will meet or exceed the requirements of [45 CFR Part 46.107].

Each IRB shall have at least five members, with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the institution. The IRB shall be sufficiently qualified through the experience and expertise of its members (professional competence), and the diversity of its members, including race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. The IRB shall be able to ascertain the acceptability of proposed research in terms of institutional commitments (including policies and resources) and regulations, applicable law, and standards of professional conduct and practice. The IRB shall therefore include persons knowledgeable in these areas. If an IRB regularly reviews research that involves a category of subjects that is vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons, consideration shall be given to the inclusion of one or more individuals who are knowledgeable about and experienced in working with these categories of subjects.

Each IRB shall include at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in nonscientific areas.

Each IRB shall include at least one member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution. Unaffiliated members by definition may not be affiliated with the University nor have a family member (1st degree relative) who is affiliated with TJU.

No IRB may have a member participate in the IRB's initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the IRB. For PharmDs and clinical pharmacologists, preparing and dispensing a study drug does not constitute a COI.

An IRB may, in its discretion, invite individuals with competence in special areas to assist in the review of issues that require expertise beyond or in addition to that available on the IRB. These individuals may not vote with the IRB.

Each IRB shall have access to a legal representative from the Legal Office.

Board Secretaries are appointed as voting or non-voting members.

4. Procedures

After establishing an IRB per these requirements, OHR Leadership will ensure that these requirements continue to be met if a member leaves the IRB. OHR leadership is responsible for training the new members.

If the Chair is not available, the Vice Chair will chair the meeting. If both the Chair and Vice Chair are not available, an interim Chair will be appointed for the meeting.

Members are expected to attend at least 75% of meetings yearly. If that expectation is not met, the Director, OHR or the Chair may meet with the individual to discuss ways to improve attendance.

Before an IRB meeting, there is a reviewer assignment meeting. At these meetings the following is addressed:

- The number of protocols to be reviewed
- The distribution of the reviews
- Any IRB membership issues
- The need for consultants

A designated OHR staff member will report changes in IRB rosters to OHRP as required OHR staff members will prepare and maintain a current list of the IRB members identified by name; earned degrees; representative capacity; indications of experience such as board certifications or licenses sufficient to describe each member's chief anticipated contributions to IRB deliberations; and any employment or other relationship between each member and the institution. The roster will be up to date and available should OHRP request to see it.

200 IRB Organization (OP)
Policy OP 202: Recruiting, Appointing and Performance Evaluation of IRB
Members, Chairs, and Vice Chairs
Rev.: 10/28/2020

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. Responsibilities

Director/Associate Director
IRB Chair(s)
Senior Compliance Officer

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 Center City'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 Jefferson Scientist/Non-Scientist Members: Potential IRB Center City 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.

Potential Board members who are Jefferson 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 Jefferson 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 is formally appointed to the Board and is listed on the roster. 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.

Alternate members must have the same IRB training as primary members. The Jefferson IRBs tend to have well in excess of 5 members, so generally any alternate may substitute for any primary member as long as quorum and all other membership requirements are met. This does not apply to the assignment of reviewers. If a primary member has specific experience relevant to a particular study (e.g. prisoner advocate), the alternate should have similar expertise. As such, the rosters will not indicate specific individuals for whom the alternate may substitute. When alternates substitute for a primary member, the alternate member should have access to the same material as the primary member.

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 Senior Compliance Officer.

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 Jefferson 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 at least 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 Jefferson.
- 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 Senior Compliance Officer.

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 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 Center City 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.

200 IRB Organization (OP)
Policy OP 203: IRB Consultants
Rev.: 5/22/2020

1. Purpose

To describe the procedure for utilizing consultants to assist in IRB review of research.

2. Responsibilities

Director/Associate Director, OHR
IRB Members
Consultants

3. Procedure

Per 45 CFR 46.107(e), an IRB may, in its discretion, invite individuals with competence in special areas to assist in the review of issues that require expertise beyond or in addition to that available on the IRB. These individuals may not vote with the IRB (and are not counted toward quorum, but may participate in the discussion).

The Director/Associate Director, OHR may determine that a consultant is needed for the review of a research study. This will usually occur at the time of reviewer assignment with consultation with the Chair/Vice Chair. Any IRB member may recommend that a consultant may be needed.

Consultants must have a completed confidentiality agreement and conflict of interest (COI) disclosure (see GA 106, Conflicts of Interest). Consultants who are not affiliated with Jefferson will also provide curriculum vitae. Any prospective consultant with a conflict of interest will not be engaged for such reviews.

Appropriate study-related material will be provided to the consultant for review. For full reviews, IRB members will be notified at the convened meeting that a consultant has reviewed the study. The consultant may present the review. Pertinent comments/information will be incorporated into the meeting minutes and the consultant's written review of the study will be maintained in the IRB study file.

200 IRB Organization (OP)
Policy OP 204: IRB Review of Protocols
Rev.: 6/21/2019

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. Responsibilities

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. Generally, appointment to the IRB is for a three-year term. A member may be re-appointed. All appointed members of Jefferson IRBs are voting members.

4. Procedures

A week prior to the IRB meeting, the Director, OHR, 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 at least 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*

200 IRB Organization (OP)
Policy OP 205: IRB Member Responsibilities
Rev.: 5/22/2020

1. Purpose

To define the responsibilities of IRB members.

2. Responsibilities

Senior Compliance Officer
Director/Associate Director, OHR
IRB Members

3. Procedure

The primary responsibility of each IRB member is to review human subjects research to determine if it is ethically and scientifically sound and to protect the rights and welfare of human subjects. Each IRB member may be assigned to be the primary reviewer for a study. IRB members must have the appropriate expertise and training per policy GA 133, Human Research Training and must remain unbiased. It is preferred that individuals remain IRB members for at least 3 years.

The specific responsibilities of various IRB members are as follows:

3.1 Unaffiliated Members

Each IRB shall include at least one member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution [45 CFR 46.107(c)]. The role of the unaffiliated member is to advocate for the interests of the community as a whole.

3.2 Non-Scientific Members

Each IRB shall include at least one member whose primary concerns are in non-scientific areas [45 CFR 46.107(b)]. The primary role of the non-scientific members is to review the research, especially consent, from the perspective of the subject.

3.3 Scientific Members

Each IRB shall include at least one member whose primary concerns are in scientific areas [45 CFR 46.107(b)]. The primary role of the scientific members is to ensure that the research is medically and scientifically sound. Members may also

3.4 Chairs/Vice Chairs

The primary role of the chair is to facilitate the IRB meetings and to participate in assigning studies to the appropriate reviewers. The chair may initiate the suspension or termination of a study per policy RR 407, Suspension or Termination of Human Subjects Research. The vice chair, or another delegated, qualified member, assumes these responsibilities in the chair's absence.

3.5 Primary Reviewers

The primary reviewer must review all submission materials and present the review to the IRB. The review is maintained in the IRB study file.

200 IRB Organization (OP)
Policy OP 206: IRB Meeting Administration
Rev.: 6/21/2019

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. Responsibilities

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. (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 will not be accepted or distributed for review.

4.2 IRB meetings and Materials Sent to Members Prior to the Board Meeting:

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 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 roster.
- 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:
 - Waiver or alteration of the consent process (not required for exempt studies);
 - Research involving pregnant women, human fetuses and neonates;
 - Research involving prisoners;
 - 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 a 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:

- 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.

- 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.

300 Quality Assurance (QA)
Policy QA 301: Quality Assurance/Quality Improvement Program
Rev.: 11/11/2021

1. Purpose

To establish a program of oversight of human research activities that:

- Involves audits to assess compliance with University policy, regulations, ethical principles, and good clinical practice (GCP).
- Supports and further educates investigators and study personnel.
- Protects the rights of human subjects.
- Creates a culture of responsible conduct of clinical research.

2. Responsibilities

OHR Personnel
Investigators and Study Personnel

3. Procedures

3.1 Site Audits

Routine Audits are selected using a risk based approach focusing on studies with the highest opportunity for risk and the amount of external oversight. Various types of studies are selected (full, expedited, phase 1, pediatric, significant risk devices, etc.).

For Cause Audits are generally brought to the attention of the OHR quality improvement group by the IRB, OHR personnel, and study personnel. Studies that involve for-cause terminations or suspensions, noncompliance, or unanticipated problems requiring reporting to federal agencies are also included. After assessing the information provided, the OHR quality improvement group will decide if an audit or other action is appropriate.

The Site Quality Improvement Form contains the items which are reviewed during an audit. The corrective action plan (CAP) is used to document compliance with University policy, regulations, ethical principles, and good clinical practice (GCP), to further educate investigators and study personnel, and to disseminate areas for improvement to the education and training group.

The CAP findings are also be used to assess opportunities for improvements to the Human Research Protection Program as a whole. As needed, OHR will make appropriate modifications to the HRPP including the revision of policies and forms, announcements, website changes, and dissemination of the findings to the education and training group. The improvements will be re-assessed through future audits.

Completed CAPs are approved by senior quality improvement group personnel. Any findings that are serious or continuing will be communicated to senior OHR personnel and TJU Policy 110.15, Institutional Review Board Review of Noncompliance Issues will be followed.

The CAP will call for both corrective and preventative actions including:

- Fixing an existing issue
- Taking action to prevent future issues
- Re-education and/or re-audit

The CAP is presented to the study team who must provide a written response addressing any findings. When the final CAP has been approved by both parties, it is signed by the investigator and the OHR quality improvement personnel.

3.2 Consent Observation

Consent observations may be done on a routine or for cause basis. The consent process with a study subject or a mock consent may be observed. The Consent Observation Form contains the items which are reviewed and is provided to the person obtaining consent and the investigator as needed. Any findings that are serious or continuing will be communicated to senior OHR personnel and TJU Policy 110.15, Institutional Review Board Review of Noncompliance Issues will be followed.

3.3 Quality Improvement Program for the IRB

The quality improvement program for the IRB includes:

- Training and continuous education (CITI) for the OHR personnel
- IRB member continuing education program to keep members informed of regulatory and procedural changes as well as timely topics
- Review, maintenance and assessment of policies and procedures

- HIPAA in Research training
- Encouragement to qualify as a Certified IRB Professional (CIP)
- Audits of IRB processes and documentation

3.4 Audits of IRB Processes and Documentation

The IRB internal audit forms contain the items which are reviewed during an audit. The OHR quality improvement group will audit the following on an annual basis:

- IRB Rosters
- IRB Minutes (ideally minutes will be selected which document the review of various types of studies)
- Exempt study IRB files. Note: Full and expedited IRB files are reviewed during quality improvement site audits.
- OHR policies and procedures as needed
- Any other policies and procedures as necessary;

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 Senior Compliance Officer for implementation.

4. References

Site Quality Improvement Form
Consent Observation Form
OHR Internal Audit Forms

300 Quality Assurance (QA)
Policy QA 303: Inspections by the FDA and Other Regulatory Agencies
Rev.: 4/12/2019

1. Purpose/Policy

The FDA and other regulatory agencies have the authority to inspect investigator sites and IRBs. The purpose of this policy is to ensure that the correct steps are taken before, during, and after an inspection.

2. Responsibilities

Investigators
Research Coordinators

OHR Personnel
IRB Chair/Vice Chair

3. Procedures

3.1 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 Jefferson to audit specific documents and procedures.

For external audits involving the FDA or OHRP, the following individuals must be immediately notified by the Jefferson PI or his/her designee:

- Senior Compliance Officer
- Director, OHR
- Legal Office and Corporate Compliance Officer
- Center City IRB
- Department Chair
- Hospital Administration, if applicable

In addition, for sponsored research, the Jefferson PI or his/her designee shall notify:

Study Sponsor consistent with the terms of the study agreement, unless the regulatory agency directs otherwise. If the regulatory agency directs Jefferson to withhold such notice, the Jefferson PI or PI designee shall immediately notify the Legal Office.

The Principal investigator and IRBs should review the FDA's BIMO manuals CPGM for Clinical Investigators and CPGM for Institutional Review Boards respectively, in preparation for inspections.

The Principal Investigator, 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.

3.2 Participating in an Audit

The OHR Administrative staff, investigators and key personnel are 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 study related documentation, inspectors or auditors should be asked to provide identification and proof of their authority or authorization to conduct the audit (e.g. FDA 482) No entity other than those listed on the consent for the study may have access to any document that includes subject identifiers. Personnel shall be responsible for redaction of such information from files prior to the audit, if required.

Auditors will be escorted throughout the inspection while on Jefferson campus and provided with an adequate working area to conduct the audit. Jefferson personnel 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, a representative of the Legal Office or the Senior Compliance Officer to do so. The Principal Investigator should maintain a copy of all documents provided to the regulatory agency to be taken off-site.

3.3 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. The Legal 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. If the Principal Investigator is unsure whether a response is required or preferred, the Principal Investigator should contact the Director, OHR and the Legal Office.

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

Designated personnel 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.

The regulatory agency will issue the final report (e.g. FDA Establishment Inspection Report (EIR) and may require actions similar to the following: OAI (Official Action Indicated), VAI (Voluntary Action Indicated), NAI (No Action Indicated). Possible consequences include the study may be put on hold, re-inspection, rejection of study data, warning letter, restriction/disqualification of investigator.

4. References

CPGM for Clinical Investigators
CPGM for Institutional Review Boards

300 Quality Assurance (QA)
Policy QA 304: Study Team Training
Rev.: 7/2010

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. Responsibilities

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 Jefferson.

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

Jefferson 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 Jefferson 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.

Jefferson 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)

300 Quality Assurance (QA)
Policy QA 305: Verification by Outside Sources that No Material Changes Have
Been Made to an IRB-Approved Protocol
Rev.: 4/2008

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. Responsibilities

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.

400 Research Review (RR)
Policy RR 401: Initial Review - Criteria for IRB Review and Approval
Rev.: 9/16/2020

1. Purpose

This policy addresses federal and ethical criteria that the IRB must apply when reviewing and approved research.

2. Responsibilities

OHR Personnel
IRB Members

3. Procedure

3.1 Review of Studies by Jefferson 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.

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 Jefferson IRB or obtains expert 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. The IRB may determine that an approval period of less than one year is appropriate, depending on risk assessment. The approval period will be recorded in the meeting minutes and in the approval letter.

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, or individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons, additional safeguards should be considered by the IRB to protect the rights and welfare of these subjects. 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 noted in the minutes, but they may not vote on the protocol.

3.3 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.

3.4 Criteria for Initial IRB approval for research (45 CFR 46.111 and 21 CFR 56.111)

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.

3.4.1 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.
- Whether additional disclosures are required for inclusion in the consent process.
- That the consent process will be documented according to legal and regulatory requirements.

3.4.2 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:
 - The consent document contains all the required elements. The participant or the participant's legally authorized representative will sign the consent document.
 - A copy of the consent document will be given to the person signing the consent document.
 - 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:
 - 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.
- 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.

3.4.3 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.
 - 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.

3.4.4 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.

3.4.5 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.

3.4.6 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.

3.4.7 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.
- 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.

3.5 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.

Both the IRB and the Protocol Review Committee (PRC) in the Sidney Kimmel Cancer Center (SKCC) review studies for inclusion of women and minority populations with the goal of promoting accurate representation of the communities involved in human research at Jefferson. Every six months, the PRC reviews studies for inclusion of women and racial and ethnic minorities. If the recruitment does not appear to be meeting inclusion expectations, PRC will notify the PI and request an explanation for the lack of diversity in enrollment and a plan for how to address. This process is a requirement of the NIH core grant that funds the SKCC.

The IRB also conducts a demographic review at the time of continuing review and will request comment from the PI if there is concern regarding lack of diversity in enrollment.

3.6 Review of Department of Defense Supported Research

See OHR Guidance G-620, "Department of Defense (DoD) Requirements for the Conduct of Human Subjects 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 relations 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, or individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons.
- 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. References

OHR OHR-8 Internal Form

Informed Consent Document for Human Subjects Research Policy GA 106

Policy and Procedure for the Determination of Conflicts of Interest

45 CFR 46.111 (a), (a) 2

21 CFR 56.111 (a), (a) 2

FDA Guidance: IRB Waiver or Alteration of Informed Consent for Clinical Investigations Involving No More than Minimal Risk to Human Subjects, July 2017

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

400 Review of Research (RR)
Policy RR 402: Continuing Review by Convened IRB
Rev.: 5/22/2020

1. Purpose

To describe the process for the continuing review of research by convened IRB (i.e., “full” review).

2. Responsibilities

OHR Personnel
Investigators and Key Personnel
IRB Members

3. Procedure

The IRB shall conduct continuing review of research requiring review by the convened IRB at intervals appropriate to the degree of risk, the degree of uncertainty regarding the risk; the vulnerability of the subject population and the experience of the Investigator, the IRB’s previous experience with the Investigator and/or sponsor and whether the study involves novel therapies, at least annually, except as described in this policy. The IRB will maintain records of continuing review activities, including the rationale for conducting continuing review of research that otherwise would not require continuing review as described in this policy.

3.1. Determination of the Need and Interval for Continuing Review

Active studies must have current IRB approval. To maintain this approval, the IRB shall conduct continuing review of research requiring review by the convened IRB at intervals appropriate to degree of risk, not less than once per year, except as described:

Unless an IRB determines otherwise, continuing review is not required for the following research:

1. Research determined to be eligible for expedited review
2. Research that is exempt from the Common Rule
3. Research that has progressed to the point that it involves only one or both of the following, which are part of the IRB-approved study:
 - a. Data analysis, including analysis of identifiable private information or identifiable biospecimens, or

- b. Accessing follow-up clinical data from protocol-specific procedures that subjects would otherwise undergo as part of clinical care.

4.2 Submitting Continuing Review Materials to the IRB

Research related activities may not occur in the absence of IRB approval except where necessary to eliminate apparent immediate hazards to the human subjects. To maintain active IRB approval, an investigator must submit the OHR-9 Continuing Review form with all associated materials to the IRB. This must be done until the study ends or until it is determined that continuing review is no longer required. Investigators are sent automated emails prior to the study expiring. The continuing review ideally should be submitted at least 6 weeks before the current expiration date to avoid lapse in approval. If a continuing review is not submitted after the expiration date, a termination notice ultimately will be issued.

If the continuing review is not approved prior to the expiration date, enrollment and other research related activities must cease. If the investigator, in conjunction with the IRB, determines that the subjects on the study would suffer a hardship if study-related 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 submitting a continuing review. However, the data collected during this period of lapsed IRB approval may not be used for research purposes without IRB approval.

To re-open a lapsed study an OHR-9 Continuing Review form with all associated materials must be submitted to the IRB. If a Continuing Review is not received within 60 calendar days of the expiration date, a study can be administratively terminated. If an expired study has been completed, an OHR-9 Final Report should be submitted.

3.2. 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. The only way to reactivate an expired study is to submit a continuing review.

3.3. Suspension of IRB Approval

IRB approval for the conduct of a study may be suspended at any time if the IRB determines that protections of human subjects have been compromised or if risks have reached an unacceptable level. Some examples of reasons for the IRB suspending a study are: a greater 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 federal, University or IRB policies.

3.4. Continuing Review

The purpose of the continuing review is to review the accumulated research data from the previously approved period according to all applicable regulatory criteria. The information submitted on the OHR-9 and associated documents are reviewed by one or more IRB members with appropriate expertise.

Continuing review includes, but may not be limited to the following activities:

3.4.1 Site Visits and Third Party Verification

The IRB has the authority to observe, or have a third party observe, the consent process and the conduct of research it has approved, and to verify that the study is being conducted as per the protocol approved by the IRB and according to federal and local regulation.

3.4.2 Review of Serious Adverse Events (SAEs) and Unanticipated Problems (UAPs)

The investigator is responsible for submitting SAEs and UAPs to the IRB as described in OHR Policy GA 120. The Policy describes which SAEs and UAPs must be submitted to the IRB for immediate review, and which are included in the continuing review. The IRB reviews the SAEs, UAPs, and other requested safety information included with the continuing review to determine if the risk profile has changed and if additional protections or actions are necessary to ensure adequate protection to research participants.

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

3.4.3 Significant New Findings

During the course of an approved study, the IRB may review reports generated from data safety monitoring boards, sponsor communication, adverse events, current literature and other sources to determine if: the risk determination of the research has changed; the risk/benefit ratio is still acceptable; new information needs to be conveyed to the subjects, or; a segment of the population may be bearing an undue burden of research risk.

3.4.4 Reports from Investigators, Key Personnel and Employees

It is the responsibility of all employee, investigators and key personnel to promptly report to 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. OHR will act on any such information in order to protect the research subjects. The IRB may determine that the IRB approved informed consent form requires revisions.

3.4.5 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 will be received and reviewed by the Director/Associate Director, OHR. All reports of alleged non-compliance with federal human subjects regulations deemed to be credible will be handled according to University Policy 110.15, Institutional Review Board Review of Noncompliance Issues.

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.

3.4.6 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 approval, the IRB may request an independent assessment of information or data provided in the continuing review. Sources 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 by the IRB.

The assigned IRB 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.

The IRB will maintain records of continuing review activities, including the rationale for conducting continuing review of research that otherwise would not require continuing review as described in this policy.

4. References

45 CFR 46.108

45 CFR 46.109

45 CFR 46.115

400 Research Review (RR)
Policy RR 403: Review of Exempt Studies
Rev.: 9/4/2020

1. Purpose

To define the requirements for classifying a study as exempt from IRB review, and the procedure for making the determination and conducting the review.

2. Responsibilities

OHR Personnel
Investigators and Key Personnel
IRB Members

3. Procedure

A new study may be designated as exempt from IRB review provided it meets one of the criteria cited in 45 CFR 46.104.

The specific categories and other criteria for exemption are cited in the OHR-18. The investigator/key personnel completes and submits the OHR-18, Application for Exemption from IRB Review to the IRB. The investigator cannot make the exemption determination, as this falls within the purview of the IRB. The application is assigned to an IRB reviewer who reviews the application and makes the exemption determination. The assigned reviewer cannot have a conflict of interest in the study in order to review it and make the exemption determination. The Principal Investigator is notified of the exemption determination. The exemption determination is recorded in the IRB exemption letter.

Research for which limited IRB review is a condition of exemption is specified in the OHR-18, and applies to exemption categories 2, 3, 7, and 8. However, Jefferson does not intend to conduct research under categories 7 and 8, nor does it intend to implement broad consent as defined in 45 CFR 46. Thus, categories 7 and 8 are not included in the OHR-18. Under limited IRB review, the IRB makes an additional determination that when appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

Exempt studies do not require continuing review by the IRB. The investigator/key personnel submits any amendment to the research as well as notification of completion of the research to the IRB. The IRB maintains oversight of exempt studies by sending automated email reminders to PIs every 6 months querying whether the exempt study is still active and whether there have been any study-related events that the IRB should be informed about. The OHR quality improvement group also performs annual internal audits of exempt studies.

Exempt studies, while not within the purview of federal human subjects regulations, are held to Jefferson's ethical standards. The following standards are evaluated by the OHR reviewer based on review of the pertinent submission documents.

- The activity involves research
- The research holds out no more than minimal risk to participants.
- Selection of subjects is equitable
- Privacy of subjects is maintained
- Adequate provisions are in place to maintain confidentiality of identifiable information (Jefferson's Privacy Officer may be consulted as needed concerning adequacy of plans to protect the identifiers from improper use or disclosure)
- If there are interactions with participants, the IRB will determine whether or not there should be a consent process and that:
 - Participation is voluntary.
 - Name and contact information for the researcher is provided.
 - There is a description of procedures.
 - The consent process is adequate and based on IRB consent form templates.

400 Research Review (RR)
Policy RR 404: Expedited Review of New and Continuing Research
Rev.: 9/14/2020

1. Purpose

To define the expedited review procedure for new studies and continuing reviews.

2. Responsibilities

OHR Personnel
Investigators and Key Personnel
IRB Members

3. Procedure

Determination and Processing of Expedited Review

OHR personnel use the OHRP guidance document “Categories of Research that may be Reviewed by the Institutional Review Board through an Expedited Review Procedure” (November 1998) to determine if a study meets the criteria for expedited review. The rationale for designating a study as expedited is that all of the study procedures fall within the categories outlined in the OHRP document and the study qualifies as minimal risk. Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

An IRB may use the expedited review procedure to review the following:

Some or all of the research appearing on the OHRP list, unless the reviewer determines that the study involves greater than minimal risk;

Minor changes in previously approved research during the period for which approval is authorized; or

Research for which limited IRB review is a condition of exemption is specified in the OHR-18. Under limited IRB review, the IRB makes an additional determination that when appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

Under an expedited review procedure, the review is always conducted by one or more experienced IRB members. In reviewing the research, the reviewers may exercise all of the authorities of the IRB except that the reviewers may not disapprove the research. A research activity may be disapproved only after full

Board review. (“Disapprove” as used in the Common Rule is to be distinguished from “Not Approve”, a Jefferson-specific term. Disapprove indicates a final decision, whereas Not Approve is a temporary action accompanied by reviewer comments provided to the investigator, who can resubmit a revised submission.) All expedited transactions are retained in the minutes of each meeting

Studies determined to meet the criteria for expedited review will be reviewed by the OHR Director, Associate Director, Chair, Vice Chair and/or designated IRB members as appropriate. All expedited reviewers will be trained by senior OHR personnel. The reviewers will receive the same materials that a primary reviewer receives (see Policy OP 206).

The expedited reviewer will review the submission and make the recommendation to approve or not approve the study. The comments are provided to the investigator/study personnel.

If in the opinion of the reviewer, the study should be disapproved (as the term is used in 45 CFR 46.110), the study must be re-submitted in full, and reviewed by a convened Board.

The convened IRB is notified of all studies approved by the expedited procedure through the IRB meeting minutes. The Board is not required to vote on these items. They are documented for information, auditing and record-keeping purposes only. When an expedited study is approved, an approval letter and stamped materials are released to the Principal Investigator, and the study may begin.

At the time of initial review and approval of an expedited study, the study may be designated for no further continuing review (NFCR) as per 45 CFR 46.109(e)(i), unless the IRB reviewer feels there is a reason to require a continuing review. If this is the case, the reviewer should document the reasons on the RQ-1 reviewer questionnaire. The approval letter will indicate that the expedited study has been approved for a defined period of time and will include the expiration date.

The IRB maintains oversight of NFCR studies by sending automated email reminders to PIs every 6 months querying whether the study is still active and whether there have been any study-related events that the IRB should be informed about. The OHR quality improvement group also includes NFCR studies in their site audits.

400 Review of Research (RR)
Policy RR 407: Suspension or Termination of Human Subjects Research
Rev.: 9/14/2020

1. Purpose

To define the process for suspending or terminating previously approved research.

2. Responsibilities

Director/Associate Director, OHR
IRB Members

3. Definitions

Suspension of IRB Approval: A temporary halt in IRB approval of some or all research activities of a given study.

Termination of IRB Approval: A permanent halt in IRB approval of all research activities of a given study.

4. Procedure

Per 45 CFR 46.113, Suspension or termination of IRB Approval of Research, an IRB shall have authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects. Any suspension or termination of approval shall include a statement of the reasons for the IRB's action and shall be reported promptly to the investigator and appropriate institutional authorities within 5 business days. For studies under DHHS and/or FDA requirements, suspension or termination of approval shall be reported to OHRP and/or FDA within 30 days.

Reasons for suspension or termination include, but are not limited to:

- Research is not being conducted as approved by the IRB.
- Research is not being conducted according to regulations or IRB policy.
- Unexpected harm to research subjects.
- Research misconduct issues.

If there is a suspected reason for suspending or terminating a study, additional information may have to be collected. This may include an audit by the OHR quality improvement group.

Suspensions and terminations may be determined 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. OHR will notify the investigator in writing of the decision and rationale. The investigator will have the opportunity to respond in writing or at the IRB meeting when the issue is reviewed. If a convened IRB did not make the determination to suspend or terminate a study that originally received full review, the action must be reported to a convened IRB for review.

All terminations or suspensions will be reported according to University Policy 110.15, Institutional Review Board Review of Noncompliance Issues.

When a study is suspended or terminated, the PI must submit a plan to OHR for approval. The plan must address the following:

- The method and timeframe for notifying subjects.
- Plans to protect the rights and welfare of subjects which may include:
 - Transferring subjects to another site/investigator.
 - Clinical care outside of the research setting.
 - If permitted by OHR, continuing necessary research activities.
 - Follow-up of subjects.
 - Withdrawal from the trial in an orderly fashion, including any appropriate safety testing or procedures.
 - Notifying subjects of adverse events or new safety information as appropriate.

400 Review of Research (RR)
Policy RR 408: Review of Amendments
Rev.: 5/22/2020

1. Purpose

To define the review procedure for amendments to previously approved research.

2. Responsibilities

Director/Associate Director, OHR
OHR Personnel
IRB Members
Investigators

3. Procedure

Changes in a study 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.

3.1 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. If protocol modification is initiated without prospective IRB review to eliminate apparent immediate hazards to a subject, it must be reported to OHR promptly (within 3 working days).

3.1.1 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

3.2 Receipt of Amendments

Amendments for studies are received by the OHR Data Coordinator and logged into the computerized agenda for the appropriate IRB meeting. OHR personnel will preview the amendment and make a determination as to category of review.

3.3 Review of Amendments

Amendments requiring 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 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).

3.4 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.

3.5 Full and Expedited Review of Amendments

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. 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 re-submitted in full, and reviewed by a convened Board.

The following categories of amendment must receive convened IRB review:

- Amendment changes risk/benefit ratio of study
- Amendment substantially alters science of study
- Amendment provides new information that may affect a subject's decision to continue participation

Also to be considered when making the determination:

- Is enrollment open or closed?
- Are subjects currently receiving treatment?
- Is the amendment to be implemented at Jefferson, or is it being submitted for administrative purposes only?

Modifications that are minor do not include the addition of 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
- Reasonable 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 are released to the Principal Investigator, and the amendment may be implemented.

400 Review of Research (RR)
Policy RR 409: Study Completion
Rev.: 6/21/2019

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. Responsibilities

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 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 Co-Chair of that IRB and be given expedited review. If the Final Report is considered to be complete and approved by the Co-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. References

OHR-9 Continuing Review/Final Form

**400 Research Review (RR)
Policy RR 410: Review of Advertisements
Rev.: 4/2008**

1. Purpose

Provide direction for the review and approval of advertisements.

2. Responsibilities

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.

400 Research Review (RR)
Policy RR 412: Recruiting Methods, Enrollment Incentives, and Subject Payment
Rev.: 5/22/2020

1. Purpose

To define the criteria the IRB will use to assess subject recruitment, enrollment incentives, and subject payment. The criteria support equitable selection, unbiased study personnel, and a non-coercive informed consent process by ensuring proper subject recruitment, advertising, and study related payments.

2. Responsibilities

Director/Associate Director, OHR
OHR Personnel
IRB Members
Investigators and Key Personnel

3. Procedure

The IRB will use the following criteria to assess human subjects research. The IRB will use these criteria to determine if the proposed plan needs to be revised.

3.1 Criteria Applicable to the Research Subject

- The inclusion/exclusion criteria.
- Where 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 subjects seems reasonable and proportionate for the procedures the subject will undergo and the length of the study.
- That the payment information is clearly explained in the consent form.

Note: It is prohibited for a sponsor to compensate participants by offering a coupon good for a discount on the purchase price of the product once it receives marketing approval.

3.2 Criteria Applicable to the University, Investigators and Key Personnel

The following are not permitted:

- 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 Criteria Applicable to Recruiting Subjects from another Health Care Provider

The health care provider must:

- Approve contacting his/her patients for research purposes.
- Obtain the patient's permission to be contacted by the study personnel.

- Introduce the study to the patient.

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 health care provider, or the health care provider and the investigator. In some cases, the letter may be signed by a physician representative, such as the department or division head or the clinical practice director, on behalf of the entire practice.

The recruitment letter must contain the following:

- Introduction of the investigator and the topic of the research.
- Purpose of the research.
- Brief description of the subject's involvement and inclusion criteria.
- An opt in or opt out mechanism such as a number to call or a postcard to return within a specified time period.
- A statement that patients may be contacted if they do not opt out.

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 Criteria Applicable to Study Advertisements

The IRB will review:

- The information contained in the advertisement.
- The mode of its communication.
- The final copy of advertisements of any media.

The advertisement must not:

- State or imply an 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 labeling.
- Use terms, such as “new treatment,” “new medication,” or “new drug,” without explaining that the test article is investigational.

The advertisement must be 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.
- A summary of the eligibility criteria.
- 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.

3.5 Subject Payment

The IRB should assure that all payment to subjects, including amounts and schedule, is described in the payment section of the consent form. No reference to payments should be made in the benefits section.

The IRB will review payment information to ensure that it does not create undue influence to enroll or continue participation in the study, and is appropriate to the study duration and procedures. This is especially important for pediatric studies as the payment is made to the parent and not the child who will actually be the subject in the study.

Payment should be prorated for visits/test completed. Generally, payment may not be made only to subjects who complete the study, but may be paid out when the subject leaves or would have completed the study.

A subject may be provided with test article free of charge or continue to be provided with an effective test article after leaving the study, but this should not

be considered as payment. Free or discounted test article should not steer a subject toward a specific test article, e.g. only be offered for one of the test articles under investigation. Free or discounted test article, once approved, should not be offered as this may imply that approval is guaranteed.

400 Research Review (RR)
Policy RR 413: Review of Research Involving Investigational Drugs and Devices
Rev.: 5/22/2020

1. Purpose

To define the IRB submission and review criteria for human subjects research involving drugs and devices.

2. Responsibilities

Director/Associate Director, OHR
IRB Members
Investigators and Key Personnel

3. Procedure

The investigator must complete and submit all required forms and documents to ensure that the IRB drug and device information needed to review the study.

These forms may include but are limited to:

- OHR-2, Summary of Interventional Human Subjects Research
- OHR-25, Device Worksheet
- FDA IND and IDE correspondence and documentation

If the research is being conducted under an IND/IDE, the investigator must provide the sponsor protocol or sponsor or FDA correspondence showing the IND/IDE number.

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 exemptions below. If none of the exceptions below are met, then the sponsor must obtain an IND/IDE number.

Note that per 21 CFR 312.2(b)(6), a clinical investigation involving an exception from informed consent under 21 CFR 50.24 is not exempt from the requirements of 21 CFR 312.

3.1 IND Exemptions

3.1.1 Exemption 1

Per 21 CFR 312.2(b)(1), the clinical investigation of a drug product that is lawfully marketed in the United States is exempt if all of the following apply:

- (i) 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.
- (ii) 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.
- (iii) 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.
- (iv) The investigation is conducted in compliance with the requirements for institutional review set forth in 21 CFR 56 and with the requirements for informed consent set forth in part 21 CFR 50.
- (v) The investigation is conducted in compliance with the requirements of 21 CFR 312.7.

Note that per 21 CFR 312.2(b)(4), the FDA will not accept an application for an investigation that is exempt under this exemption category 1.

3.1.2 Exemption 2

Per 21 CFR 312(b)(2), A clinical investigation involving one of the following in vitro diagnostic biological products: (a) blood grouping serum, (b) reagent red blood cells, (c) anti-human globulin, is exempt if all of the following apply:

- (a) It is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established, diagnostic product or procedure.
- (b) It is shipped in compliance with 312.160.

3.1.3 Exemption 3

Per 21 CFR 312(b)(3), A drug intended solely for tests in vitro or in laboratory research animals is exempt from the requirements of this part if shipped in accordance with 312.160.

3.1.4 Exemption 4

Per 21 CFR 312(b)(5), A clinical investigation involving use of a placebo is exempt from the requirements of this part if the investigation does not otherwise require submission of an IND.

3.2 IDE Exemptions

The IRB reviews the OHR-25, Device Worksheet to determine if the FDA regulations governing device research apply and if device is non-significant risk and meets the requirements for an abbreviated IDE.

Also, see policy SC 501, Determining Whether a Device Study Involves a Significant Risk or Non-Significant Risk.

400 Research Review (RR)
Policy RR 414: Institutional Conflicts of Interest
Rev.: 4/2018

1. Purpose

To describe circumstances in which a research study must be reviewed by an external IRB due to an institutional conflict of interest in the study.

2. Responsibilities

Director/Associate Director, OHR
Principal Investigator
Conflict of Interest Committee

3. Background

There may be situations where Jefferson has a financial interest in a research study that is determined to be greater than minimal risk and to be conducted at Jefferson. In order to eliminate any real or apparent bias in the regulatory review and oversight for a study under these circumstances, the Jefferson IRB must divest itself of primary regulatory oversight for the study. This necessitates that the study be reviewed by an external IRB that will assume regulatory responsibility and oversight for the study for its duration. This IRB is deemed the “IRB of record.”

4. Procedures

The Conflict of Interest Committee makes all determinations regarding the existence of institutional financial conflicts of interest (FCOI) in regard to human research studies. If the Committee makes this determination in regard to a particular study, the principal investigator must first submit the study for IRB pre-review by an unaffiliated IRB member who will determine the risk designation of the study. An unaffiliated IRB member is an individual who holds a member position on a Jefferson IRB, but does not have a relationship with Jefferson, e.g., is not an employee of Jefferson, is not affiliated with the Jefferson, and does not have a family member (1st degree relative) who is affiliated with Jefferson (See, OP 201 at page 112). If the study is deemed minimal risk by an unaffiliated IRB member, it may be reviewed by an IRB at Jefferson. If the study is deemed greater than minimal risk by the unaffiliated IRB member, it must be submitted to an external IRB that will serve as the IRB of record for the duration of the study. The external IRB will be one with which Jefferson has an established service agreement.

Jefferson will rely on the external IRB for the duration of the research study. The service agreement stipulates the allocation of responsibilities between Jefferson and

the external IRB in regard to ensuring the study is compliant with all applicable regulations.

The IRB of record will communicate to Jefferson any important issues such as serious and/or continuing non-compliance, unanticipated problems involving risks to subjects or others, and issues of non-compliance. Any necessary reporting to federal agencies will be accomplished as per the service agreement.

If an institutional FCOI is identified for a greater than minimal risk study after the Jefferson IRB has approved and assumed regulatory oversight for the study, the principal investigator must submit the study to an external IRB as soon as possible, and in any case, no later than six weeks from time of notification from the COI Committee that an institutional FCOI exists. The Jefferson IRB will continue to oversee the study until the external IRB has approved the study, at which point Jefferson's primary regulatory oversight for the study will cease.

400 Research Review (RR)
Policy RR 415: Undergraduate Research
Rev.: 1/21/2019

1. Purpose

To differentiate between undergraduate student educational research projects and undergraduate student academic research projects and describe how undergraduate student academic research projects will be overseen and regulated.

2. Responsibilities

Director & Associate Director, OHR
Chair, East Falls IRB
Undergraduate Faculty

3. Background

In general, the primary aim of undergraduate student research projects is educational. This is to be differentiated from graduate and professional academic research, one of whose primary aims is to contribute to the body of academic and generalizable knowledge. Generalizable knowledge is knowledge that can be applied in diverse settings outside the confines of Jefferson. The Jefferson IRB, which includes the East Falls IRB, follows the federal definition of human research stipulated in DHHS regulations at 45 CFR 46 (“The Common Rule”) when determining whether research conducted at Jefferson falls within the purview of the IRB and thus requires IRB approval prior to initiation. Key to this definition is the concept of generalizability, which also can be gauged by the researcher’s primary intention to publish or publicly present the research findings beyond the boundaries of the classroom or institution. As this usually is not the intention of undergraduate student research projects, this research does not fall under Common Rule oversight, and thus does not require IRB approval.

To be clear, undergraduate student research is not the same as “exempt” research. “Exempt” is a term specifically used in the Common Rule to designate research that does constitute human subjects research, but, because of the minimal level of risk that it imposes upon human subjects, does not need to comply with the Common Rule, and is thus exempt from its requirements. Undergraduate student research, on the other hand, usually does not constitute human subjects research, as discussed above, and so the term “exempt” does not apply.

This being said, the Office of Human Research believes that an iterative process for undergraduate student research is useful both from an educational as well as a compliance standpoint. The process is outlined below.

4. Procedure

Because the undergraduate student senior thesis project resembles an academic research study and represents the culmination of the undergraduate student's training in a major, it is considered academic research and is subject to this policy. In contrast, research-type activity that occurs in the course of a class or over several classes, and that relies upon immediate proposition and enactment, will be considered primarily as undergraduate student educational activity and will not be subject to this policy. The East Falls IRB Chair ("Chair") will have discretion in making determinations that deviate from the above statements, and may request that an OHR-35 be submitted where necessary to address special situations, specifically, determining which undergraduate student research projects (in addition to senior thesis projects) constitute academic research.

The Undergraduate Student Research Checklist (form OHR-35) will serve to document each senior thesis project or other undergraduate student project determined to be academic research by the Chair. The OHR-35 will be administered by the faculty member who is assigning the project to the undergraduate student. The faculty member will be responsible for signing, obtaining the student's signature, and submitting a copy to the Chair at posted deadlines that will be determined by the Chair. The Chair will maintain OHR-35s in an appropriate manner as well as a database of all undergraduate student research conducted prospectively at East Falls.

The OHR-35 will act both as documentation of the senior thesis or other academic research project and also as decision tool for the Chair in determining whether the project will need formal IRB review.

5. Undergraduate Student Compliance in Academic Research

When involved in the conduct of academic research, undergraduate students should be aware that they must conduct themselves in adherence with all Jefferson standards and policies regarding appropriate behavior, safety and integrity. In particular, undergraduate students must adhere to the Academic Integrity policy and the HIPAA Privacy Policy (#122.0), as it pertains to collecting protected health information from individuals for the purpose of conducting undergraduate student research.

Students also should be familiar with the basic principles of conducting ethical research, as embodied in the Belmont Report. The Chair is available to conduct workshops for students in applied research ethics upon faculty request.

500 Reviews Requiring Special Consideration (SC)
Policy SC 501: Determining Whether a Device Study Involves a Significant Risk or
Nonsignificant Risk
Rev.: 10/2/2017

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. Responsibilities

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

The January 2006 FDA “Information Sheet Guidance for IRBs, Clinical Investigators and Sponsors: Significant Risk and Nonsignificant Risk Medical Device Studies,” at <http://www.fda.gov/oc/ohrt/irbs/devrisk.pdf> provides guidance on how to determine the differences between significant risk and nonsignificant risk medical device studies. It also contains an updated list of examples of significant and nonsignificant risk devices.

- 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.
- 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

- 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).

- **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. Note that the OHR-25 is not required if a drug and a device (e.g. a drug and its delivery system) are under the same IND.

The IDE status for the study is documented with a copy of the IDE approval letter from the FDA.

500 Reviews Requiring Special Consideration (SC)
Policy SC 502: Review of Cancer Trials Approved Under NCI Central IRB
Independent Review Model
Rev.: 12/1/2015

1. Purpose

To describe the procedures by which Jefferson participates in the National Cancer Institute (NCI) Central IRB (CIRB) review of multicenter oncology trials conducted by NCI-established cooperative groups.

2. Responsibilities

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 Jefferson 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 (Jefferson) 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 Jefferson 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 Jefferson 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 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.

Jefferson 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 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"

500 Reviews Requiring Special Consideration (SC)
Policy SC 503: Review and Approval of a Humanitarian Device Exemption
Rev.: 1/20/2020

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 not more than 8000 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 an 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 an 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. Responsibilities

Institutional Review Boards
Principal Investigators
OHR Personnel

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 discussed 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. References

21 CFR 814

Humanitarian Device Exemption (HDE) Program, Guidance for Industry and Food and Drug Administration Staff

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"

500 Reviews Requiring Special Consideration (SC)
**Policy SC 504: Populations Requiring Special Consideration (Women, Prisoners,
Children)**
Rev.: 5/22/2020

1. Purpose

To define investigator and Institutional Review Board (IRB) requirements for populations requiring special consideration (45 CFR 46 Subparts B, C, and D).

2. Responsibilities

OHR Personnel
IRB Members
Investigators and Key Personnel

3. Definitions

The definitions used are those found in 45 CFR 46.

4. Procedure

4.1 General Regulatory Requirements

Research involving pregnant women and women of childbearing potential, human fetuses and neonates, prisoners, and children, requires additional protections most prominently defined in 45 CFR 46, Subpart B, C, and D. For federally funded research, the IRB will only approve research that satisfies the conditions of the applicable subpart sections and will extend these protections to all human research as applicable.

4.2 Pregnant Women and Women of Childbearing Potential

Investigators and the IRB must ensure that research involving pregnant women and women of childbearing potential meets the requirements in 45 CFR 46 Subpart B.

Research not otherwise approvable per 45 CFR 46.204 or 205, but which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of pregnant women, may be approvable if all the conditions of 45 CFR 46.207 are met.

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 review and consider

any possible teratogenic effect on the fetus due to involvement of a male subject. The investigator's brochure will be reviewed for relevant reproductive risks from animal studies.

The protocol must be reviewed for opportunities to reduce the risk benefit ratio for both the mother and the fetus. The protocol should have clear plans for follow-up of the pregnant woman up to and after delivery. The risks to the mother and the fetus should be considered separately. The minutes of the IRB meeting should reflect the discussion regarding the protection of the mother and the fetus.

The inclusion of women of childbearing potential as subjects may result in pregnancy. The Investigator and IRB must evaluate the necessary safeguards that such as frequent pregnancy tests, reliable means of contraception, and abstinence.

Consent requirements are as follows:

For studies with pregnant women with minimal risk.	The consent of the mother is required.
For studies with pregnant women with possibility of benefit only to the fetus.	The consent of both parents is required.
For studies with neonates.	The consent of one parent is required.
For studies with neonates of uncertain viability.	The consent of one parent is required.
For studies with non-viable neonates.	The consent of both parents is required. There are no surrogates or exceptions per protocol or waiver. Notes A and B below still apply.
For studies with minimal risk or greater than minimal risk and possible benefit to the child.	The consent of one parent is required.
For studies with greater than minimal risk and no direct benefit to the child, or for studies involving serious health conditions.	The consent of both parents is required.
A. When the consent of both parents is required.	In general, if one parent is deceased, unknown, not practically available, incompetent, incapacitated or if one parent has full legal responsibility, the consent of only one parent is required.
B. If pregnancy is the result of incest or rape.	The consent of the father is not required.

As applicable, the consent document must include a statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or

fetus, if the subject is or may become pregnant) that are currently unforeseeable [45 CFR 46.116 (c) (1)].

4.3 Human Fetuses and Neonates

Investigators and the IRB must ensure that research involving human fetuses and neonates meets the requirements in 45 CFR 46 Subpart B.

Investigators and the IRB must ensure that research involving viable neonates after delivery meets the requirements in 45 CFR 46 Subparts B and D.

Investigators and the IRB must ensure that research involving neonates of uncertain viability and nonviable neonates meets the requirements in 45 CFR 46.205.

Investigators and the IRB must ensure that research involving after delivery, the placenta, the dead fetus or fetal material meets the requirements in 45 CFR 46.206.

Research not otherwise approvable per 45 CFR 46.204 or 205, but which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of fetuses or neonates, may be approvable if all the conditions of 45 CFR 46.207 are met.

4.4 Prisoners

Investigators and the IRB must ensure that research involving prisoners meets the requirements in 45 CFR 46 Subpart C.

This section includes procedures for research involving subjects who are prisoners or may reasonably be expected to become prisoners at some time during enrollment.

In addition to the definitions found in 45 CFR 46, OHRP has provided the following clarification regarding the 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.

Composition of Institutional Review Boards where Prisoners are Involved.

In addition to other regulations governing the constitution of the IRB, when reviewing research involving prisoners, the IRB shall also meet the following specific requirements:

- A majority of the Board (exclusive of prisoner members) shall have no association with the prison(s) involved, apart from their membership on the Board.
- At least one member shall be a prisoner, or a prisoner representative with appropriate background and experience to serve in that capacity, except when a study is reviewed by more than one Board, only one Board need satisfy this requirement.

The main scenarios that must be considered are:

- A subject now meets the definition of a prisoner after enrolling in a study not approved as a prisoner study.
- A subject who meets the definition of a prisoner is proposed for enrollment in a study not approved as a prisoner study.

In both scenarios the investigator must notify the IRB in writing as soon as possible. The IRB will then review the protocol again at its earliest opportunity according to 45 CFR 46 Subpart C and this policy.

If a subject now meets the definition of a prisoner after enrolling in a study not approved as a prisoner study:

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. If it is determined that the subject be withdrawn from the study, if the incarceration of additional subjects is probable, the consent form should indicate that incarceration may result in the termination of the subject’s participation by the investigator without the subject’s consent.

The IRB will determine one of the following:

- IRB review and approval is not required if the research interactions and interventions, including the collection identifiable information, will not occur during the incarceration period.
- Approve the continued participation of the subject if all applicable requirements will be met and there will be no significant increase in risk.
- Approve research participation for non-prisoner participants, but approve participation of prisoner-participants as pending until all applicable

requirements are met including confirmation from OHRP that the proposed research falls within the categories of research permissible under 45 CFR 46.306. All study specific activities for the prisoner-subject, including the collection of data, must stop until all requirements are met.

- Determine that the prisoner-subject must be withdrawn from the study because it will not be possible to meet applicable requirements. When this occurs, plans should be made for safe withdrawal of the subject from the study.

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.

When a subject who meets the definition of a prisoner is proposed for enrollment in a study not approved as a prisoner study, the IRB must consider the following:

- Situations involving non-prisoners who require similar protections such as those living within the community and sentenced to court-supervised monitoring or treatment and those wearing monitoring devices.
- A Department of Health and Human Services (HHS) supported, minimal risk epidemiologic study, in which prisoners are not the focus, but will be enrolled, and the sole purpose of the study is either:
 - i. To describe the prevalence or incidence of a disease by identifying all cases.
 - ii. To study potential risk factor associations for a disease.

As with any amendment, the IRB should also re-review a study approved only for prisoner-subjects when the enrollment of non-prisoners is being proposed. All applicable requirements of 45 CFR 46 Subpart C may continue to be met and the IRB should ensure that the rights and welfare of the non-prisoner subjects will also be protected.

Before any HHS supported research involving prisoners can begin, the IRB must submit a certification letter to HHS through the Office for Human Research Protections (OHRP) that the conditions in 45 CFR 46 Subpart C have been met. The certification letter must provide the following information:

That an IRB designated under the Federalwide Assurance has determined that the appropriate conditions have been met (45 CFR 46.305) and that the research falls within the permissible categories (45 CFR 46.306). OHRP does not require

that the certification letter include a specific listing or rationale behind the IRB findings, but the IRB may wish to include a brief, protocol-specific explanation of the IRB's rationale for each finding.

Which of the categories of permissible research involving prisoners in 45 CFR 46.306(a)(2) is applicable to the proposed research.

A statement that indicates that the IRB was constituted as per requirements in 45 CFR 46.304. OHRP does not require that the certification letter include information about the manner in which the IRB fulfills the requirements of 45 CFR 46.304, but the name of the prisoner representative may be included.

FWA number.

IRB registration number for the designated reviewing IRB.

Site(s) where the research will be conducted. If prisoner research site is "engaged in research", provide FWA #.

HHS Grant Award number.

HHS Funding Agency Name.

Funding Agency Grants/Program Officer Name and Telephone #.

Title of DHHS Grant.

Title of Protocol.

Version date of the informed consent document to be used with prisoners.

Date(s)/chronology of all IRB Meeting(s) in which the protocol was reviewed (initial, amendment, addendum, continuing review, etc.).

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.

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 a 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.

The following should also be submitted:

The protocol application, including the protocol and any IRB submission material.

The grant application, including any grant award updates.

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

OHRP will make its own determination based on the information provided.

The IRB must inform the principal investigator in writing that no prisoner-subjects can be enrolled in the research until the letter from OHRP is received that acknowledges receipt of the prisoner certification letter 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).

4.5 Children

Investigators and the IRB must ensure that research involving children meets the requirements in 45 CFR 46 Subpart D.

Note: 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.

NIH Research: For research involving children supported or conducted by the NIH, the NIH Policy and Guidelines on the Inclusion of Children as Participants in Research Involving Human Subjects (March 6, 1998) must be followed.

Research in children requires that the IRB carefully consider the risk and benefit to children involved in research. The IRB and investigator should have adequate experience in pediatric research.

The IRB must find that the research meets the applicable requirements as follows:

Research not involving greater than minimal risk (45 CFR 46.404).

Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects (45 CFR 46.405).

Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition (45 CFR 46.406).

Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children (45 CFR 46.407).

Research involving wards of the state (45 CFR 46.409).

Note: Per 45 CFR 46.409(b), If the research is approved for wards, the IRB shall require appointment of an advocate for each child who is a ward, in addition to any other individual acting on behalf of the child as guardian or in loco parentis. One individual may serve as advocate for more than one child. The advocate shall be an individual who has the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child's participation in the research and who is not associated in any way (except in the role as advocate or member of the IRB) with the research, the investigator(s), or the guardian organization.

Requirements for permission by parents or guardians and for assent by children that must be followed are in 45 CFR 46.408 and OHR Policy IC 704, Child Assent and Parental Permission for Participation in Research. Signature requirements appear above.

5. References

45 CFR 46 Subparts B, C, D

500 Reviews Requiring Special Consideration (SC)
Policy SC 507: The Enrollment of Women and Minorities as Subjects in Clinical Research
Rev.: 7/2010

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. Responsibilities

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

Jefferson 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:

- i. 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.

- ii. 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.
- iii. 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.

500 Reviews Requiring Special Consideration (SC)
Policy SC 508: Pennsylvania Reporting Requirements
Rev.: 5/22/2020

1. Purpose

To provide guidance on Pennsylvania state laws related to human subjects research.

2. Responsibilities

Director/Associate Director, OHR
Investigators and Key Personnel

3. Procedure

The principal investigator is responsible for following all applicable federal and state laws and Jefferson policies, and must contact the Director/Associate Director, OHR for any necessary clarification. The Director/Associate Director, OHR will work with the Legal Office as needed to provide the necessary information to the investigator.

TJUH policies 113.58, Human Immunodeficiency Virus (HIV) Testing and 113.12, Suspected Abuse, Neglect, Domestic Violence or Exploitation - Assessment And Management, must also be followed as appropriate.

Special Considerations Concerning Confidentiality Related to Required Disease, Abuse, and HIV Reporting:

3.1 Confidentiality of Records

Consent forms must include a statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained. Limits on confidentiality, including the Commonwealth of Pennsylvania's requirement for reporting of suspected child abuse or neglect, and 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."

3.2 Mandatory Reporting of Diseases, Infections, and Conditions

Researchers should be aware that the laws of Pennsylvania require health care professionals and health care facilities to report specific diseases, infections and conditions to the Pennsylvania Department of Health or the appropriate local health authority in the required manner and timeframe (PA Code, Title 28, Chapter 27.2)..

The up to date list can be found on the Pennsylvania Department of Health, List of Reportable Diseases.

3.3 HIV/AIDS Related Considerations

No HIV-related test shall be performed without first obtaining the informed, documented, 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 Pennsylvania Department of Health.

Consent requirements for HIV-related tests shall not apply to the following:

- i. 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
- ii. The performance of an HIV-related test for the purpose of medical research not prohibited by the Pennsylvania Department of Health if the testing is performed in a manner by which the identity of the test subject is not known and may not be retrieved by the researcher.

Reference 35 P.S. 7605 for the complete regulations.

3.4 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

500 Reviews Requiring Special Consideration (SC)
Policy SC 509: International Research
Rev.: 5/22/2020

1. Purpose

To establish guidelines to ensure that research fully or partially outside the United States, regardless of funding source, is conducted in a compliant and ethical manner. Researchers must follow all applicable regulations including those of the sponsoring agency, Jefferson and OHR policies, and ethical principles, including at least one of the following:

- The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research of the U.S. National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research.
- 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 Common Rule (45 CFR 46).

Jefferson researchers are also expected to abide by the tenets of the International Congress of Harmonization Good Clinical Practice guidelines.

2. Responsibilities

OHR Personnel
IRB Members
Investigators and Key Personnel

3. Procedure

3.1 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 either obtain Jefferson IRB approval or establish a reliance agreement with the local Ethics Committee in the host country that will assume oversight for the study. If the study is federally funded, Jefferson cannot not rely solely on the local IRB. In this instance, either both Jefferson IRB and the EC will review the study, or Jefferson IRB will serve as the designated IRB and the EC will rely upon the IRB's review. If an Ethics Committee or other similar review

committed does not exist, then a letter of support from a community leader, liaison, or official from the institution where the research will take place must be obtained and submitted to the Jefferson IRB which would then serve as the designated IRB for the study. Note that some countries require multiple levels of ethics review (e.g., national, regional, local).

The PI also must obtain a letter of support from the facility at which the research will be conducted, if the facility is not under the jurisdiction of the local Ethics Committee. All documents from the country in question must be translated into English before being provided to Jefferson IRB for the purposes of verification and auditing.

Investigators are required to be knowledgeable about and comply with local laws while conducting their research. They also must take into account local customs and cultural context which may require them to modify certain aspects of the research with IRB/EC approval. Consultation with researchers or other individuals 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 in the research, such as being subjected to retaliation from local authorities or community members.

The PI must provide information about local context to the IRB to affirm that the research is culturally appropriate. The IRB will use the information to determine whether any modifications are needed to make the research more culturally appropriate. This information may be obtained or supplemented by legal or cultural consultants to the IRB for its review of the research.

3.2 IRB

The Jefferson 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) of the country in which the research will be conducted, it must be documented that the EC is guided by at least one of the above stated ethical documents. If the study is federally funded, Jefferson cannot not rely solely on the local IRB. In this instance, either both Jefferson IRB and the EC will review the study, or Jefferson IRB will serve as the designated IRB and the EC will rely upon the IRB's review.

OHRP maintains a compiled document of guidelines that govern human subjects research in other countries, as well as standards from a number of international and regional organizations (OHRP International Compilation of Human Research Protections). OHR directs researchers to these guidelines and requires compliance with local standards cited by OHRP when conducting international research in the countries to which they pertain.

If the research receives federal funding from the U.S., any international institution involved with the research will be required to have a Federalwide Assurance (FWA) with the Office for Human Research Protections (OHRP) prior to initiation of the research in that country.

Conflicts arising between U.S. federal law and national and/or other applicable laws of the country in which the research is to be conducted are referred to Jefferson's Legal Office for guidance and resolution.

The IRB will confirm the qualifications of the Jefferson researchers and research personnel conducting research in the designated country.

When the IRB is the designated IRB for the research, it also will be responsible for:

- Initial review, continuing review, and review of modifications to previously approved research.
- Post-approval monitoring.
- Non-compliance and unanticipated problems involving risk to participants or others. While the IRB is nominally responsible for handling complaints, it is likely that this will be impracticable, given cultural and language differences and geographical distance. In these instances, the IRB will rely on the Principal Investigator and the local Ethics Committee, community leader or liaison, or institutional or governmental official to mediate the process and provide a report to the IRB of the complaint and how it was addressed.

Any problems encountered with the research should be reported to the study sponsor, relevant regulatory bodies and all reviewing IRBs and/or Ethics Committees as appropriate. Research that is federally funded and is FDA regulated must comply with both DHHS and FDA regulations.

For research conducted jointly under Jefferson IRB and local Ethics Committee and any other involved IRBs providing oversight, the Jefferson IRB will be responsible to apply the above-listed duties only to those specific research procedures conducted by Jefferson researchers and Affiliates, unless otherwise documented through reliance agreement or agreements with individuals unaffiliated with Jefferson. The local Ethics Committee and any other involved IRBs will assume responsibility for all other research conduct, as applicable.

3.3 Consent

Obtaining consent in non-U.S. populations presents certain challenges. Especially in non-Western populations, conceptions of individuality and

permission may be substantially different. The investigator should be sensitive to differing norms pertaining to informed consent and design the consent process accordingly, while adhering to applicable regulations.

All consent documents must be translated into the local language. These translations should be certified accurate per IC 705, Informed Consent – Non-English Speaking Subjects and Translations. There may be different laws regarding determination of who may serve as a Legally Authorized Representative (LAR) and the age of adulthood and consent that both the Principal Investigator and the IRB must take into consideration when applying regulatory standards. There may also be cultural norms pertaining to gender and decision-making that will need to be observed.

In some cultures, it may be inappropriate to document consent by using standard written consent. The 2018 Common Rule provides for an additional route of consent when research is to be conducted with members of a distinct cultural group or community in which signing forms is not a standard practice. For minimal risk research in these groups, an appropriate alternative mechanism for documenting consent can be used [46.117(c)(1)(iii)].

3.4 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.

600 Guidance (G)
Guidance G 601: Definition of Key Personnel in Human Subjects Research
Rev.: 5/15/2014

1. Purpose

This policy defines key personnel as listed on the Proposal Transmittal Form (OHR-1) for purposes of IRB oversight.

2. Responsibilities

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.

600 Guidance (G)

Guidance G 607: Certificates of Confidentiality

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. Responsibilities

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.

600 Guidance (G)
Guidance G 608: Sociobehavioral Research
Rev.: 5/22/2020

1. Purpose

To provide guidance for issues specific to sociobehavioral research.

2. Responsibilities

IRB Members
Investigators and Key Personnel

3. Guidance

3.1 Federal Regulations

Federal regulations apply not only to biomedical research, but also to sociobehavioral research in such areas as human behavior, social science, anthropology, epidemiology, and education. Studies of these types often present only minimal risk and may be exempt from IRB review (RR 403) or given an expedited review (RR 404).

3.2 Psychological/Social Risk

Sociobehavioral 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 the risk of a breach of confidentiality. Sociobehavioral studies often do not benefit the subject but rather science or society. In assessing the potential risks presented by a sociobehavioral study, investigators and IRBs should ensure that the design of the study provides an adequate level of protection against these potential risks.

3.3 Deception in Sociobehavioral 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 sociobehavioral 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.

600 Guidance (G)
Guidance G 610: Quality of Life Issues
Rev.: 12/21/2021

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. Responsibilities

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

600 Guidance (G)
Guidance G 615: IRB Fees
Rev.: 5/22/2020

1. Purpose

To provide guidance regarding IRB fees.

2. Responsibilities

Director/Associate Director OHR
OHR Personnel
Investigators and Key Personnel
ORA Personnel

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.

600 Guidance (G)
Guidance G 616: Independent Monitoring of Investigator-Initiated Clinical Trials
Rev.: 6/21/2019

1. Purpose

To provide guidance to investigators for establishing acceptable monitoring procedures for investigator-initiated clinical trials.

2. Responsibilities

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 Jefferson-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 any annual review required 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 Jefferson employee or someone who is not employed by Jefferson. 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 Jefferson 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.

600 Guidance (G)
Guidance G 618: HIPAA and Activities Preparatory to Research
Rev.: 11/11/2021

1. Purpose

To define and provide guidance regarding HIPAA permitted activities preparatory to research and some recruitment activities.

2. Responsibilities

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 Jefferson.

4. Overview

For Activities Preparatory to Research, Jefferson, 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 Jefferson 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 an OHR-29 with a non-Jefferson 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 Legal Office for a BAA.

The completed OHR-29 may be submitted to the Privacy Office at privacyoffice@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. References

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"

600 Guidance (G)
Guidance G 619: Radioactive Materials
Rev.: 11/11/2021

1. Purpose

To provide guidance for approval and use of radioactive materials.

2. Responsibilities

Investigators
Key Personnel
IRB Members
Director, Office of Radiation Safety

3. Definitions

Radioactive Drug is defined in 21 CFR 310.3(n) and includes a “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. Procedure

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.

Categories of Use

The use of ionizing radiation sources in or on human research studies can fall into one of the following categories:

- Category 1: 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).

- Category 2: To study the safety and effectiveness of a radioactive drug or radiation emitting device for diagnostic, therapeutic, or similar purposes (i.e., clinical trials).
- Category 3: 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.
- Category 4: 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 Category 1 Guidance

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) Jefferson Radiation Safety Committee (RSC) or the Radiation Safety Officer (RSO) (as appropriate – RSC procedures permit RSO only approval in limited circumstances), (2) the Jefferson Radioactive Drug Research Committee (RDRC), and (3) the Jefferson 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, Jefferson must confirm that the test articles have appropriate regulatory approval or meet exemptions for such approval.

FDA regulations found in 21 CFR apply to this category of research. Oversight at Jefferson is handled by the Radioactive Drug Research Committee which is chartered by the FDA under 21 CFR 361 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 [21 CFR 361.1(b)(1)(iv)]:

- Qualified study investigators

- Properly licensed medical facility to possess and handle radioactive materials
- 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 an appropriate Institutional Review Board (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 [21 CFR 361.1(b)(1)(iii)] and is within the limits specified in 361.1(b)(3)(i) as shown below. Furthermore, as stated in 10 CFR 361.1(b)(3), the amount of radioactivity to be administered shall be such that the subject receives the smallest radiation dose which is practical to perform the study without jeopardizing the benefits to be obtained from the study.

Radiation Dose Limit Guidelines (for this category)

Age of Subject	Radiation Dose Limit
Under 18 years	300 millirem (3 millisievert) 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 (5 mSv) annual total dose commitment.
18 years or older	3,000 mrem (30 mSv) 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 (50 mSv) annual total dose commitment. 5,000 mrem (50 mSv) to other organs from a single administration, and 15,000 mrem (150 mSv) annual total dose commitment.

[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 (Note: RSC approval may be made contingent upon subsequent IRB approval.)
- Approval by the RDRC

4.2 Category 2 Guidance

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 RDRC 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 Jefferson 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 (Note: RSC approval may be made contingent upon subsequent IRB approval.)

4.3 Category 3 Guidance

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 Jefferson 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 (Note: RSC approval may be made contingent upon subsequent IRB approval.)

4.4 Category 4 Guidance

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. The RSO may nevertheless review study protocols to make a determination as to whether the proposed studies are Category 3 or Category 4.

4.5 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 childbearing 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.

The completed OHR-32, Radiation Research Review Form is submitted to:

Radiation Safety Officer, TJU/TJUH
Nevil Building, Suite 820
919 Walnut St.
Philadelphia, PA 19107
Phone: 215-955-1950
Phone: 215-955-7813
Fax: 215-923-9039

Copies of the proposed protocols themselves will also need to be provided. In some cases, the Investigator’s Brochure may also be requested.

The current RSO is John C. Keklak, and forms and study materials may be submitted to him at john.keklak@jefferson.edu .

600 Guidance (G)
Guidance G 620: Department of Defense (DoD) Requirements for the Conduct of
Human Subjects Research
Rev.: 9/9/2020

1. Purpose

To describe the requirements for IRB review and investigator responsibilities when conducting human subjects research sponsored or funded by the DoD.

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. 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.

2. Responsibilities

OHR Personnel
Investigators and Key Personnel
IRB Members

3. Guidance

3.1 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.

3.2 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.

3.3 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.

3.4 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

3.5 Multisite Research

- When conducting multi-site research, a formal agreement between organizations is required to specify the roles and responsibilities of each party.

3.6 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.

3.7 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 ombudsperson 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:
 - Stop a research project in progress
 - Remove individuals from a study
 - Take any steps to protect the safety and well-being of participants until the IRB can assess.

3.8 Recruitment and Compensation

- Jefferson does not intend to conduct research that will recruit military volunteers.
- 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.

3.9 Consent

- As with all studies requiring consent, the consent process must ensure the comprehension of the subject, and stress voluntary participation in order to foster informed decision-making by participants.
- 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:
 - A waiver of the consent process is prohibited unless a waiver is obtained from the Assistant Secretary of DoD for Research and Engineering.
 - 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.
- In addition to the basic and required consent disclosures, consent documents must include:
 - A statement that the DoD or a DoD organization is funding the study.
 - A statement that representatives of the DoD are authorized to review research records.

3.10 Research on Pregnant Women

- 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.

3.11 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.
 - 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.
 - "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 for 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.

3.12 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.

3.13 Research on Fetal Tissue

- Fetal research must comply with US Code Title 42, Chapter 6A, Subchapter III, Part H, 289g.

3.14 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.

3.15 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.

3.16 Non-exempt Classified Research is not performed at Jefferson. In the unlikely event such research is contemplated by a Jefferson investigator, the

investigator should carefully review DoD instruction 3216.02 and contact the Director, OHR prior to initiating any aspect of a proposal.

4. References

DoD Instruction 3216.02
32 CFR 219

600 Guidance (G)
Guidance G 621: Safeguarding and Protection of Children in Research Studies
Rev.: 5/22/2020

1. Purpose

A substantial portion of research conducted by Thomas Jefferson University involves pregnant women, mothers and children. Therefore, consistent with its mission, the university is committed to reviewing, approving and overseeing research that ensures the safety and well-being of all children who come into contact with research personnel, including students, faculty, employees or contracted personnel, consultants, contractors, or volunteers. The term “children” has a meaning consistent with the definition found in the US Code of Federal Regulations as “persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted” [45 CFR 46.402; 21 CFR 50.3(o)].

The purpose of this guidance is: to compile the various policies, guidelines, codes, and assurances that contribute to the protection and safeguarding of children involved in research; to promote awareness of the Institutional Review Board’s (IRB’s) commitment to the protection of children from harm, neglect and abuse, whether physical, emotional or psychological; and to alert the research community that Jefferson has systems in place to enforce these policies and procedures.

2. Responsibilities

OHR Personnel
IRB Members
Investigators and Key Personnel
Office of Research Conduct and Compliance (ORCC)
Office of Research Administration (ORA)
Research Administration Center of Excellence (RACE)

3. Guidance

a. A designated Compliance Officer (CO), who has appropriate knowledge and skills to promote child-safe environments and respond to safety concerns, has responsibility for accepting and investigating any report of a known or suspected violation of applicable policies or a concern (no matter what the cause) about the safety and well-being of a child involved in research involving Thomas Jefferson University.

b. When research implemented by Jefferson will involve children, the consent form for the research will detail any potential risks to a child due to the study intervention. Furthermore, the consent, a copy of which will be given to the parents/guardians of

participating children, will include contact information for the Principal Investigator and the Office of Human Research (OHR) to facilitate the communication of child safety concerns. Additionally, when the OHR receives concerns of child safety not covered under human subjects regulations, the concerns will be forwarded to the CO for attention and follow-up.

c. Prior to initiating research that will involve children (either directly as a participant or indirectly as the offspring of a study participant), the IRB will ensure that those implementing the research have appropriate training (e.g., from CITI--the Collaborative Institutional Training Initiative--or other source) which promotes an understanding of child safeguarding roles and the internationally accepted research rules related to protecting children.

d. When Jefferson has a need for employing or contracting new personnel for its research activities, the rules associated with the Thomas Jefferson University "Recruitment-Employment Policies and Practices" will apply. Consistent with the Pennsylvania Child Protective Services Act, the University's procedures include a provision for special screening of an individual who would be in regular contact with children in the form of care, guidance, supervision or training. The screening includes the Pennsylvania State Police criminal background check, the Pennsylvania Department of Welfare child abuse criminal background clearance, and a Federal Bureau of Investigation (FBI) fingerprint based federal a criminal records check. Employment or contractor engagement cannot occur if any of the screenings indicate background that results in an individual being at high-risk for behavior contrary to safeguarding and protecting children.

e. All Jefferson researchers must adhere to HIPAA standards and applicable international standards when collecting and storing confidential research data.

f. Jefferson's IRBs apply applicable regulations governing human research and, when necessary to adequately protect children, IRB members may recommend that a study protocol encompass special protections for children involved in research.

g. Jefferson Principal Investigators conducting research involving children should periodically conduct safeguarding risk assessments to ensure the research is conducted in an appropriate environment and locations where processes are applied to ensure safe, inclusive environments for children. When subcontractors are involved in the research, Principal Investigators shall insure that subcontractors meet the same expectations.

h. When Jefferson and its subcontractors involve children who have reached the age of reason (usually about 7 years of age) in research, opportunities will be provided for such children to express what risks are a concern to them. Further, assent (i.e., affirmative agreement to participate in research) should generally be sought from children judged capable of providing it. In addition, a parent generally will be present when a child under 7 is involved in a research activity, and the

researcher will be receptive to recommendations from the parent about safeguarding and protecting the child during a research activity.

i. Jefferson will consider whether any independent oversight is necessary to ensure adequate protection of a child involved in research. For example, if a child has a “court appointed special advocate,” the advocate may help ensure that the child’s needs and interests are met. Measures may also be implemented to promote a child-friendly and protective environment during a research activity. Such an environment is understood to mean one in which child abuse (physical, sexual, emotional or resulting from neglect) is unlikely; proactive steps have been taken to prevent all forms of violence against children; and child protection is a priority and results in a prompt response when a child is at risk for physical and/or mental violence, injury and/or abuse, neglect and/or negligent treatment, maltreatment and/or sexual exploitation, and/or sexual abuse.

j. Anyone involved in research implemented by Jefferson, including subcontractors, who suspects a violation of any of these policies or has a concern that research activities present a risk to children should register the violation, complaint or concern with the OHR or its Research Compliance Officer as set forth in applicable policies. Any compliance matter may also be reported to Jefferson’s Chief Compliance Officer through the Jefferson Alertline--888-5-COMPLY (888-526-6759). A complaint, suspicion or concern will be investigated by the appropriate official and a decision will be reached about the facts associated with the complaint, suspicion or concern. The appropriate official will present a recommendation for prompt action to the violator’s supervisor should it be determined that a violation of applicable policies has occurred or there is a need for changing processes or procedures to better safeguard and protect children involved in research.

k. Reporting a violation (or suspected violation) of applicable policies or a child safety concern is strongly encouraged, and one means to protect a whistleblower is anonymous reporting (as outlined above). Additionally, the appropriate official need not make the name of an individual who reports a possible violation or child safety concern known unless there is an atypical and justified reason for doing so. Further, it is the intent of Jefferson to protect the whistleblower--to the best of its ability--from retaliation for reporting a violation, suspected violation or concern related to this policy.

l. Jefferson is committed to assurance of the Jefferson Code of Conduct & Ethical Behavior for students, faculty, employees or contracted personnel, consultants, contractors, or volunteers engaged in its research. The following are specific expectations:

- i. When Jefferson is involved in research being conducted outside of Thomas Jefferson University’s research area and participants are recruited from another country, the Jefferson Principal Investigator will ensure that applicable Jefferson child protection policies are met as well as the rules of a

- recognized Ethics Committee and/or other review committee of the country in which the research is being conducted.
- ii. Community-based approaches for publicizing research involving children are the preferred means of communicating an approved research project involving children, and generally social media sites (such as Facebook) will not have messages directed at children or otherwise be used unless the specifics of use of such social media sites have been detailed in an application for review and approved by the appropriate IRB and/or Ethics Committee.
 - iii. Any students, faculty, employees or contracted personnel, consultants, contractors, or volunteers engaged in the research undertaken by Jefferson shall not have sexual relations involving anyone under the age of 18 years old who is involved in the research. Neither should such individuals associated with Jefferson engage in sexual relations with any young person that is 18 to 25 years of age and is connected with research involving Jefferson (with a rare exception being marriage to such an individual in this age group).
 - iv. Students, faculty, employees or contracted personnel, consultants, contractors, or volunteers engaged in the research undertaken by Jefferson are always expected to behave in a manner consistent with a commitment to promoting the safety and well-being of children.

700 Informed Consent (IC)
Policy IC 701: Informed Consent and HIPAA Authorization: General Requirements
Rev.: 11/11/2021

1. Purpose

To describe the general requirements for obtaining and documenting informed consent.

2. Responsibilities

OHR Personnel
Investigators and Key Personnel
IRB Members

3. Procedure

Informed consent must be legally effective and prospectively obtained (45 CFR 46.116; 21 CFR 50.20). Except as described in Policy IC 706, before involving a human subject in research, an investigator shall obtain the legally effective informed consent of the subject or the subject's legally authorized representative (LAR). The consent must be IRB approved and contain the appropriate privacy authorization language (HIPAA).

Separate medical treatment consent must also be obtained for any procedure cited in Hospital Policy 117.03, Informed Consent (also see list below).

The consent form document may be either of the following:

- A written informed consent form that encompasses the elements of informed consent and the required elements of a HIPAA authorization. The investigator shall give the subject or LAR adequate opportunity to read it before it is signed. Alternately, this form may be read to the subject or LAR. The subject or LAR shall receive a written copy of the signed and dated consent document.
- A written "short form" stating that the elements of informed consent have been presented orally to the subject or the subject's LAR, and that the key information was presented first to the subject, before other information was provided. The IRB shall approve a written summary of what is to be said to the subject or LAR. When this method is used, there shall be an impartial witness to the oral presentation. The subject or LAR will sign the short form. The witness shall sign both the short form and the summary, and the person actually obtaining the informed consent shall sign the summary. A written copy of the signed and dated summary and the signed and dated short form shall be given to the subject or LAR.

A guidance document is available with details about commonly encountered consent scenarios. It includes information about which consent forms to use and which signatories are required. The document is called Consent Guidance, and it is located on the OHR website in the IRB Reference Documents section. In addition, please reference the policies about specific scenarios.

Electronic signatures are acceptable if the signatures are legally valid within the jurisdiction where the research is to be conducted. For FDA regulated research, electronic signatures must meet the requirements of 21 CFR 11.

To ensure that the correct, IRB approved versions of consent forms and other subject materials are used, the following must be done:

- Documents that are readily copied (e.g. consent forms, questionnaires): These documents will be stamped by the IRB when approved. Copies of the stamped document will be given to the subjects.
- Document that are not easily stamped or copied (e.g. electronic documents, laminated materials and booklets provided by the sponsor): If a paper version is made for submission purposes and approved, it will be stamped by the IRB. The actual versions given to the subjects will not be individually stamped. However, the study teams must ensure (e.g. by the use of version date/number) that the version approved by the IRB is identical to the version given to the subjects.

The approval and expiration dates appear on the first page of the document. The expiration date appears on the signature page(s). Except where necessary to eliminate apparent immediate hazards to the human subjects, no research related activities may occur after midnight on the date of expiration.

The investigator must not deviate from the consent plan approved by the IRB.

Privacy is generally the right of a person to be free from intrusion into matters of a personal nature, including control over how personal information is collected, used, maintained, shared, disclosed, and destroyed. The principles of respect for persons and beneficence in the Belmont Report support the need for privacy. Both 45 CFR 46.111 and 21 CFR 56.111 require the IRB to determine that there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data as appropriate.

Researchers and the IRB must respect the privacy of potential research subjects and research subjects. Extra care to protect privacy must be taken during recruitment and consent. This is when the voluntary nature of participation and the extent of privacy must be made clear. Once a subject has consented, the researcher should continue to maintain subject privacy. This may include allowing for

appropriate flexibility, such as only contacting a subject using the requested method or at the requested time of day.

Privacy also includes an individual's desire not to be approached or contacted. Other than research related activities specifically designed to safely withdraw a subject from a study, once a potential subject or subject has indicated their decision, it must be respected. Any further questions or contact could be considered coercion. Once a subject is no longer in the study, the privacy of the patient and confidentiality of the data must be protected according to the protocol.

3.1 General Requirements for Informed Consent

These requirements apply to both written and oral consent.

- Before involving a human subject in research, the principal investigator must ensure that the legally effective informed consent of the subject or the subject's LAR is obtained.
- An investigator shall seek informed consent only under circumstances that provide the prospective subject or LAR sufficient opportunity to discuss and consider whether or not to participate and that minimize the possibility of coercion or undue influence.
- The information that is given to the subject or LAR shall be in language understandable to the subject or LAR.
- The prospective subject or LAR must be provided with the information that a reasonable person would want to have in order to make an informed decision about whether to participate, and an opportunity to discuss that information with research personnel.
- For standard informed consent:
 - Informed consent must begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject or LAR in understanding the reasons why one might or might not want to participate in the research. This part of the informed consent must be organized and presented in a way that facilitates comprehension.
 - Informed consent as a whole must present information in sufficient detail relating to the research, and must be organized and presented in a way that does not merely provide lists of isolated facts, but rather facilitates the prospective subject's or LAR's understanding of the reasons why one might or might not want to participate.

- No informed consent may include any exculpatory language through which the subject or LAR is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence.

3.2 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.

- One of the following statements about any research that involves the collection of identifiable private information or identifiable biospecimens:
 - A statement that identifiers might be removed from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the subject or LAR, if this might be a possibility; or
 - A statement that the subject's information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies.

3.3 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.
- A statement that the subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit;

- A statement regarding whether clinically relevant research results including individual research results, will be disclosed to subjects, and if so, under what conditions; and
- For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen).

3.4 Elements of HIPAA Authorization

If PHI will be collected, HIPAA authorization language must be in the consent form or separate document unless the IRB approves a waiver. HIPAA authorization language is in the OHR-8 consent form template. The required elements of a HIPAA authorization can be found in 45 CFR 164.508 (c).

3.5 Obtaining Informed Consent – General Requirements

The PI has ultimate responsibility for ensuring that consent is properly obtained. Informed consent must be obtained before any study specific procedures are performed.

The consent form is reviewed with the subject and the subject is given the opportunity to read and discuss the consent form, ask questions, and consider participation.

To indicate consent, the subject or LAR signs and dates the consent form. The person obtaining/assisting with consent and the investigator also sign and date the consent form at this time.

For minimal risk studies, and if the IRB has approved the investigator signature option in the OHR-8 for studies without MCARE procedures (see below), the investigator does not have to be present during the consent process, but should be available for questions as necessary. In this case, the investigator signs and dates the consent form as soon as possible after the subject has consented.

The original, signed consent form is maintained in the subject's study file. A copy of the signed consent form is provided to the subject. It must be documented that a copy was provided to the subject.

3.6 Obtaining Informed Consent – MCARE

These MCARE requirements apply to all Jefferson studies regardless of location. The IRB has the discretion to modify the MCARE requirements for the OHR-8 on a per study basis.

If a study involves MCARE procedures (see below), a physician investigator or “qualified practitioner” must review the purpose, procedures, risks, benefits, and alternatives to participation with the study participant. The other elements of consent may be provided by properly trained and qualified key personnel.

For the purpose of this policy, the term "qualified practitioner" means a co-investigator or key personnel who is one of the following: Physician Assistant, Certified Registered Nurse Practitioner, Midwife, Certified Registered Nurse Anesthetist, another physician or a physician participating in a medical residency or fellowship training program who has knowledge of the patient's condition and the procedure to be conducted on the patient and shall be acting under the supervision of, at the direction of, or in collaboration or cooperation with, the physician.

At the time of consent, all signature lines are completed. In part, the investigator’s signature is certifying that the appropriate individual(s) reviewed the consent information with the study participant (see the OHR-8, Informed Consent template). The appropriate investigator signature option must be included in the consent form.

The following list of procedures is based on MCARE law and Hospital Policy 117.03, Informed Consent.

1. Administration of anesthesia (local, general, conscious sedation, etc.)
2. Performance of surgical procedures
3. Administration of chemotherapy and therapeutic radiation
4. Administration of blood and/or human source products
5. Refusal to allow transfusion of blood and/or human source products
6. Insertion of a surgical device or appliance
7. Performance of abortion
8. Performance of sterilization
9. Performance of any HIV-related testing (See Policy #113.58, HIV Testing, for specific documentation requirements)
10. Performance of ECT
11. Administration of an experimental medication, use of an experimental device, use of an approved medication or device in an experimental manner or the removal of bone, fluids or tissue for use in research or in the manufacture of a product. Experimental procedures and consent forms must be approved by the Institutional Review Board (“IRB”). Note: Only an IRB approved informed consent is required.
12. Invasive procedures, such as halo placement, central venous catheterization, pulmonary artery catheterization
13. Performance of vaginal delivery/cesarean section

3.7 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.

3.8 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.

3.9 Posting of Clinical Trial Consent Form

For each clinical trial conducted or supported by a Federal department or agency, one IRB-approved informed consent form used to enroll subjects must be posted by the awardee or the Federal department or agency component conducting the trial on a publicly available Federal Web site that will be established as a repository for such informed consent forms.

If the Federal department or agency supporting or conducting the clinical trial determines that certain information should not be made publicly available on a Federal Web site (e.g. confidential commercial information), such Federal department or agency may permit or require redactions to the information posted.

The informed consent form must be posted on the Federal Web site after the clinical trial is closed to recruitment and no later than 60 days after the last study visit by any subject, as required by the protocol.

4. References

45 CFR 46.111

45 CFR 46.116

45 CFR 46.117

45 CFR 164.508

HHS Guidance: Use of Electronic Informed Consent

Hospital Policy 117.03, Informed Consent

700 Informed Consent (IC)
Policy IC 702: Documentation, Waiver and Alteration of Informed Consent
Rev.: 11/1/2018

1. Purpose

To describe the requirements for documenting informed consent.

2. Responsibilities

OHR Personnel
Investigators and Key Personnel
IRB Members

3. Policy Statement

Before involving a human subject in research, an investigator shall obtain the legally effective informed consent of the subject or the subject's legally authorized representative (LARs) unless waiver or alteration is approved by the IRB.

4. Procedure

4.1 Note: A guidance document is available with details about commonly encountered consent scenarios. It includes information about which consent forms to use and which signatories are required. The document is called Consent Guidance, and it is located on the OHR website in the IRB Reference Documents section. In addition, please reference the policies about specific scenarios.

4.2 Documentation of Informed Consent

Each subject or his/her legally authorized representative (LAR) must sign and date a written 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 written copy of the signed document that has also been signed by an 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. For information on electronic signatures, see OHR Policy IC 701.

The IRB may approve procedures for documentation of informed consent that involve: (1) a written consent form signed by the subject; (described below); (2) a short form written consent form with oral presentation (see OHR policy IC 701); or (3) in limited circumstances a waiver or alteration of a written consent form (see OHR Policy IC 706). It is the responsibility of the IRB to determine which of

the procedures described below is appropriate for documenting informed consent.

4.2.1 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 an investigator. The investigator must 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 must 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 are generally presented with an informed consent document written in a language understandable to them (see OHR Policy IC 705).

4.2.2 Subjects Physically Unable to Sign a Consent Form (e.g. paralyzed)

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 or other documentation 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.

4.2.3 Illiterate Subjects

Consent documents may be read to subjects who understand the language, but cannot read the language.

4.2.4 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 investigator must obtain the subject's informed consent for this limited participation in the study (assuming such a situation was not described in the original informed consent form). 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 investigator 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.

4.2.5 Use of Electronic Copy or Mail to Document Informed Consent

The IRB may approve a process that allows the informed consent document to be delivered by mail or electronic copy 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.

If written information (e.g. consent form) has been approved for the study, the subjects must be presented with a revised version of the written information unless otherwise specified by the IRB. Attention should be drawn to the revisions in the written information (e.g. highlight). In the event that re-consent is required, the revisions must be discussed with the subject. All appropriate signatures must be obtained and a written copy provided to the subject. All information provided to the subjects must be approved by the IRB.

6. References

45 CFR 46.116

FDA Guidance: IRB Waiver or Alteration of Informed Consent for Clinical Investigations Involving No More than Minimal Risk to Human Subjects, July 2017

OHRP Compliance Activities: Common Findings and Guidance #45.

FDA Guide to Informed Consent, Information Sheets, 1998 pp. 34-35.

700 Informed Consent (IC)
Policy IC 704: Child Assent and Parental Permission for Participation in Research
Rev.: 11/11/2021

1. Purpose

To define the procedures to ensure that effective assent and consent are obtained when children are participating in research.

2. Responsibilities

OHR Personnel
Investigators and Key Personnel
IRB Members

3. Definitions

3.1 **Assent** means a child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.

3.2 **Children** are persons who have not attained the legal age for consent to treatments or procedures involved in the research/clinical investigation, under the applicable law of the jurisdiction in which the research/clinical investigation will be conducted.

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. .

- 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.
- 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.

3.3 **Guardian** means an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care.

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. 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.

- 3.4 **Legally authorized representative (LAR)** means an individual or judicial or other body authorized under applicable law to consent on behalf of prospective subject to the subject’s participation in the procedure(s) involved in the research. If there is no applicable law addressing this issue, legally authorized representative means an individual recognized by institutional policy as acceptable for providing consent in the non-research context on behalf of the prospective subject to the subject’s participation in the procedure(s) involved in the research.

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 must meet the definition of a parent or guardian..

- 3.5 **Parent** means a child’s biological or adjudicated, adoptive parent. Where ‘parent’ is used in this policy, it includes guardians and legally authorized representatives (LARs) as defined in the policy.
- 3.6 **Permission** means the agreement of parent(s) or guardian to the participation of their child or ward in a research/a clinical investigation.
- 3.7 **Ward** means a child who is place in the legal custody of the State or other agency, institution, or entity, consistent with applicable Federal, State, or local law. 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.

If parental consent is given for a minor’s participation in research and the legal status of the child changes (the child is adopted or becomes a ward), the consent previously provided will continue to be valid unless the new legal guardian withdraws the child from participation in the study.

4. Procedure

As required by regulation, the assent of a child must be accompanied by the permission of a parent/guardian/legally authorized representative. Generally, children age 7 – 17 should be given the opportunity to assent. The IRB will determine the appropriate assent requirements and documentation pursuant to determinations made with the OHR-26 form. The investigator is responsible for determining if the subject (minor or individuals with impaired decision making capacity) is capable of assent.

4.1 Assent

The IRB shall determine that adequate provisions are made for soliciting the assent of the children, when in the judgement of the IRB the children are capable of providing assent. In determining whether children are capable of assenting, the IRB shall take into account the ages, maturity, and psychological state of the children involved. The IRB will also consider the risks and benefits to the child. This judgement 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 Common Rule 45 CFR 46.116 (a) (5) (i) indicates, “Informed consent must begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject or legally authorized representative in understanding the reasons why one might or might not want to participate in the research.” This summary of key information, or a separate assent document, may be used for assent. The study will be explained to the subject at the appropriate level of understanding. Subjects who would have difficulty understanding a written consent document will not be required to read a written consent document. Those at a higher level of understanding will be given the opportunity to read the summary of key information, or the entire consent form as appropriate. A separate assent form approved by the IRB is also acceptable. The signature and date of the parent/guardian are obtained on the consent form. The signature and date of the minor subject are obtained on the consent form, or on the separate assent form.

The IRB may waive the requirement for assent if:

- The capability of some or all of the children is so limited that they cannot reasonably be asked to provide assent
- The intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research

Even where the IRB determines that the subjects are capable of assenting, the IRB may still waive the assent requirement for some of the same reasons consent would be waived (45 CFR 46.116)

If a child dissents, this should be respected and documented. If the research may provide direct benefit to the child, the dissent of the child may be overruled by the parent and the child can be enrolled in the research with the parental permission.

4.4 Parental Permission

As required by regulation, the permission of a parent/guardian/legally authorized representative must be obtained before a child may participate in research. Parental permission follows the same process as obtaining consent. A consent form may be used as a parental permission form.

When possible, the permission of both parents should be obtained. The permission of both parents must be obtained for the following types of research 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:

- Research involving greater than minimal risk and no prospect of direct benefit to individuals subjects, but likely to yield generalizable about the subject's disorder or condition (45 CFR 46.406).
- Research meeting criteria at 45 CFR 46.407 that is not otherwise approvable under the other regulatory categories in Subpart D which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children.

The permission of only one parent is required for:

- Research not involving greater than minimal risk. (45 CFR 46.404)
- Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects. (45 CFR 46.405)

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 parental permission requirements, provided an appropriate mechanism for protecting the child participants 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. A possible mechanism would be seeking a court appointment of an alternative guardian or LAR.

4.4 Research Involving Children Conducted in other Jurisdictions

If the research includes enrollment of child participants in other states or countries, and a Jefferson IRB is the designated IRB, the principal investigator is responsible for providing OHR with acceptable verification of the following as it pertains to child participants in those states or countries:

- The age at which participants have the ability to consent to research and medical treatments and procedures.
- Who may act as a guardian or LAR for children participating in research.
- Privacy requirements. The principal investigator may consult with the Privacy Office.
- Regulations on genetic research when applicable.

OHR will consult with the Legal Office as necessary. For research conducted in other jurisdictions where an external IRB is serving as the designated IRB, Jefferson will defer to the external IRB for review of the above issues.

5 References

45 CFR 46.102
45 CFR 46.116
45 CFR 46 Subpart D
21 CFR 50.3
21 CFR 50 Subpart D

700 Informed Consent (IC)
Policy IC 705: Informed Consent – Non-English Speaking Subjects and
Translations
Rev.: 5/22/2020

1. Purpose

To define the policy and procedures for informed consent translations.

2. Responsibilities

Investigators
Research Coordinators
IRB Members
OHR Administrative Staff

3. Procedure

In general, non-English speaking subjects should not be excluded from studies with possible therapeutic benefit unless there is a valid scientific, ethical or logistical reason. Per 45 CFR 46.116, the consent information that is given to a subject must be in language understandable to the subject. This means that non-English speaking subjects must be provided with consent information that is in a language that is understandable to them. This will typically be done with translated, written documents that are approved by the IRB unless appropriate waiver criteria are met (45 CFR 46.116 and 46.117). Ad hoc oral translations are not permitted. All consent documents must be submitted to and approved by the IRB before being used to consent a subject.

3.1 Non-English Speaking Subjects

The consent documentation for non-English speaking subjects can be divided into two categories:

1. When non-English speaking subjects are expected (e.g. common in the study population), the full English consent form is translated into the subject's language. Both the English and translated versions are submitted to the IRB for approval.
2. When a non-English speaking subject unexpectedly presents for possible inclusion in a study, the short form process is used. For the short form process, the full English consent form is discussed with the subject using a translator. The short form is in the subject's language and verifies that the elements in the English version have been discussed with the subject. There are short forms in several languages on the Office of Human Research (OHR)

website. Only the study specific information prompted for should be added to the short form. The short form in the subject's language must be provided to the IRB for approval with the full English version of the consent form (if not yet approved). In the case of newly translated short forms, the certification of translation (see below) must also be provided to the IRB. For information about the required signatories on each document, see the Consent Guidance document located on the OHR website in the IRB Reference Documents section.

After a subject consents using the short form process, the IRB will determine the requirements for providing an English translation of the study information (e.g., no further translation or a translation of a study summary or the full English consent). The determination will be based on the duration and risk of the study. The subject's receipt of the translated study information should be documented, but re-consent and signatures are not required.

3.2 Re-Consent of Non-English Speaking Subjects

If the consent form for the study has to be amended and subjects must be re-consented, the short form process should not be used, because now any non-English speaking subjects already in the study would be expected. There are 2 options in this case: 1. Amend the full English consent form and have it translated or 2. Create an English addendum, which just states the changes to the consent form and have it translated. In either case, the consent form must be approved by the IRB.

3.3 Obtaining Translations of Consent Documents

Consent forms may be translated by a translation agency or an individual. Translation agencies will provide a certification of translation. For individuals, the certification of translation consists of the translator's name, qualifications and a statement that the translation is accurate. All translated consent documents must be submitted to the IRB for review and approval. If there are no substantive changes to a short form on the OHR website, only the translated form must be submitted to the IRB. For other translated documents, provide the English version, the translated version and the certification of translation.

3.4 Translators for the Consent Discussion

The translator present during the consent process can be a professional translator, study personnel, other non-study staff, or a family member. The translation phone may also be used. The translator must have an adequate understanding of both languages in order to translate the full meaning of the consent form including medical and scientific terms. The translator must be present for the entire consent discussion and available throughout the study if needed.

3.5 Witnesses and Translators

When required for consent involving non-English speaking subjects, the witness must be bilingual to confirm that the information was presented correctly to the subject. The witness must be present for the entire consent discussion and available throughout the study if needed. When using the translation phone, the translator may act as the witness. This must be documented but the signature of the translator is not required.

4. References

45 CFR 46.116

45 CFR 46.117

700 Informed Consent (IC)
Policy IC 706: Waiver and Alteration of Informed Consent and HIPAA
Authorization
Rev.: 11/11/2021

1. Purpose

To describe the procedures by which an IRB may waive or alter informed consent or authorization to use and/or disclose protected health information.

2. Responsibilities

OHR Personnel
Investigators and Key Personnel
IRB Members

3. Policy Statement

In certain circumstances, the IRB may waive the requirement to obtain informed consent or approve a consent procedure that omits some, or alters some or all of the elements of informed consent.

4. Procedure

4.1 Waiver and Alteration of Informed Consent

- **Waiver**

An IRB may waive the requirement to obtain informed consent, provided that pertinent regulatory criteria are met.

An IRB may approve a consent procedure that omits some, or alters some or all, of the elements of informed consent, provided the IRB satisfies the requirements below. An IRB may not omit or alter any of the general requirements of informed consent (see IC 701).

- **Requirements for Waiver and Alteration**

In order for an IRB to waive or alter consent, the IRB must find and document that:

- The research involves no more than minimal risk to the subjects;
- The research could not practicably be carried out without the requested waiver or alteration;

- If the research involves using identifiable private information or identifiable biospecimens, the search could not practicably be carried out without using such information or biospecimens in an identifiable format;
- The waiver or alteration will not adversely affect the rights and welfare of the subjects; and
- Whenever appropriate, the subjects or legally authorized representatives will be provided with additional pertinent information after participation.

IRB waiver or alteration of informed consent must be documented in the IRB meeting minutes. This is not required for exempt studies.

- **Waiver or Alteration of Consent in Research Involving Public Benefit and Service Programs**

For waiver or alteration of consent in research involving public benefit and service programs conducted by or subject to the approval of state or local officials

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:

- Public benefit or service programs;
- Procedures for obtaining benefits or services under those programs;
 - Possible changes in or alternatives to those programs or procedures; or
 - Possible changes in methods or levels of payment for benefits or services under those programs; and
- The research could not practicably be carried out without the waiver or alteration.

4.2 Screening, Recruitment, or Determining Eligibility

An IRB may approve a research proposal in which an investigator will obtain information or biospecimens for the purpose of screening, recruiting, or determining the eligibility of prospective subjects without the informed consent of the prospective subject or the subject's legally authorized representative, if either of the following conditions are met:

- The investigator will obtain information through oral or written communication with the prospective subject or legally authorized representative, or
- The investigator will obtain identifiable private information or identifiable biospecimens by accessing records or stored identifiable biospecimens.

In these instances, the IRB does not have to make the regulatory determinations for waiver/alteration of consent. However, if a researcher is communicating directly with a potential participant either through written or verbal means and with intent to collect personal information to be used for the above-mentioned reasons, the investigator should make a good faith effort to communicate the goal of this information-gathering to the individual.

4.3 Waiver of the Requirement to Obtain Written Consent

An IRB may waive the requirement for the investigator to obtain a signed informed consent form for some or all subjects if it finds any of the following:

- The only record linking the subject and the research would be the informed consent form and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject (or legally authorized representative) will be asked whether s/he wants documentation linking him/her with the research, and his/her wishes will govern;
- That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context; or
- If the subjects or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not a typical practice that the research presents no more than minimal risk of harm to subjects and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained.

In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects or legally authorized representatives with a written statement regarding the research.

4.4 Waiver of Authorization to Use and/or Disclose Protected Health Information:

Investigators 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 Subject 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.

The OHR-3, Request for Waiver of Subject Authorization to Collect Protected Health Information submitted to request a waiver of consent.

5. References

45 CFR 46.116
45 CFR 46.117

700 Informed Consent (IC)
Policy IC 707: Surrogate Consent
Rev.: 11/11/2021

1. Purpose

To ensure that surrogate consent is obtained according to federal regulations and local law, and that the process and associated forms are properly approved by the IRB.

2. Responsibilities

OHR Personnel
Investigators and Key Personnel
IRB Members

3. Definitions

Legally authorized representative (LAR) means 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. If there is no applicable law addressing this issue, legally authorized representative means an individual recognized by institutional policy as acceptable for providing consent in the non-research context on behalf of the prospective subject to the subject's participation in the procedure(s) involved in the research.

4. Procedure

In general, surrogate consent is used with adults with a temporary condition that impairs decision making capacity.

The investigator must determine if surrogate consent is a possibility for the study. The Office of Human Research (OHR) may be consulted as needed. Please refer to the OHR-8B for an acceptable list of surrogates.

The IRB submission must include the following documents to be used during the consent process:

- The consent form and the surrogate consent form (OHR-8B). For surrogate consent, the surrogate consent form is used as the signature page.
- A separate assent form for the subject may also be required and used as directed by the IRB.

The IRB will determine if surrogate consent is appropriate. In its decision, the IRB will consider:

- The risks vs. the benefits
- The plan to assess the capacity of the subject to consent or assent
- The necessity and plan for assent
- In cases of abuse, neglect or endangerment, the plan to disqualify an individual to serve as a surrogate.

The PI is responsible for reporting cases of abuse, neglect or endangerment as required by local law and must document the decision to disqualify an individual to serve as a surrogate.

Surrogate consent is documented on the surrogate consent form, OHR-8B which lists the acceptable surrogates in order of priority. If the subject is determined to be capable of assent, assent is also obtained at this time.

If the subject actively refuses assent, the investigator must assess the following:

- The subject has been found legally incapable of decision making through the use of formal assessment.
- The study has potential benefit to the subject.
- There is no conflict of interest of the surrogate.

If all of these conditions are met, surrogate consent may be used. If any of these conditions are not met, the subject's wishes will be respected and the subject will not be enrolled.

In the event of a disagreement among potential surrogates, the investigator will attempt to facilitate a consensus. If consensus cannot be reached, the subject cannot be enrolled in the study unless further mediation is sought for the parties in disagreement.

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.

If the subject is initially capable of providing informed consent, but it is likely that the subject will lose this capacity during the study, the subject should appoint a surrogate before beginning the study. The appointed person can then assume the surrogate role as necessary and for the duration of the study, unless the subject

again attains decision/cognitive capacity and can resume autonomous decision-making.

If the initial consent is provided by the surrogate, and the subject is later determined to be decisionally capable, assent or consent should be obtained as appropriate. If the subject does not consent to continued participation, the subject will be withdrawn from the study, and the data obtained will not be used without the subject's written agreement and signature.

4.1 Research being Conducted in Other Jurisdictions

If the research includes enrollment of participants in other states or countries, the principal investigator is responsible for providing OHR with acceptable verification of the following:

- The circumstance under which surrogate consent is allowable.
- Who may act as a surrogate
- Other legal requirements. The principal investigator may consult with the Legal Office.

OHR will consult with the Legal Office as necessary.

5. References

45 CFR 46.102

700 Informed Consent (IC)
Policy IC 708: Research in Emergency Settings (Prospective Review)
Rev.: 5/22/2020

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 to emergent use of a drug, biologic, or medical device, which is addressed in OHR Policy GA 112.

2. Responsibilities

Director/Associate Director, OHR
IRB Members

3. Procedure

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 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.

3.2 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.

3.3 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.

3.4 The clinical investigation could not practicably be carried out without the waiver,

3.5 The proposed research plan defines the length of the potential therapeutic window based on scientific evidence;

3.6 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.

3.7 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 21 CFR 50.24 (a)(7)(v) of this section.

3.8 Additional protections of the rights and welfare of the subjects will be provided, including at least:

- Consultation carried out by the study team, its designees, and/or other stakeholders 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. References

21 CFR 50
Federal Register 61(192): 51531-51533.

700 Informed Consent (IC)
Policy IC 709: Treatment and Cost of Research Related Injury
Rev.: 4/12/2019

1. Purpose

To define what treatment and compensation will be provided to research subjects as a result of a research-related injury.

2. Responsibilities

Investigators
IRB Members
OHR Personnel
Research Coordinators
Director, ORA
Senior Associate Provost for Clinical Research
Legal Office

3. Policy Statement

Jefferson is required to conform with Federal regulations pertaining to informed consent, and pertinent accreditation standards. Federal regulations require that one of the provisions of consent is that prospective subjects be provided with the following information: “for research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments will be provided if an injury occurs and if so, what they consist of, or where further information may be obtained.” Those regulations also prohibit any informed consent, oral or written, from including “any exculpatory language through which the subject or their representative is made to waive or appear to waive any of the subject’s legal rights, or releases or appears to release the investigator, the Sponsor, the institution, or its agents from liability for negligence” (21 CFR 50.20; 45 CFR 46.116).

4. Definitions

4.1 **Funding Source** means the organization or person providing financial or other support for a study. Other support may be provided by the provision of drugs/devices for the study. The Funding Source may be internal such as from a Jefferson department, or external from non-Jefferson owned individuals or entities, such as a pharmaceutical company.

4.2 **Sponsor** means a person who takes responsibility for and initiates a research study. The Sponsor may be an individual or pharmaceutical company, governmental agency, academic institution, private organization, or other organization. The Sponsor does not actually conduct the study unless the

Sponsor is a Sponsor-Investigator. The FDA delineates specific responsibilities for the study Sponsor, see 21 CFR 312 Subpart D. Some of the highlights of those responsibilities are the Sponsor must (i) choose qualified investigators §312.50; (ii) ensure proper monitoring of the investigation and ensure that the FDA and all participating investigators are promptly informed of significant new adverse events or risks §312.50; and (iii) any transfer of responsibilities are done appropriately §312.52.

4.3 Sponsor-Investigator means an individual who both initiates and conducts clinical research, and under whose immediate direction the investigational drug/device is administered or dispensed. The requirements applicable to a Sponsor-Investigator include both those applicable to an investigator and a Sponsor

4.4 Sponsor-Investigator means an individual who both initiates and conducts clinical research, and under whose immediate direction the investigational drug/device is administered or dispensed. The requirements applicable to a Sponsor-Investigator include both those applicable to an investigator and a Sponsor.

4.5 Subject Injury Costs means costs for treatment of illness or injury suffered by a research subject that directly results from participation in the research.

5. Procedure

5.1 Subject Injury Cost Applicable Rules

The Centers for Medicare and Medicaid Services (CMS) has taken a position that a promise to pay for Subject Injury Costs in a contract (even conditional payment), of itself, is sufficient to be considered a liability insurance policy or plan such that Medicare would not be the primary payor (Medicare Secondary Payor (MSP) provisions). As a result, CMS requires that if a Sponsor chooses to pay Subject Injury Costs for subjects covered by Medicare, then the Sponsor must be treated as the primary payor for those costs. The MSP provisions require that Medicare is the secondary payor. The same principles apply to Medicaid, the payor of last resort.

For Commercially Sponsored Research, applying the CMS position, Jefferson shall prohibit scenarios that could result in Medicare becoming a primary payor when another “primary plan” exists. In order to avoid Medicare Secondary Payor violations for subject injury claims, contractual obligations shall require Commercial Sponsors to pay for all subject injuries without an obligation to first bill insurance programs, followed by a Commercial Sponsor payment for denied claims. Medicare will not be charged for Medicare eligible subjects and therefore Medicare will remain a “secondary payor.” Commercial Sponsors shall be the Primary Payor for all subject injuries. For clarity, Jefferson will NOT agree to initially

bill Medicare, Medicaid HMO plans or any other governmental healthcare insurance or any other payor for Subject Injury Costs, and then bill the Commercial-Sponsor for what the governmental healthcare programs or other payors do not pay. The reason for the above is that Jefferson accepts funding from Medicare and other governmental health care programs and under the National Coverage Determination (NCD) for Routine costs in Clinical Trials (310.1), Medicare provides coverage for items or services needed for reasonable and necessary care arising from the provision of an investigational item or service in particular, for the diagnosis or treatment of complications. Additionally, because Medicare may pay for certain costs in the study, but other payors will not and the Sponsor provides those items or services for those study participants, Medicare must not be billed for those items and services provided for non-Medicare study participants.

For government or philanthropic grant funded research and Jefferson funded research (also known as departmentally funded), Jefferson will not promise to pay Subject Injury Costs and will not become a primary payor, but will make every effort to seek reimbursement from a subject's health plan. The subject will be responsible for any deductibles and co-payments required under his/her health plan and for any claims ultimately denied by the health plan.

Jefferson and its investigators share responsibility for complying with the laws, rules, regulations, and operating guidance relating to treatment of research-related injury and compensation for Subject Injury Costs. The purview of the IRB is to provide an ethical and regulatory review of the research, including evaluating the subject injury language.

5.2. Funding Types

- Commercially Sponsored Research

Although Commercial Sponsors are not legally required to pay for Subject Injury Costs for any subject, Jefferson will require that Sponsors pay for Subject Injury Costs. These terms shall be negotiated as part of the clinical trial agreement. If the Commercial Sponsor elects not to pay for any Subject Injury Costs, additional endorsement of the research must be obtained from the Department Chair and the Senior Associate Provost for Clinical Research justifying that the research subjects should bear the costs that may arise as a result of research-related injury.

- Governmental or Philanthropic Grant Funded Research

In situations where the Funding Source is a grant from the government or a philanthropic institution or foundation, Jefferson will offer reasonably necessary treatment for a research-related injury or illness, but Jefferson will not pay for Subject Injury Costs. Jefferson will make every effort to seek

reimbursement from a subject's health plan, but the subject will be responsible for any deductibles and co-payments required under his/her health plan and for any claims ultimately denied by the health plan.

- Jefferson Sponsored Research (also known as Departmentally Funded)

Jefferson Sponsored Research means research studies that are sponsored by Jefferson and whose Funding Source may be internal or external. For Jefferson Sponsored Research, Jefferson shall provide medical care to subjects and handle Subject Injury Costs on the same terms as government or philanthropic grant funded studies.

- Other Compensation

No other compensation for claims in connection to research-related injuries, such as lost wages, pain and suffering, and other types of additional expenses beyond medical treatment related to the research-related injury, will be offered for any type of research including Commercially Sponsored Research, governmental or philanthropic grant funded research or Jefferson Sponsored research.

- Informed Consent Form and Clinical Trial Agreement (CTA)

Subject Injury Costs provisions will be added to the informed consent form and Clinical Trial Agreement. The wording of the CTA and the consent form must be consistent. The CTA should be compared to the consent form that is approved by the IRB to ensure that the language between the two documents is consistent, though not necessarily identical. If the language is inconsistent, one of the documents should be modified appropriately to reflect the agreement of the parties. In the event of an inconsistency between an executed CTA and the IRB approved informed consent form, the CTA will not be released to the PI, and/or the study account will not be established until both documents are aligned.

5.3 Clinical Trial Agreement (CTA) Template

For all Commercially Sponsored research, Jefferson's CTA template provision for Subject Injury Costs is as follows:

In addition to its obligations under Article/Paragraph ____, Indemnification of this Agreement/Letter of Indemnification, if a study subject suffers an adverse reaction, illness, or injury which, in the reasonable judgment of Institution, was directly caused by a study drug or study device or any properly performed procedures required by the protocol ("Study Injury"), Sponsor shall reimburse for the reasonable and necessary costs of diagnosis and treatment of any study subject Study Injury, including hospitalization, but only to the extent such

expenses are not attributable to: (i) Institution's gross negligence or willful misconduct, or (ii) the natural progression of a documented underlying or pre-existing condition or events, unless exacerbated by participating in the study. The Sponsor shall not delay or withhold reimbursement from any such study subject based upon the belief that the Study Injury was due to the Institution's negligence. In that event, Sponsor's sole remedy shall be with respect to Institution under the Indemnification provisions of this Agreement.

In addition, it is the policy of Jefferson that, other than what is set forth in the above-mentioned template language, no CTA shall permit the Sponsor to limit its own indemnification, or shift to subjects its indemnification risk with respect to claims or causes of action that arise from the conduct of the sponsor, whether related to the manufacturing, distribution or quality of a test article, or with respect to the actions of the Sponsor in design, conduct and reporting of the research. Further, no CTA shall permit the Sponsor to limit compensation for subject injury based on the subjects' actions such as not following the directions of the study.

5.4 Subject Injury Costs

Jefferson's position for Subject Injury Costs for government or philanthropic grant-funded research or Jefferson-Sponsored research shall be as follows:

Jefferson will offer subjects reasonable and necessary care to treat injuries directly resulting from a subject taking part in this research. Jefferson may bill the subject's insurance company or other third parties, if appropriate, for the costs of the care provided for the injury, but the subject will be advised that he/she may also be responsible for some of the costs. There are no plans for Jefferson to compensate subjects for the injury. Subjects do not give up their legal rights by consenting to take part in the research.

All consent forms that involve research with **greater than minimal risk** must contain and some of the consent forms that involve research with **minimal risk** may contain the language related to subject injury and cost set forth in the Informed Consent Form Template (OHR-8) provided on the OHR website.

5.5 Principal Investigator Responsibilities

- Coverage for Research-Related injury:

The PI shall be responsible to know how research-related injuries will be covered, e.g., medical expenses for research-related Injury (the cost of reasonably foreseeable medical care in the event of a research related injury) will be covered (i) by the Commercial Sponsor, (ii) by government, philanthropic or other grant, or (iii) by the subject. As noted above, for Commercially-Sponsored clinical trials, the Sponsor will cover the costs; for

Jefferson Sponsored clinical trials, the subject will be responsible for the costs of subject injury.

- Informing Subjects:

Investigators are responsible for ensuring the appropriate language is included in the consent form and discussing obligations for research related injuries as part of the informed consent process. The consent form language must be consistent with contractual obligations.

- Determination of Injury:

The PI of the study is responsible for evaluating a subject who claims to have a research-related injury or illness and reporting this to the IRB (see policy OHR 120) and the Legal Office. Investigators should report all claims and outcomes to the IRB and Legal Office regardless of whether it is determined to be research-related or not. If the injury is determined to be research-related, a meeting will be held with the PI, representatives from the IRB, contracting office, clinical trial billing, and the Legal Office to determine the additional steps which need to be taken and to designate a point of contact for the research subject in addressing the claim.

6. References

21 CFR 50.20

45 CFR 46.116

21 CFR 312 Subpart D

National Coverage Determination (NCD) for Routine Costs in Clinical Trials (310.1)